Design and Implementation of Smart Room

Article · May 2020

DOI: 10.22214/ijraset.2020.5327

1 author:

Muhammad Ibrahim
Mewar University
1 PUBLICATION **0** CITATIONS

SEE PROFILE

iJRASET
International Journal For Research in Applied Science and Engineering Technology

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 8 **Issue:** V **Month of publication:** May 2020

DOI: http://doi.org/10.22214/ijraset.2020.5327

www.ijraset.com

Call: 08813907089 | E-mail ID: ijraset@gmail.com

International Journal for Research in Applied Science & Engineering Technology (IJRASET)
ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.429
Volume 8 Issue V May 2020- Available at www.ijraset.com

Design and Implementation of Smart Room

Muhammad Ibrahim Zubair[1], Ritesh Kumar Ojha[2], Abbati Muhammad Ado[3]
[1, 3]*Post Graduate Scholar,* [2]*Assistant Professor, Electronics and Communication Engineering Department, Mewar University, Chittorgarh, India.*

Abstract: ***Our modern life today is simply over dependent on technology and its application. The cornerstone of such development in industrial and commercial sectors of our life is the automation process as a field of modern technology. This paper concerns on commercial residential application of automation technique to design and implement advanced conventional room known as smart room using Arduino UNO as the main microcontroller board .Smart room incorporates room appliances control automation wirelessly using HC-05 Bluetooth module and android application; automatic security alarm system involving buzzer; and a real time weather status display via 16x2 LCD using DHT11 sensor. The user controls all room appliances and also display temperature and humidly status on the LCD by sending numerical character from his Smartphone Bluetooth terminal to the microcontroller wirelessly, furthermore the security system works automatically upon detecting an intruder.***

Keywords: Arduino Uno, LCD, Smart phone, HC-05 Bluetooth module, Sensor

I. INTRODUCTION

Room appliances Automation; security of our rooms; and whether status information; remain vital to our daily day-to-day activities. Elderly and handicapped people find it tedious or are not able to move frequently for controlling room appliances such as: fans, bulbs, television etc. Intruders and thieves continue to invade our rooms, unknowingly to us and as a result we lost our properties, belongings and peaceful mind of a secured room when we are outside our rooms. Similarly, we often look through our windows each morning to understand the weather status which would enable us to know the cloth we will wear, where shall we visit and what we will do over the day etc. With the advancement of technology and our over dependence on our smart mobile phones, The smart room technology will be a much needed extension of our conventional rooms to contains all needs mentioned and to cater for many problem that do affect our residence. Over the years different technologies have evolved for smart room technology implementation among which are: Bluetooth, WIFI and ZigBee for communication purposes and different devices such as: smart phones, laptops etc controlling various appliances. This paper designs and implements smart room using Bluetooth technology and is economically low cost for easier implementation.

II. LITERARUTE REVIEW

In [1] the research paper designs and implement smart home, it consists of an android application which would send control signal via ESP8266 WIFI module to an Arduino microcontroller for automating and controlling of accessories using relay board. [2] The paper presented home automation system (HAS).

Bluetooth HC-05 module was used to establish the communication purposes. Android Application sends signal or voice command to Arduino to control up to four appliances using 4-channel relay board. [3], the paper employs IOT technology; it implemented home automation and home security technique. ESP8268 WIFI module and other sensors are interface with Arduino, the sensors read the condition of the home appliances and upload it to a cloud platform so that user can access it. The microcontroller provided the control.

[4] Home automation and security ware discussed and implemented using GSM module, Arduino and Android application. A counter displays the number of people entering the home on LCD, in automation mode, appliances are turned on/off depends upon if a person is available in the home while in security mode, light and an alarm are turned and SMS message alert is sent upon detecting intruder. Similarly, Smartphone application can be use by residence for appliances automation. [5] Home Automation of appliances cantered on Arduino UNO as the main controller was designed and implemented, features include water level indication using ultrasonic detector and plant irrigation system monitoring using soil moisture detector was used. Bluetooth module HC-06 was used.

[6] The author demonstrated home automation of appliances over the internet as channel of communication. It employs raspberry microcontroller as a server and upon receiving control signal from Smartphone application from any place, it activates the operation of relay to an appliance.

III. PROPOSED DESIGN

From the literature review above, most of the design concern only about automation of appliances in homes and employs WIFI module which relatively is cost high and difficult in implementation, require expertise to handle and monitor, and problem of network connectivity would always remain a setback. The design here gives expansion upon automation of appliances to add intelligent security system and real time weather status in a room and it involves Bluetooth which is easier in implementation than WIFI module and better cost economic.

The figure below shows the block diagram of Smart Room Technology:

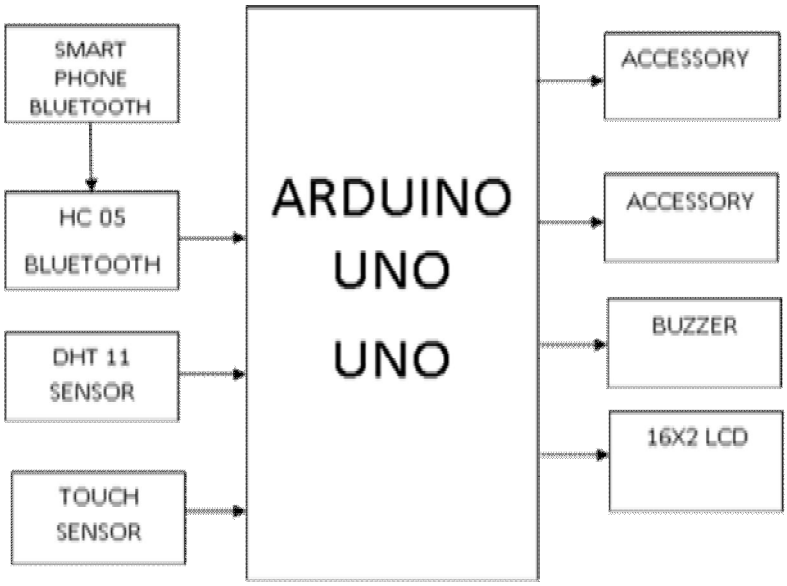


Figure 1: Block Diagram of Smart Room

IV. COMPONENTS AND SPECIFICATIONS

A. *Hardware Used*

1) *Arduino Uno Board:* This is an open source general purpose microcontroller board based on ATMEGA 328 Microcontroller. The board has 14 digital input/output pins, six analog inputs pins, programmable using Arduino UNO IDE and can be powered through USB port or External 7v to 20v power adaptor. The board however can be used in extension with other boards for some applications. The board has other technical specification and other pins of different application.

Figure 2: Arduino Uno

2) *Hc-05 Bluetooth Module:* This is manufactured for wireless communication, it is based on IEEE8802.15.1 standard protocol, through which one can build wireless personal area network. It uses frequency-hopping spread spectrum radio technology to send data. This module can be used in a master and slave configuration. It has 6 pins: Key/EN ;VCC ;GND ;TXD ;RXD and STATE. Similarly, the module has RED LED to show connection status, before user device is connected, the light blinks fast and continuously, after the device is connected it slows down to blink slowly. HC 05 operates on 3.3V voltage supply but can work with 5V supply since it has in-build voltage regulator. Default baud rate is 38400bps.

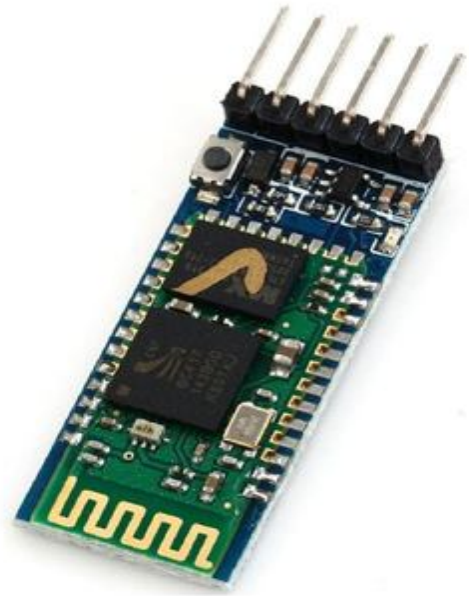


Figure 3: HC-05 Bluetooth module

3) *16x2 LCD:* Liquid crystal display (LCD) is very popular in embedded and IOT projects because of its cheapness, availability and easily to be programmed for display of an image or characters on its flat screen. LCD does not produce their own light rather depends on some reflectors to produce image in a single color. It is named 16x2 because it has 16 columns and 2 rows meaning it can contain 16*2=32 images or characters in total and each is made of 5x8 pixel dots.

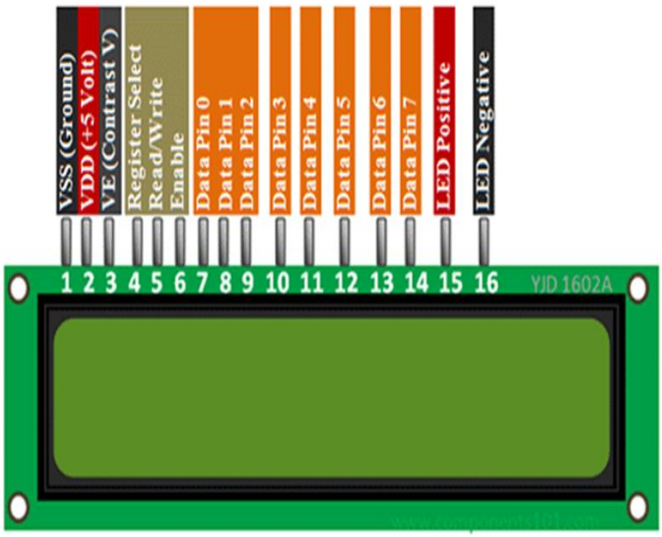


Figure 4: 16x2 LCD Pin Descriptions and Specification[7]

4) *DHT11* Sensor: This consists mainly of resistive humidity measurement component and negative temperature coefficient component. It is a single wire humidity and temperature detector that produce fully calibrated digital humidity and temperature values output serially with a single wire protocol. The sensor is manufactured in a single row of 3 0r 4 pins package and operates from 3.5v to 5.5v supply. It measures temperature range of 0-50^{0}C with an accuracy of +2^{0}C% and humidity ranging from 20-90% with an accuracy of 5%.

Figure 5: DHT11 Sensor

5) *Touch Sensor:* Also known as tactile sensor, it is mostly a proximity sensor reduced to lowest distance. Touch sensors are used to detect and sense touch, they operate as a closed switch upon touched. They perform action similar to human being's skin.

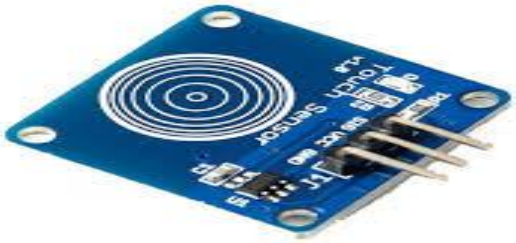


Figure 6: Touch sensor

6) *Relay Module:* This is designed for mostly microcontroller such as Arduino UNO board, PIC, etc. Relay is an electrically operated switch that is used to control or operate both AC and DC output devices upon receiving a pulse signal. A channel relay module has six pins: VCC (+5V), GND, Digital input, normally closed and normally open. The relay output is always connected to normally closed pin, upon receiving pulse it got triggered to normally open.

Figure 7: relay module

V. SOFTWARE ARCHITECTURE

The microcontroller was programmed in an open source ARDUINO UNO IDE, the programmed was written as a sketch and uploaded to the Arduino UNO board. The detail algorithm is below:

A. Automation and Weather status Display Algorithms

1) *Input:* Character "KEY" from android application
2) *Output:* Status of pin
a) Initialize input and output pins
b) If serial available, read and store it in to variable "KEY"
c) Switch "KEY"
d) Case "1": switch ON first accessory
e) Case"2": switch OFF first accessory
f) Case"3": switch ON second accessory
g) Case"4": switch OFF second accessory
h) Case"0": display weather status information on LCD
i) End

B. Automatic security Program Algorithms

1) *Input:* character "INPUTVAL" from android application
2) *Output:* status of pin
a) Initialize input and output pins
b) Declare character ALARM VALUE
c) Analog read input quantity and stores in "INPUTVAL"
d) If INPUTVAL is greater than ALARMVALUE, Set output pin HIGH
e) If INPUTVAL is less than ALARMVALUE, Set output pin LOW
f) Repeat continuously

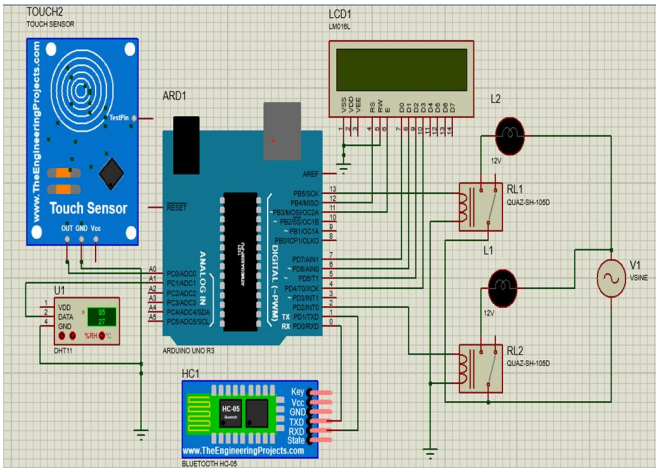


Figure 8: Circuit Diagram

VI. RESULTS

The proposed plan of this paper leads to its real implementation and all the goals required of the smart room was observed and tested. Excellent communication between our smart phone android application and Arduino UNO was obtained first, the accessories were then fully controlled independently and simultaneously by sending the right numerical command also the LCD displayed the real time weather status information on the LCD by sending the appropriate command. Finally, the security system was tested, the touch sensor was touched and buzzer alarm sound was heard. The system is very important for Room residence, economic friendly and easily implemented.

VII. CONCLUSION

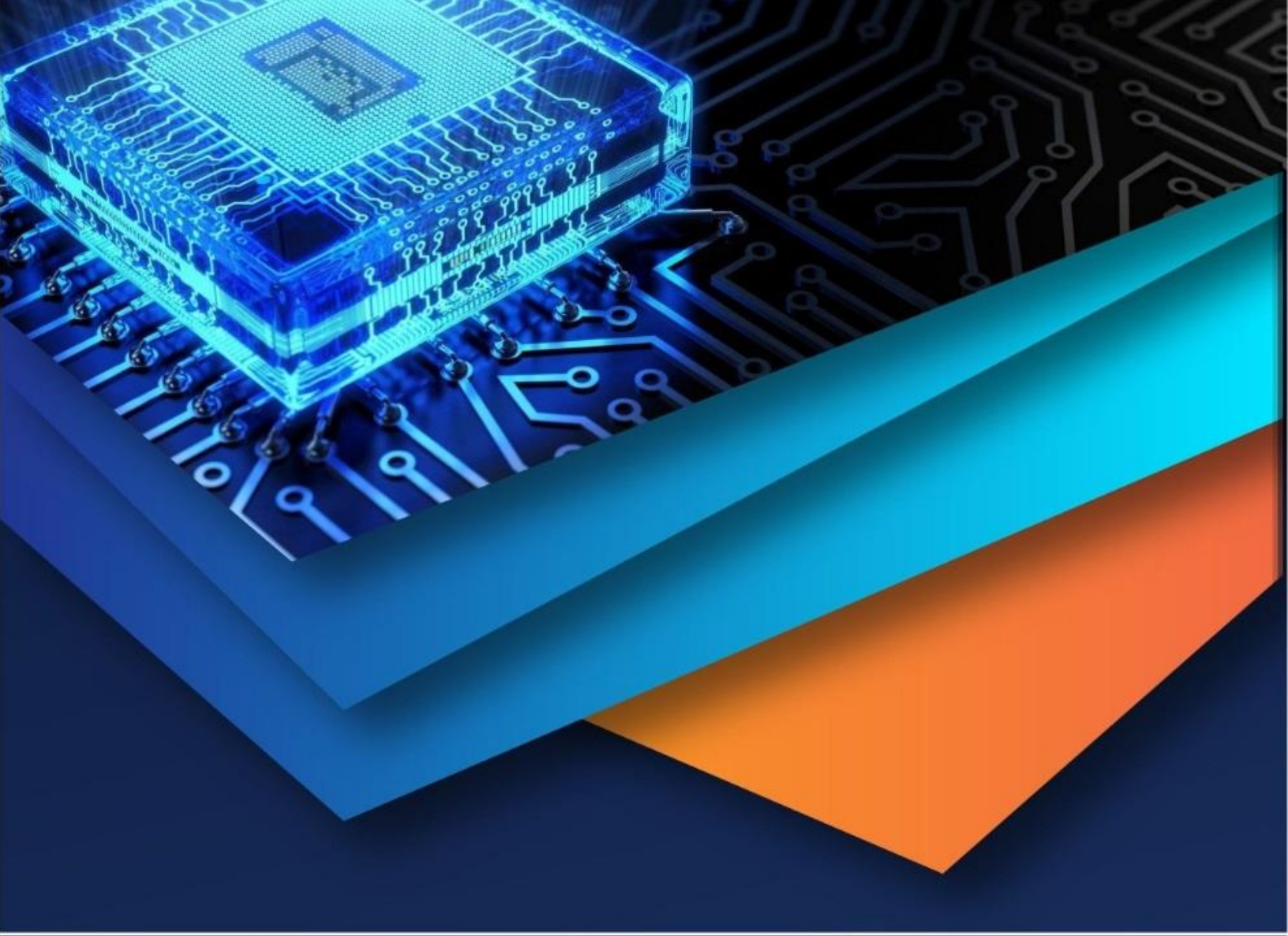
Smart room is an advance extension of commercial room to make life very comport for its residence. In the paper, design of smart room was discussed along with a block diagram and all hardware and software ware discussed appropriately. The system was also implemented and tested and it comprises of room accessories automation, security system and real time weather status display. The Bluetooth module provides the communication channel between the smart phone application and Arduino UNO microcontroller. The project demonstrated the high objective of energy saving needs, cost effectiveness and easily programmed, implemented and maintained.

VIII. ACKNOWLEDGMENT

The research was supported by department of electronics and communication, Mewar University of Rajasthan and presented at the university's EXPO fest competition. we are grateful to Mr. Ritesh ojha for supervising and assisting the project to its completion.
We are also thankful to our colleagues Gurzal, Auwal, Abubakar and Aliyu for their support and encouragement.
Lastly, my deepest appreciation to the head of department Mr. Gaurav for sharing his wisdom, support and making sure the department provided all the needful of the project.

REFERENCES

[1] H.B.Shinde, 312222Abhay Chaudhari, Prafull Chaure, Mayur Chandgude and Pratik Waghmare (2017) " Smart Home Automation System using Android Application" International Research Journal of Engineering and Technology (IRJET) Apr -2017 Volume: 04 Issue: 04, Pp:2408- 2411
[2] Sheetal Prusty (2017) "ARDUINO BASED HOME AUTOMATION USING ANDROID APPLICATION" International journal of Intelligent Computing and Applied Sciences, ISSN (Print): 2322-0031, Vol. 5, Issue 1, 2017, Pp:23-26
[3] Siddharth Wadhwani, Uday Singh, Prakarsh Singh and Shraddha Dwivedi "Smart Home Automation and Security System using Arduino and IOT" International Research Journal of Engineering and Technology (IRJET), e-ISSN: 2395-0056 Volume: 05 Issue: 02, Feb-2018, Pp 1357-1359
[4] Surinder Kaur, Rashmi Singh, Neha Khairwal and Pratyk Jain "HOME AUTOMATION AND SECURITY SYSTEM" Advanced Computational Intelligence: An International Journal (ACII), Vol.3, No.3, July 2016.Pp 17-23.
[5] Muhammad Asadullah and Khalil Ullah 2017 "Smart Home Automation System Using Bluetooth Technology"
[6] Himani Singh Dhami, Nidhi Chandra and Nishank Srivastava. "International Journal of Advance Research, Ideas and Innovations in Technology" ISSN: 2454-132X. Volume:03, Issue:02, 2017. Pp:521-525
[7] https://components101.com/16x2-lcd-pinout-datashee



10.22214/IJRASET

45.98

IMPACT FACTOR: 7.129

IMPACT FACTOR: 7.429

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

International Research Journal of Engineering and Technology (IRJET) e-ISSN: 2395-0056
Volume: 08 Issue: 09 | Sep 2021 www.irjet.net p-ISSN: 2395-0072

DESIGN, SIMULATION AND RESPONSE ANALYSIS OF FIR FILTER DESIGNED BY WINDOWING TECHNIQUE

Abbati Muhammad Ado[1], Jitendra Vaswani[2], Muhammad Ibrahim Zubair[3]

[1]PG Student, Electronics and Communication Engineering Department, Mewar University, Chittorgarh, India
[2]Assistant Professor, Electronics and Communication Engineering Department, Mewar University, Chittorgarh, India
[3]PG Student, Electronics and Communication Engineering Department, Mewar University, Chittorgarh, India

---

ABSRACT: *Digital filters plays very important role in digital signal processing (DSP), digital filters are systems that operates on sampled, quantized input signals (digital signals) to allow certain range of frequency to pass either low frequency or high frequency, it can also pass or reject certain band of frequency from the given input signal bandwidth, or to achieve other filtering objectives. Finite impulse response (FIR) filter and infinite impulse response (IIR) are the two types of digital filters used, One of the methods that are used for the design of FIR filter is the windowing method, this method uses a window function such as rectangular, triangular, hamming, hanning, and Kaiser Window to truncate the infinite impulse response (e.g. Sink signal) in order to get the finite impulse response. In this work a low pass FIR filter is design using four different window functions namely Rectangular, Hamming, Hanning, and Blackman. Analysis and comparison on the frequency response of each low pass FIR filter designed is done, so that conclusion can be made on the window function that gives good filter response.*

Keywords: *filter, frequency, FIR, IIR, window functions.*

1.0 INTRODUCTION

1.1 FILTER

A filter is an electronic circuit that changes the wave shape, amplitude-frequency or phase-frequency characteristics of a given signal, for the purpose of removing noise, extracting information from the signal, or to separate two or more signals that a combine together. Filters played an important role in the field of engineering especially electrical, electronics and communication fields of engineering. Filters generally are frequency selective circuit that allow only certain range of frequency to pass either low frequency or high frequency, Filters are generally categorized in to analog filters and digital filters. [1]

1.2 ANALOG FILTER

Analog filter is a type of filter that operates on continuous-time signal to remove noise from the signal, to allow certain range of frequency to pass or block it, or to achieve any filtering objectives. Analog filters circuits are made of analog components such as resistors, capacitors, inductors, and op amps. They are also characterized by their continuous impulse response described by a differential equation. Laplace transform is used to represent the transfer function of the analog filter [3]. Types of analog filters are.

i. Low pass filter (LPF)
ii. High pass filter (HPF)
iii. Band pass filter (BPF)
iv. Band reject filter (BRF)
v. Notch filter
vi. Resonance filter
vii. All pass filters.

1.3 DIGITAL FILTER

A digital filter is a type of filter that operates on a digital input signal and produced a digital output signal for filtering purposes. It is an algorithm implemented in hardware or software that plays an important role in digital signal processing (DSP) systems below. [1]

i. Speech signal processing
ii. Image processing
iii. Data transmission
iv. Data compression
v. Biomedical signal processing
vi. Digital audio signal processing

Digital filters operates on sampled, quantized input signals (digital signals) to allow certain range of frequency to pass either low frequency or high frequency, it can also pass or reject certain band of frequency from the given input signal bandwidth, or to achieve other filtering objectives

[3]. Finite impulse response (FIR) filter and infinite impulse response (IIR) are the two types of digital filters used depending on the requirement of the system or application in which the filter is to be used.

1.3.1 Types of digital filters

i. Finite impulse response (FIR) filter

This is a type of digital filter in which its impulse response is of finite duration. [1] This filter can be represented by the difference equation below.

$$y(n) = \sum_{k=0}^{N-1} h(k)x(n-k)$$

From the difference equation of the FIR filter above, the impulse response h (k) is of finite values from 0 to N, the equation also indicates that the output of the filter y (n) depends on the present and past values of the input signal. Now the transfer function of the FIR filter can be obtained by taking the z-transform of the impulse response as below.

$$H(z) = \sum_{k=0}^{N-1} h(k)z^{-k}$$

The diagram below is block diagram of digital FIR filter, with the input, output, delays, coefficients, and sum.

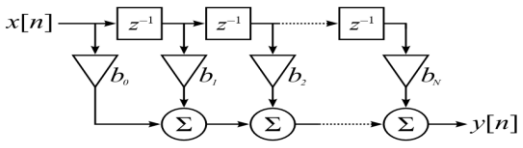


Fig. 1.0 FIR filter block diagram

ii. Infinite impulse response (IIR) filters

This is a type of digital filter in which its impulse response is of infinite duration, the input and output signals to IIR filter are related by the convolution sum below.

$$y(n) = \sum_{k=0}^{\infty} h(k)x(n-k)$$

Now the problem with the equation above is that it cannot be implemented by computation because of the infinite impulse length that started from zero to infinity, instead the equation is express in a recursive form which is called the difference equation of the IIR filter as given below.

$$y(n) = \sum_{k=0}^{N} bkx(n-k) - \sum_{k=1}^{M} aky(n-k)$$

Where a_k and b_k are the coefficients of the IIR filter.

From the difference equation above, the output signal y (n) depends on the present and past values of the input signal as well as past output values, this shows that the IIR filter has a feedback system. [1]

2.0 LITERATURE REVIEW

Various articles and research papers were reviewed which formed the literature review of the thesis. However for the purpose of this publication some part of the literature review is discuss as below, Manjinder Kaur1 and Sangeet Pal Kaur in their research paper "FIR low pass filter designing using different window functions and their comparison using MATLAB" the simulation result shows that the triangular window produced inefficient low pass filter result compare to other window function, hence should not be choose for efficient FIR low pass filter design. Among all the window functions the Blackman Harris window is the best choice for FIR filter design using window function because it produces less side lobes and zero leakage factor. [4]

In another research work done by N. M. Shehu, A.S. Gidado, and M.I. Faruk on "response analysis of FIR high pass filter design using window methods" they make a comparative analysis based on the magnitude response, phase response, and pole-zero plots of the FIR high pass filter designed using three window functions namely: Rectangular, Kaiser, and Tukey window functions. The simulation result shows that the rectangular window function is the best for the design of FIR high pass filter because its magnitude response is close to the specified cut-off frequency. [5] [6]

Sumbal Zahoor and Shahzad Naseem in their research paper worked for an optimized and efficient design of digital FIR band pass filter from software to hardware implementation using Hamming, Hanning, Blackman, and Kaiser as the window functions. The Kaiser window function is the best choice based on the simulation result as it showed less transition band and minimum main lobe width, based on the same specifications(N = 15, β = 0.5, fc1 = 0.4, fc2 = 0.5) given for the design of the FIR band pass filter using the mentioned window functions above. And for realization of the transfer function the best-chosen structure is the direct-form structure, this design method reduces arithmetic complexity and hardware resources, hence produced optimized FIR band pass filter. [7, 8]

In the work of Er. Sandeep Kaur, and Er. Sangeet Pal Kaur, on "Design of FIR filter using hanning window, hamming window and modified hamming window". Based on the simulation result of their work, the FIR filter designed using the modified coefficients of the hamming window

function give a better and efficient design than the hanning and hamming window functions, because it provided smaller main lobe width, and sharp transition band. [9]

Also, in a published paper by Mr. Ankan Bhattacharya on FIR filter design, a modified window function and a hamming window function were used in the design, a frequency response of low pass, high pass, band pass, and band stop FIR filter of the modified window function and the hamming window function were shown in the simulation result, by comparison the modified window function give efficient and best design. [10]

3.0 METHODOLOGY

A MATLAB software was used for the design and simulation of the low pass FIR filter, the codes of the design are implemented on the software, and simulation result of various plots of the low pass FIR filter designed were observed. At the first stage of the design methodology, the design specifications of the filter such as order, range of values, cut off frequency, angle, etc. were given. A sink function was define and plotted with it frequency response, rectangular window function was defined and plotted as well, truncation of the sink function was done by multiplying it with rectangular window function, the frequency response of the multiplication result is the low pass FIR filter designed using rectangular window function by windowing technique. Subsequently a different window function Hamming was used, the result is the low pass FIR filter designed using Hamming window function, the other two window functions used are Hanning and Blackman window functions.

A noisy sine signal was defined with its time domain plot. The low pass FIR filter designed above using each window function was called, and used to filter the noisy sine signal above, the time domain of the noisy signal before and after filtering were plotted, the four different filtering result were compared, and conclusion was made on the filter that gives best filtering result.

3.1 DESIGN SPECIFICATIONS

The parameters or specifications used in the design of the low pass FIR filter are:

i. Order of the filter m = 50
ii. Range of values n = 0:1:m-1
iii. Sampling frequency f s = 2000
iv. Cuff-off frequency $f_c = 0.1$
v. Angles $\theta_1, \theta_2, \theta_3$
vi. Frequency of a noisy sine signal $f_1 = 50$
vii. Time domain t

3.2 DIGITAL FIR FILTER DESIGN METHODS

i. Frequency sampling method
ii. Chebyshev approximation method
iii. Windowing Method

3.3 FIR FILTER DESIGN USING WINDOWING TECHNIQUE

The design of FIR filter using windowing method involved the use of window function such as rectangular, hamming, hanning, and Kaiser Window and multiplies it with the desired infinite impulse response to obtain the finite impulse response of the filter, this truncation produces ripples and overshoot both in the passband and the stopband of the FIR filter frequency response. This ringing effect near the band edge of the FIR filter is called Gibbs phenomenon, the magnitude of this Gibbs phenomenon differs for each window function used in the design. All the window functions have different properties in time and frequency domain, having different side lobe attenuation and transition width. The best window function to be choose for the design of FIR filter is one that provide good filter response with reduced side lobes and comparatively less pass-band and stop-band ripples.[11]

Generally, in the design of any digital filter, the desired frequency response of the digital filter response $H_d(e^{jw})$ is given below.

$$H_d(e^{jw}) = \sum_{-\infty}^{\infty} hd(n)e^{-jwn}$$

By taking the inverse discrete Fourier transform (IDFT) of the desired frequency response an infinite impulse response $h_d(n)$ can be obtain below.

$$h\,d\,(n) = 1/2\pi \int_{-\infty}^{\infty} Hd(e^{jw})e^{jwn}\,dw$$

Unfortunately, this impulse response h d (n) is infinite and hence lead to unrealizable IIR filter. However, this infinite impulse response can be made finite by truncating it, this truncation is achieved by multiplying the infinite impulse response with a window function w(n) to get the finite impulse response h(n). [12]

$$h\,(n) = h_d\,(n)\,.w\,(n)$$

Now the design frequency response of the FIR filter is obtained from the finite impulse response h (n) as.

$$H\,(e^{jw}) = \sum_{n=0}^{m-1} h(n)e^{-jwn}$$

Also, the transfer function of the FIR filter can be determined by taking the Z-transform of the impulse response as. [13]

$H(z) = \sum_{n=0}^{m-1} h(n) z^{-n}$

3.4 WINDOW FUNCTIONS

Window functions are used to truncate the infinite impulse response (e.g sink function) in the design of FIR filter, some of the window functions are discuss below. [14]

i. Rectangular window function

$$W_R(n) = \begin{cases} 1, & 0 < n < L-1 \\ 0, & otherwise \end{cases}$$

ii. Hanning window function

$$W_{HN}(n) = \begin{cases} 0, & otherwise \\ 0.5 - 0.5\cos\left(\frac{2\pi n}{L-1}\right), & 0 < n < L-1 \end{cases}$$

iii. Hamming window function

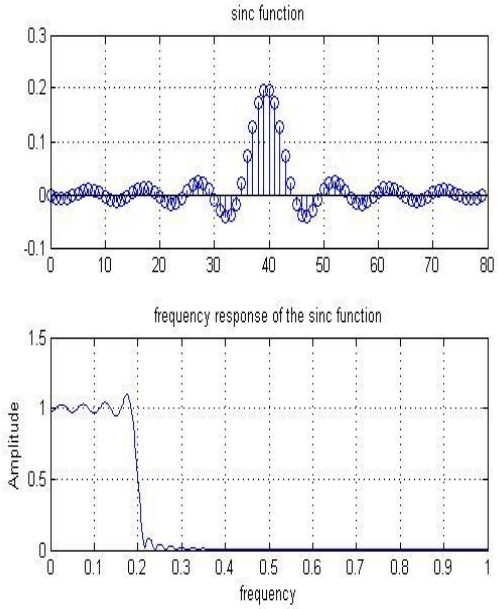
$$W_H(n) = \begin{cases} 0, & otherwise \\ 0.54 - 0.46\cos\left(\frac{2\pi n}{L-1}\right), & 0 < n < L-1 \end{cases}$$

iv. Blackman window function

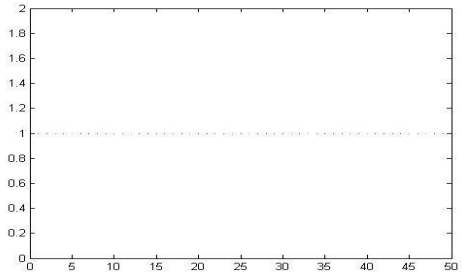
$$W_B(n) = \begin{cases} 0, & otherwise \\ 0.42 - 0.5\cos\left(\frac{2\pi n}{L-1}\right) + 0.08cos\left(\frac{4\pi n}{L-1}\right), & 0 < n < L-1 \end{cases}$$

4.0 SIMULATION RESULT AND ANALYSIS

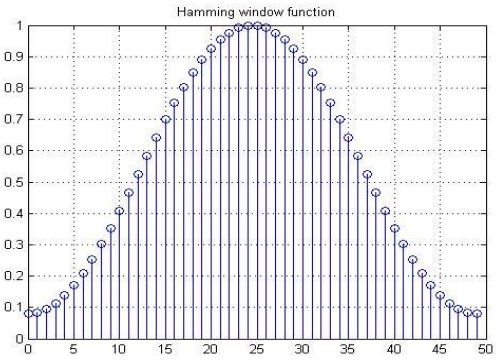
There are various plots from the simulation result using the MATLAB software, the plot of the sink signal, window functions, response of the low pass FIR filter designed, noisy sine signal, as well as the filtered sine signal are shown below.



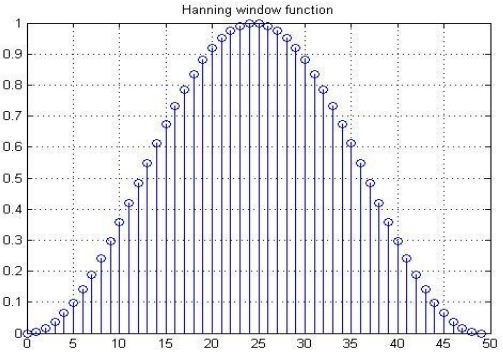
a) Time domain and frequency response of the sink function.



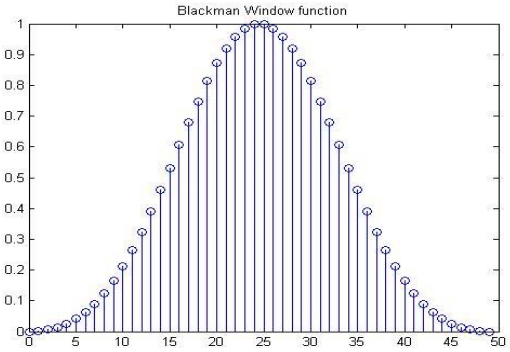
b) Plot of Rectangular window function



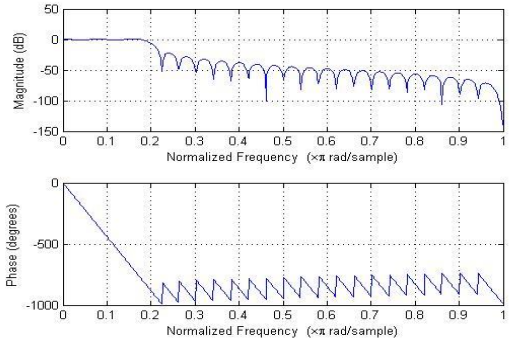
c) Plot of hamming window function.



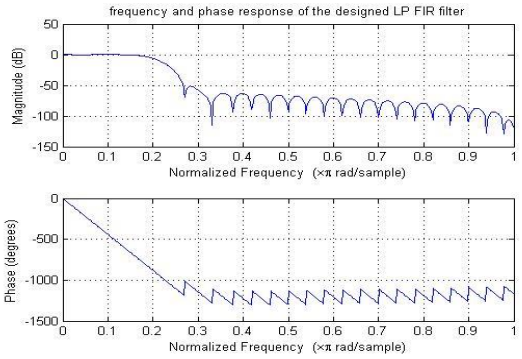
d) Plot of Hanning Window function



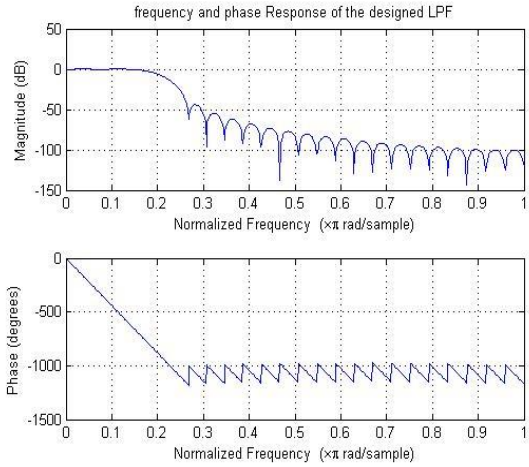
e) Plot of Blackman window function



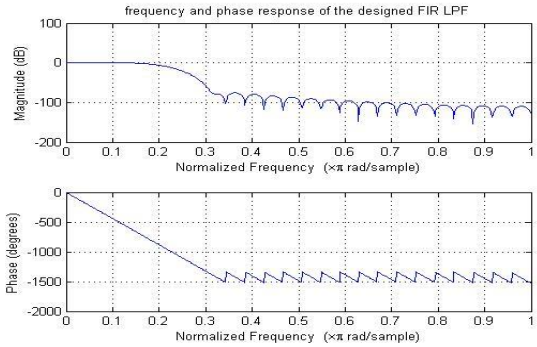
f) Response of low pass FIR filter designed using Rectangular window function.



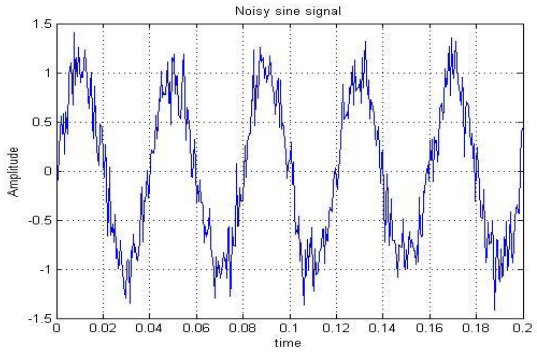
g) Response of low pass FIR filter designed using Hamming window function.



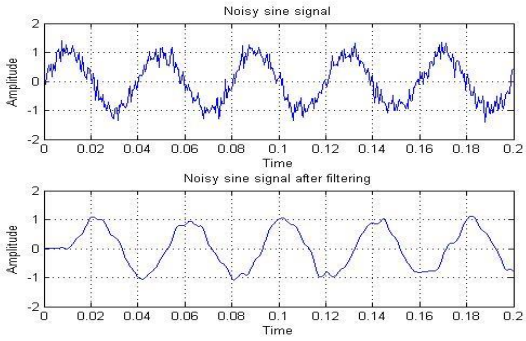
h) Response of low pass FIR filter designed using Hanning window function.



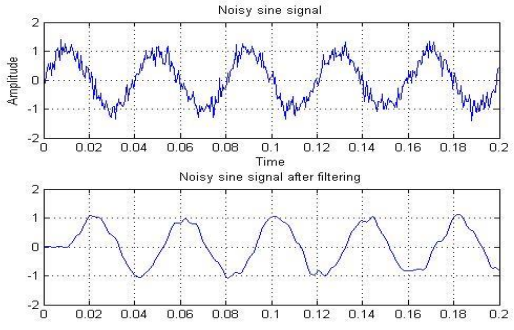
i) Response of low pass FIR filter designed using Blackman window function.



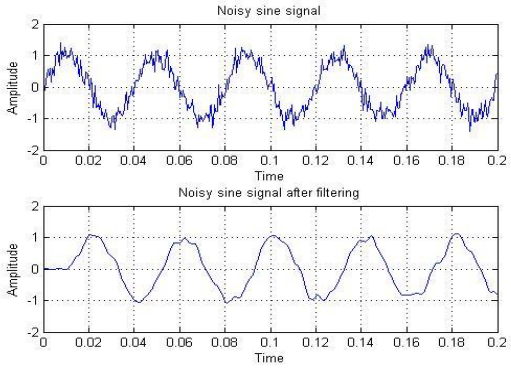
j) Noisy sine signal.



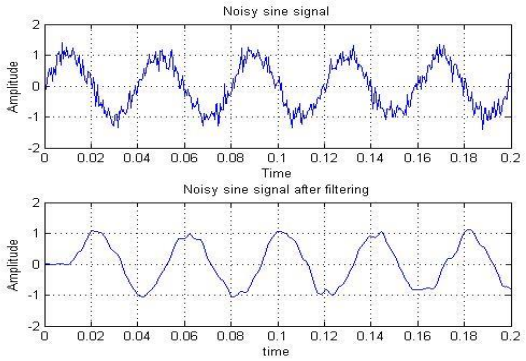
k) A comparative plot of Noisy sine signal with the filtered noisy signal using Rectangular Windowed function filter.



l) A comparative plot using Hamming windowed function filter



m) A comparative plot using Hanning windowed function filter



n) A comparative plot using Blackman windowed function filter.

4.1 ANALYSIS ON THE DESIGNED FIR FILTER RESPONSES

All the window functions Triangular, Rectangular, Hanning, Hamming and Blackman have completely different properties in time and frequency domain, having different side lobe attenuation and transition width. The best window function to be choose for the design of FIR filter is one that provide accurate type of responses with reduced side lobes and comparatively less pass-band and stop-band ripples. Considering the frequency response of the low pass FIR filter designed using rectangular window function in (f), there is a sudden transition at around 0.2 from passband to stopband region, this make the transition width very small, the stopband also consist of ripples with high side lobes as shown in the diagram. In the case of the frequency response of the low pass FIR filter designed using Hamming window in figure (g), transition from the passband to stopband start at around 0.2, with transition width 0.2 to 0.3, and a high side lobes

in the stopband region as shown above. Also, for the response of FIR filter designed using Hanning window function in figure (h), there is almost similar result with that of FIR low pass filter designed using Hamming window function, due to the slight difference in the formula of Hanning and Hamming window functions.

However, looking at the frequency response of the FIR low pass filter designed using Blackman window function in (i), transition from the passband to stopband start after 0.2 and stop after 0.3, there is also reduced in the width and height of the side lobes in the stopband, unlike that of the FIR filter designed using rectangular, Hanning, and Hamming window function that have high stopband ripples.

5.0 CONCLUSION

Based on the simulation results and it analysis, the design of low pass FIR filter using windowing technique on MATLAB software, four different window function namely Rectangular, Hamming, Hanning, and Blackman were used for the design using windowing technique, based on the analysis of the four filter responses designed, and also looking at the comparative plots of the noisy sine signal filtered using the four filters designed, the Rectangular window function is not suitable for the FIR filter design based on this specifications, because it produces filter response with less transition width and high side lobes ripples in the stopband. The Hamming and Hanning window functions almost gave similar result due to the similarity in their formula. However, Blackman window function gave better filter response than that of rectangular, Hamming, and Hanning window functions, as it produces filter response of smaller width and height of the ripples in the stopband

Although looking at the diagrams from (k) to (n), there are four comparative plots of the noisy sine signal and its filtered form using the four different low pass FIR filter designed using the four window functions, the four comparative plots almost give similar result, even though, we expect to see Blackman window function to give a better filtering result than the other three window functions. However, this depends on the nature and properties of the signal to be filtered, and which filter specifications meet the requirement or values of the signal to be filtered, such analysis need to be done before designing or chosen a filter so as to avoid filter mismatch or removing part of the signal that is not supposed to be remove.

REFERENCES

[1] Emmanuel C. Ifeachor, Bamie W. Jervis: “Digital Signal Processing, A Practical Approach”, pp 318-398, PEARSON, second edition

[2] Sanjit K. Mitra. “Digital Signal Processing, a computer-based approach 4th edition McGraw Hill,” pp 489-528.

[3] P. Dutilleux, U. Zolzer, “Chapter 2 Filters”, pp 33, 2002 John Wiley & Sons, Ltd

[4] Manjinder Kaur, Sangeet Pal Kaur, “FIR Low Pass Filter Designing Using Different Window Functions and their Comparison using MATLAB”, International Journal of Advanced Research in Electrical, Electronics and Instrumentation Engineering, Vol. 5, Issue 2, February 2016.

[5] N. M. Shehu, A.S. Gidado, M.I. Faruk, “Response analysis of FIR high pass filter design using window methods”, International Journal of Engineering Applied Sciences and Technology, 2019 Vol. 4, Issue 5, ISSN No. 2455-2143, Pages 30-35.

[6] Shehu, NM; Baraya, JT; Sani, MH, “Comparative Analysis of a High Pass Finite Impulse Response (FIR) Filter Designed and Simulated by Window Methods”, J. Appl. Sci. Environ. Manage. Vol. 23 (4) 721-725 April 2019.

[7] Sumbal Zahoor and Shahzad Naseem, “Design and implementation of an efficient FIR digital filter”, Electrical & Electronic Engineering research article, Cogent Engineering (2017), 4: 1323373.

[8] Mohammed Mynuddin, Md. Tanjimuddin, Md. Masud Rana, Abdullah, “Designing a Low- Pass Fir Digital filter by using Hamming window and Blackman window Technique”, Science Journal of Circuits, Systems and Signal Processing, Vol. 4, No. 2, 2015, pp. 9-13

[9] Er. Sandeep Kaur, and Er. Sangeet Pal Kaur, "Design of FIR filter using hanning window, hamming window and modified hamming window", International Journal of Advanced Research in Computer Engineering & Technology (IJARCET) Volume 4 Issue 5, May 2015.

[10] Mr. Ankan Bhattacharya, "A modified window function for FIR filter design with an improved frequency response and its comparison with the Hamming window", International Journal of Science, Engineering and Technology Research (IJSETR) Volume 2, Issue 5, May 2013

[11] Sanjay Sharma, "Digital Signal Processing", Katson Books.

[12] S Salivahanan, A Vallavaraj, C Gnanapriya: "Digital Signal Processing", pp 381-401, Tata McGraw-Hill, second edition, 2010.

[13] John G. Proakis, Dimitris G. Manolakis, "Digital signal Processing" PEAESON, 4th edition.

[14] Su Peng, "Design and analysis of FIR filters based on Matlab", Degree Project of Bachelor thesis, Linnaeus University, school of computer science, physics and mathematics.

iJRASET
International Journal For Research in Applied Science and Engineering Technology

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 7 **Issue:** IV **Month of publication:** April 2019

DOI: https://doi.org/10.22214/ijraset.2019.4167

www.ijraset.com

Call: 08813907089 | E-mail ID: ijraset@gmail.com

International Journal for Research in Applied Science & Engineering Technology (IJRASET)
ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 6.887
Volume 7 Issue IV, Apr 2019- Available at www.ijraset.com

An Overview on the Artificial Eye System using MEMS Technology

R. K. Ojha[1], Gaurav Sharma[2]
[1, 2]*Mewar University, Chittorgarh, Rajasthan*

Abstract: ***The world of today is full of colors and joys. To enjoy this color of nature we need the eyes. But one of the major conditions which damage the human eyes capability of seeing is blindness. Blindness effects on our education, employment and prosperity, and also participation in civil, social and political life. World's largest number of blind people is in India. Around 40 million people across the globe, who are blind, over 15 million are from India. In India, the requirement of optometrists is 40,000 but there are only 8,000. 75% cases of blindness could be avoided but for the shortage of optometrists and donated eyes for the treatment of corneal blindness.[1]***

In 21st century MEMS and NEMS is the most promising technology. Now a days it players very important role in the revolution of industrial and consumer products by combining silicon based microelectronics with micromachining technology. The main function of bionic eye is to restore basic visual cues for those people who are suffering from eye diseases such as retinitis pigmentosa. In bionic eye a micro video camera fitted to the Goggle used by patient, it will capture the image and process it. After that image are sent via wireless medium to a bionic eye, which is implanted at the back of eye, it generates optic signals to stimulates optic nerves to generate points of light, it forms the basis of images in the brain. Thus a blind one can also watch that object.

Keywords: Cause of Blindness, Bionic Eye & MEMS Technology.

I. INTRODUCTION

MEMS and NEMS is now in trend and one of the most promising technologies in this Century and has the capacity to revolutionize both industrial and consumer products by combining silicon-based microelectronics with micromachining technology. Its techniques and microsystem-based devices have the potential to dramatically effect of all of our lives and the way we live. MEMS and NEMS have become the fastest-growing area of scientific research, with inventions of new devices. Technology has done wonders which help the mankind. Prosthetics use to help overcome handicaps.

II. CAUSES OF BLINDNESS

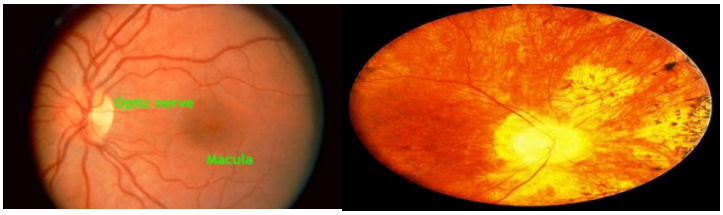
There are mainly two causes of blindness:-

1) Retinitis Pigmentosa
2) Age-related macular degeneration

A. What is a Retinitis Pigmentosa?

Retinitis pimentos (RP) is the major cause of inherited blindness, affecting 1.5 million people worldwide (a prevalence of one in 5000).RP is characterized by the progressive loss of photoreceptor cells and supporting vision and is related with night-vision difficulties. Most commonly, patients lose their sight slowly, eventually developing tunnel vision and possibly complete blindness in the late stages of the disease. Patients with RP have difficulty with mobility, navigation and night-vision.[1]

Normal Eye Defected Eye



(1a) (1b)

Fig. 1: (1a) Normal eye (1b)Defected eye

B. What is Age-Related Macular Degeneration?

Age-related macular degeneration (AMD) is the cause of almost half of all legal blindness in India. It results in vision loss in the center of the visual field and usually affects people over the age of 65. AMD causes cells in the retina, the light sensing part of the eye, to stop converting absorbed light into electro-chemical signals. As the brain does not receive the signal, a complete image is not formed Patients with AMD have difficulty performing tasks that rely on central vision, such as reading and recognizing faces.

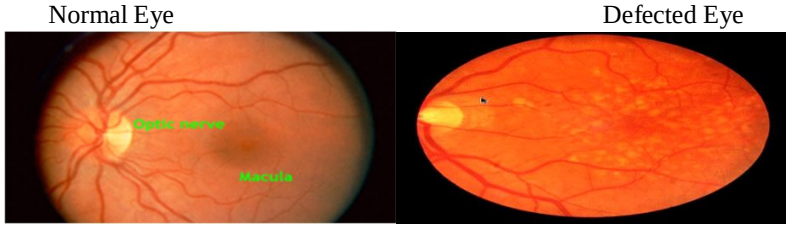


Fig 2: Normal eye(2a) ,Defected eye (2b)

III. THE HUMAN EYE

Light make us able to see the objects through the healthy Eye. When light falls on our eyes, Photo receptors absorb them and convert them in to electrochemical signals that are sent to our brain, and our brain deciphers the information in order to detect the appearance, location and movement of the objects we are sighting at. This whole process is too much complex and would not be possible without healthy Eye system and light. Without light, there is no world. The human eye is most important organ which gives us the sense of sight and it allows us to learn about the surrounding world than any of the other senses.[2]

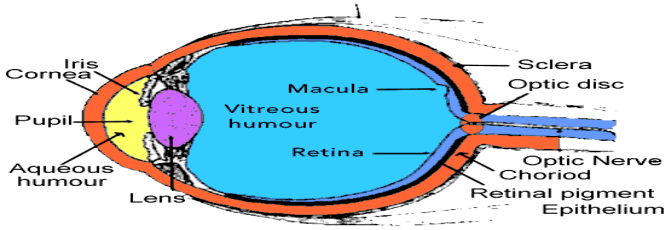


Fig: 3:- Human Eye

IV. THE BIONIC EYE

In this bionic eye system there will be a small digital camera developed using MOMS technology, an external processor and an implant with a Nano chip and stimulating electrodes, these all are surgically placed in the back of the eye. MEMS Technology paved way through a bionic eye to allow blind people to see again.

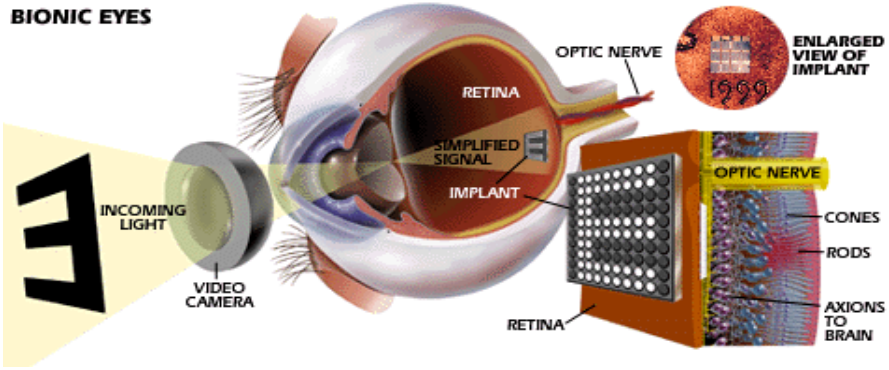


Fig: 4:-The Bionic eye

In artificial Eye system there is an embedded computer chip which is kept in the back of the patient's eye, linked up Google glasses that they wear. The captured images are beamed to the chip, which translates them into impulses and that can be interpreted by the brain. [3]

ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 6.887
Volume 7 Issue IV, Apr 2019- Available at www.ijraset.com

V. HOW BIONIC IMPLANT WORK

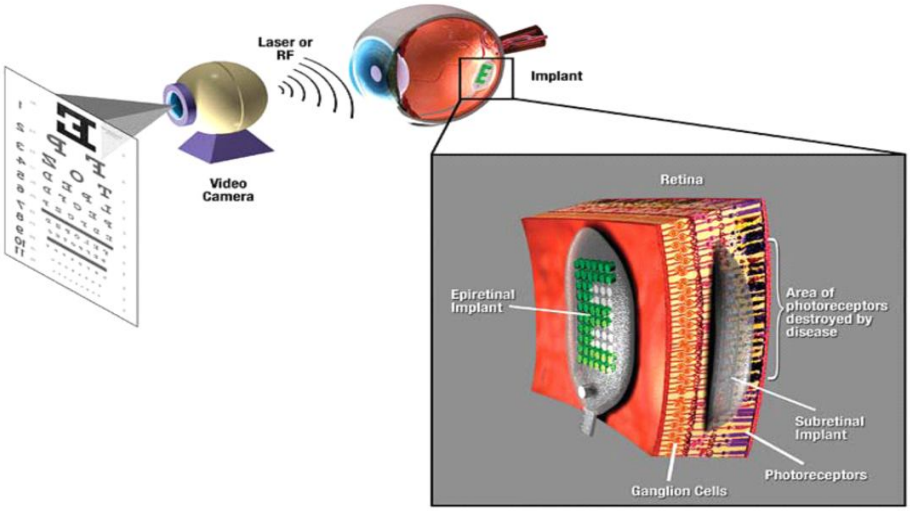


Fig 5:- Bionic eye working

The artificial eye system is connected with Google glasses, which transmits high-frequency radio signals to the embedded microchip implanted in the partially defected retina. The microelectrodes on the implanted chip convert these signals into electrical impulses to stimulate cells in the remaining healthy portion of retina that connect to the optic nerve. These impulses are then converted in to electrochemical pulses by the remaining healthy photoreceptor cells and then passed down along the optic nerve to the vision processing centers of the brain, where they are interpreted as an image.
Bionic eye system is one of the greatest boons given by the MEMS technology. The application of bionic eye system is infinite. The bionic eye presented in this paper will come as a dream come true for blind people.
The size of this device is 2 millimeters across and contains some 4000 micro photodiodes and is placed behind the retina, this collection of miniature solar cells is designed to convert normal light to electrical signals, which are then transmitted to the brain by the remaining healthy parts of the retina.
In this artificial eye the following components have been integrated with the lens using custom-built optoelectronic components.[1]

A. Control Circuits
B. Communication Circuits
C. Miniature Antennas
D. LED

The light emitting diode will form the images in front of the eyes and hence we would require around 100s of this LEDs. This will form images such as, words, charts, and photographs. The hardware used in this is a semitransparent because of which the patent will be able to navigate his surroundings without any problem. One of the main reasons for possibility of fabricating the component on single polymer based contact lens is NEMS technology. Because of this technology, we can manufacture these functional devices on such a tiny scale and then incorporate these tiny functional devices on the polymer lens.

VI. FABRICATION PROCESS USING MEMS TECHNOLOGY

The fabrication process involves integration of electronic components like control circuits, communication circuits, miniature antennas and LEDS. In order to fabricate the components for silicon circuits and LEDs, we need to make use of high temperatures and also corrosive chemicals, because of this we cannot manufacture them directly on to lens and we also have to make sure that all the component of lens are miniaturized and integrated onto about 1.5 square centimeters of a flexible, transparent polymer. This problem can be eliminated by the use of self-assembly process.[4]
In Self-assembly a disorganized system of pre-existing components forms an organized structure or pattern as a consequence of specific, local interactions among the components themselves without external direction.

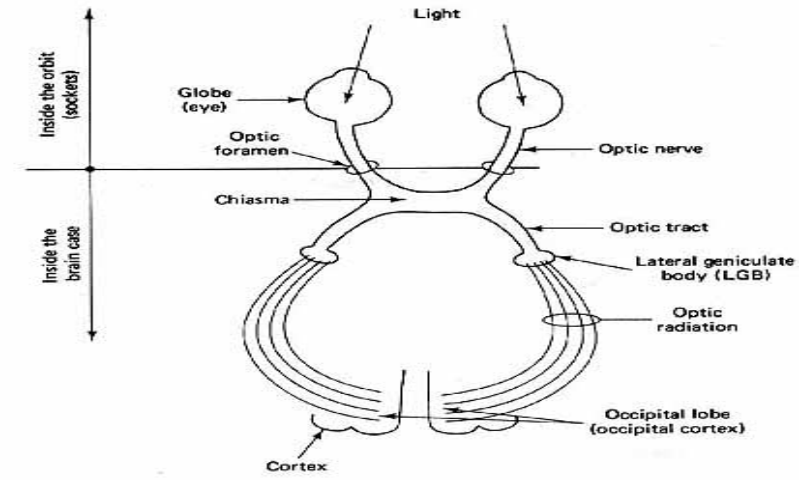


Fig:-6. site of implant

VII. POWER SUPPLY

As we know that this artificial eye system is power operated system hence it requires the power supply for its operation. One of the best sources of power for electronic component integrated with in lens would be Nano generators.

The Nano generators are very effective and small in size; it does not require petrol or diesel like other generators for its mechanical movement instead even a small finger movement of our body will be enough to produce a considerable amount of electricity required.

This generator works on the principle of piezoelectric effect, this could play a vital role in providing the power source for bionic eye cause this will avoid the use of battery which is a toxic instead we can use Nano generator which will produce electricity due to flow of blood which gives it a mechanical force.

Flexing the nanowires (actuators) through vibration (like sound waves) produces a current in the wire. When the wire bends far enough to touch a discharge electrode, the current is transferred. So, the more the nanowire gets bent or vibrated, the more current it produces.[5] The Nano wire used here in Nano generator is zinc oxide. Mechanical vibration which is needed for this generator can be obtained by blood flow or movement of iris. Based on arrays of vertically-aligned zinc oxide nanowires that move inside a novel "zigzag" plate electrode, the Nano generators provides a new way to power bionic eyes without batteries or other external power sources.

VII. APPLICATION OF BIONIC EYE

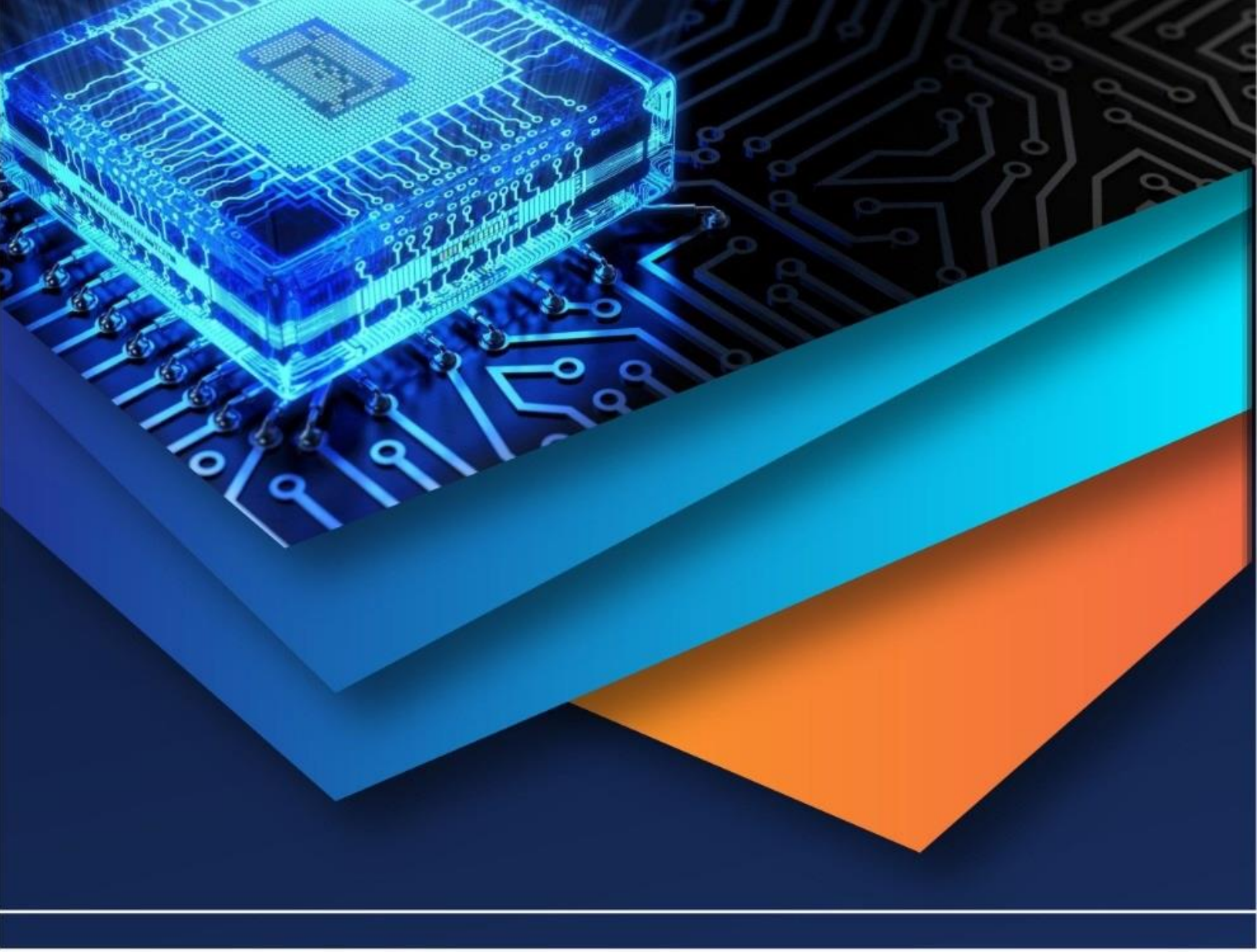
A. It can play a vital role in the field of medical electronics.
B. These lenses that can superimpose computer-generated high-resolution color graphics on a user's real field of vision.
C. Sensors built onto lenses would let diabetic wearers keep tabs on blood-sugar levels without needing to prick a finger
D. Virtual gamers could use the real world as a backdrop for their adventures.

VIII. CONCLUSION

Now, it's not a dream to restore the sight of a blind people today. Bionic Eyes have made this true. Though there are a number of challenges to be faced before this technology reach the common man, the path has been laid. This paper has tried to present the concept of Artificial Vision called "Bionic Eyes". It is just a matter of time, may be 4-5 years that the blind will be able to see through these Bionic Eyes, with thanks to Science and Technology.

REFERENCES

[1] M.S Humayun , J.D Weiland , G.Chader , "Basic research , biomedical engineering and clinical advances",2007,pp. 151-206.
[2] Xi Chen,Shiyou Xu,Nan Yao and Yong Shi, "1.6v nanogenerator for Mechanical Energy harvesting using PZT nanofibers", Nano Letters
[3] Guang Zhu, Rusen Yang, Sihong Wang and Zhong Lin Wang, School of Materials Science and Engineering, Georgia Institute of technology,Atlanta,Georgia,"Flexible High-Output Nanogenerator based on lateral ZnO Nanowire Array", Published, Copyright © American chemical Society
[4] Kosta Grammatis,Rob Spence, "Building the bionic eye; Hacking the human", Future of Journalism conference, www.eyeborgproject.com .
[5] T. Judd, K. Ehinger, F. Durand, and A. Torralba. Learning to predict where humans look. ICCV, 2009.
[6] Javier Portilla and Eero P. Simoncelli. A parametric texture model



10.22214/IJRASET

45.98

IMPACT FACTOR: 7.129

IMPACT FACTOR: 7.429

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

IJIRSET
International Journal of Innovative Research in
SCIENCE | ENGINEERING | TECHNOLOGY

e-ISSN: 2319-8753 | p-ISSN: 2320-6710

INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH

IN SCIENCE | ENGINEERING | TECHNOLOGY

Volume 9, Issue 9, September 2020

ISSN INTERNATIONAL STANDARD SERIAL NUMBER INDIA

Impact Factor: 7.512

9940 572 462 | 6381 907 438 | ijirset@gmail.com | www.ijirset.com

International Journal of Innovative Research in Science, Engineering and Technology (IJIRSET)

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.512|

|| Volume 9, Issue 9, September 2020 ||

Congestion Control Through Mobile Agent in Wireless Sensor Network

Kamal Deep [1], Mohd.Museum [2]

Research Scholar, Department of Electronics and Communication Engineering, Mewar University, Chittorgargh, Rajesthan, India[1]

Professor, Department of Electrical Engineering, Mewar University, Chittorgarh, Rajesthan, India[2]

ABSTRACT: Mobile agent technology embedding in wireless sensor network (WSN) has a new research area for researchers. Mobile agents (MA) embedded in different applications such as commercial, civil applications, climate monitoring, vehicle tracking, military surveillance,data gathering. Congestion in an network created problem of packet losses, bandwidth degradation,time consuming and energy waste on congestion In this paper, we have done a mobile agent base framework for congestion control and routing. Agents roamed in a network to communicate with the sensor. A mobile agent started moving from every node and went to an adjacent node at every time to collect information from sensor nodes and also maintain a routing table as well as node congestion status. When a mobile agent travels through the network, it selected a less-loaded neighbor node as its subsequent hop according to the node's congestion status and also updates the routing table of the node it is visiting. All the nodes are static and base station (BS) collected the information about network congestion from cluster heads (CH) and inform to the mobile agents (MA). Each Cluster head has a routing table that stores route information for every destination. The purpose of mobile Agent in WSN is to control link-level-congestion, which improves the network throughput, reduce the time delay.

KEYWORDS: Congestion, Cluster head (CH), Mobile Agent (MA), Sink node, Wireless sensor network.

I. INTRODUCTION

Wireless sensor network environment consist of thousand wireless sensor nodes and a single central node (called a sink node), all wireless sensor nodes collect information from the environment and send collected information to sink node for further processing.When all nodes will send sensed data directly to the sink node than congestion will surely occur. Congestion is affecting the data transmission process, increase packet loss, delay in the coming of data from the endpoint and degrade energy level of each node. Congestion in the network will happen if packets are transmitted in a many-to-one manner or from sensors-to-sink direction [1].Congestion in the network has some negative impact on the network performance,like increase packet loss, end-to-end delay, consume energy and other fidelity degradation. The main purpose of a mobile agent in a wireless sensor network environment to congestion control so that improvement in network throughput, reduce the time of data harmful impacts on network performance such as increase packet loss, end-to-end delay consume more energy.Since the node energy, communication bandwidth, network computing capability and other resources are generally restricted ,therefore the main purpose of a mobile agent in wireless sensor network environment to congestion control so that improvement in network throughput, reduce transmitted delay. It is likely to improve the network performance by protocol design, route algorithm chooses, data integration and load balancing, and so on[2].Therefore congestion in a wireless sensor network need to be controlled in order to prolong the system lifetime, improve fairness, high energy-efficiency, and increase the quality of service.

Each sensor has limited battery power. If the sensor nodes send their data directly to the central node, it might possible that they will lose their energy in the first round of data transmission. The mobile agent concept has employed in WSN to remove the problem of energy consumption and to obtain data gathering effectively. Therefore, before migrating MA in the network, it is very important and fundamental steps to decide the route selection for mobile agent. The mobile agent (MA) is a software code that is migrating from node to node in the network and performs data processing itself.Many applications are based on mobile agent technology such as google. It has also been proved that mobile agent technology may save up to 80% of the data transmission time.

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.512|

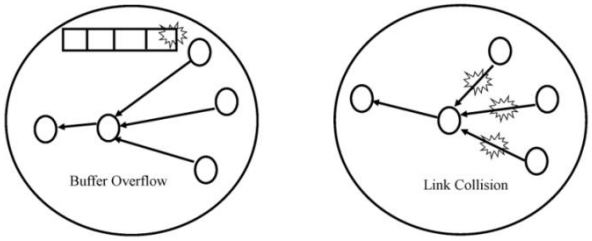
|| Volume 9, Issue 9, September 2020 ||

II. RELATED WORK

When a huge amount of sensor nodes are involve to send data, it must be a possibility of congestion in the network .Congestion is a major crucial problem in wireless sensor network because it has a negative impact on the performance of a network such as energy efficiency of sensor nodes. Congestion occurs in the network whenever a single link traffic becomes greater than its individual capacity. There are two types of congestion:

Node-level congestion: When the packet arrival rate is higher than packet service rate than Node-level congestion will occur [4].The result of this congestion is a high packet loss and queuing delay.

Link-level congestion: This type of congestion take place when multiple active sensor nodes start transmit packets at the same time within range of one another.Packets that leave the buffer might fail to reach the next hop as a result of the collision and bit error.Overall throughput and link utilization is decreased by this type of congestion while packet delay and energy waste will be increase[5] [6].
There are various congestion control protocols in wireless sensor networks.



1-Congestion at Node-level 2 - Congestion Link-level

Fig.1. Congestion types in WSNs

Congestion Avoidance and Detection (CODA) [7]: it detects the congestion by detecting the buffer size of sensor nodes and the load of the wireless channel. If channel load exceeds from a pre-defined threshold value, a sensor node informs its neighbors to decrease the transmission rate.

Congestion Control and Fairness (CCF): It [8] detects congestion at the packet service time at the medium access control MAC layer CCF uses packet service time to decrease the rate of service and congestion at every node.

Adaptive Rate Control (ARC) [8]: These protocols monitor the traffic route and how many packets are injected into the traffic stream. Every node estimates the amount of upstream nodes therefore the bandwidth is divided proportionally between route-through and locally generated traffic, with preference given to the former node. The resulting bandwidth allotted to every node is thus almost fair.

III. MOBILE AGENT BASED CONGESTION CONTROL

The attention of users in wireless sensor technology is increasing exponentially. Researchers work on the design an information retrieval system and tools that can efficiently find, collect and process the information .To achieve this goal, A mobile agent model is widely used in distributed applications. A mobile agent is a software entity that can migrate in the network with its execution code and current state to finish its works intelligently on behalf of the users. Whenever user requires information, it sends query to the base station and the base station dispatches a mobile agent to fulfil the requirement of users. As it migrates from one node to another node it saves its current state to the new host and resumes its state from the saved state. This process will save the bandwidth of wireless networks and improve the efficiency of network. Figure 2 shows the functional component of the mobile agent system, the agent manager has concern about sending and receiving mobile agents back and forth remote hosts so that the mobile agents may organize their work nearby. An agent manager is also responsible for agent creation; cloning, dispatching and destroying. The communication manager provides the facility to establish communication between two or more mobile agents. The reliability manager will also be a part of the relocation process when is necessary to prove that the agent manager has certainly received a mobile agent at the remote gatway. The directory manager is used to identify the position of an application server that the mobile agent can migrate to gatway . The security manager will to approve the process use of the gateway, and agent to the application server.

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.512|

|| Volume 9, Issue 9, September 2020 ||

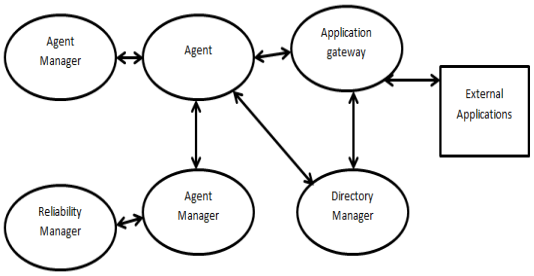


Fig.2. Mobile Agent System

Figure 3 shows mobile agent based WSN architecture .here three clusters of sensor nodes is given they have unlike sensor nodes, source node and destination node.

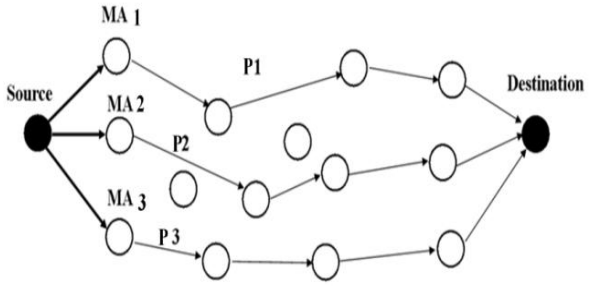


Fig.3. Congestion control routing by Mobile agent

The following steps are followed by mobile agent:-

i. The source node verified the number of available clusters and communication mobile agents in each cluster.
ii. Mobile Agents select the shortest path to move from one sensor to another sensor in order to collect information.
iii. MA1, MA2 and MA3 will check the routing table and move toward destination according to P1,P2 and P3 path respectively.
iv. Mobile Agents will also calculate Total Congestion Metric (TCM) of their respective paths on the basis of congestion status stored at destination node.
v. Destination node will send the total congestion metrics of path P1, P2 and P3 in the form of TCM1,TCM2 and TCM3.
vi. A source node will select a path having minimum congestion and transmit data to that route which has minimum congestion.

IV. MOBILE AGENT EMBEDDED IN WSN ENVIRONMENT

In our work , mobile agent technology will use in a cluster based wireless sensor network.These are the following steps:

Step 1: Node Deployment
Step 2: Clustering Algorithm in WSN
Step 3: Embedding Mobile agent in clustered WSN
Step 4: Define Itinerary planning of MA
Step 5: Defining a simulation environment
Step 6: Simulation and Performance evaluation

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.512|

|| Volume 9, Issue 9, September 2020 ||

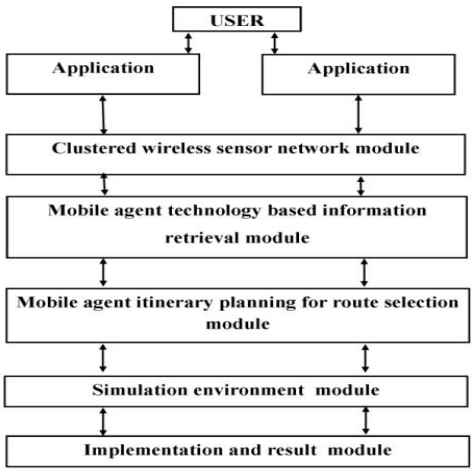


Fig.4. Mobile agent embedding in cluster based WSN

A. Clustering Algorithm for Wireless Sensor N/W

Clustering is a mechanism that divides the network into a number of groups. Each group assigned to the co-ordinator node called cluster head (CH).The coordinator node of the cluster is responsible for collecting, processing and transmitting of the detected data to the sink node. Other nodes in the cluster are member nodes, which sense and transmit detected data to the CH. Cluster head will selected using throushold value T (n) in Low Energy Adaptive Clustering Hierarchy (LEACH) [9].
revise the function of threshold value of T (n) using projected progressive approach to extend the probability of cluster head selection for other nodes. The revised function $T(n)$ is:

$$T(n) = \begin{cases} \dfrac{P}{1 - P(r \bmod (1/p)) - Pk} & n \in G \\ 0 & others \end{cases} \qquad (1)$$

P means the probability of cluster head selection, r means the number of rounds, k means the number of nodes that are not included in the cluster head selection.

It has become important to retrieve information efficiently and rapidly from distributed network. A mobile agent is software code capable of moving across the entire network. Mobile agents move into a network either on a predetermined path from sink node, or the agents itself determine the path dynamically. In A mobile agent-based wireless sensor network sink node sends a query to mobile agent for data collection in the target node, then mobile agent travel in the network, move to each cluster head one by one. In traditional client server model all data stored on server, clients can access data from server only. So one client cannot transmit data to another client directly without a server. This will create a significant problem if we increase client server model. But using mobile agent data are often shared between client machines. The mobile agent approach reduces the traffic load over the network as well as use low bandwidth.

B. Itinerary Planning by Mobile Agent for route selection in WSN

A mobile agent based applications for data gathering, it is very important steps to find out the route planning for mobile agent. An itinerary means information about routes which the agent will follow to urge information from the network with low resource usage. According to topology itineraries would be either static or dynamic and according to uses in network mobile agent is a single agent or multiple agents [10].Stationary itineraries calculated at the sink node before the MA is transmitted while in the dynamic itineraries mobile agent it defines the source nodes to be visited and the route of migration. In an approach [11] two SIP approaches, namely: Local Nearest First (LNF) and Global Nearest First (GNF) used. In LNF mobile agent visit the next node having the least distance from the current node and Global Nearest First (GNF), where mobile agent search for the next node having the smallest distance from the processing node.

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.512|

|| Volume 9, Issue 9, September 2020 ||

V. PERFORMANCE EVALUATION

There are various types of simulators which are used in a wireless sensor network, the simulator provides result analyses of our work. We simulate our work using NS-2. It is composition of two languages: Object-oriented Tool Command Language (OTcl) & C++ Library for the simulator. To setup and run a simulation, the source code is written in the article then the article - interpreter will interpret the program using C++ library. When the simulation is complete, the simulation results will store in the form of text-based on specified output files that contain detailed simulation data, which can be used to analyze directly in the term of X graph or can be visualized in graphical user interface using Network Animator (NAM) [12].

The proposed work is simulated using 2000*2000 m^2 areas, with 20 nodes and the base station are located at "550,140". The initial energy of each of the normal node is 100 J.

A. Simulation Environment

Step1: Random Node Deployment

Sensors are randomly deployed in a wireless sensor network. All sensor nodes have assigned with equal energy and the location of the base station is far from wireless sensor area. Next step shows that the network of sensor is divided into clusters using a clustering algorithm.

Fig.6. Random node deployment of sensor nodes.

Step 2: Revised LEACH clustering algorithm in WSN.

Here a modified LEACH clustering algorithm is applied to create different clusters in the network. This algorithm is location based algorithm and divides region, according to the X-axis.

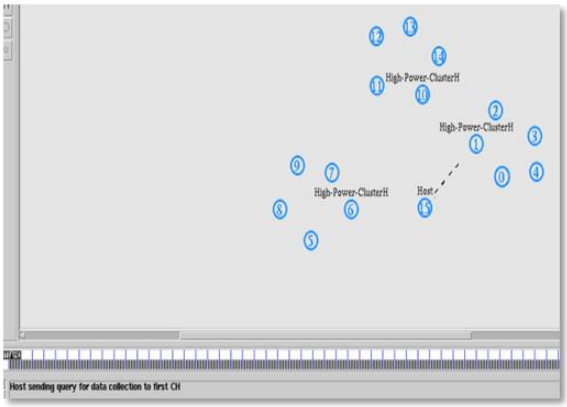


Fig. 7. Clustered WSN without MA

First of all base station (sink) will find total clusters in the network and then broadcast a TCM (Total Congestion Metric) message to each cluster head in order to find the congestion status.

Step 3: Embedding Mobile agent in a clustered WSN

Base Station will find congestion status and then dispatch mobile agent to that particular path which have less congestion. Mobile agent starts moving toward the cluster head (CH).

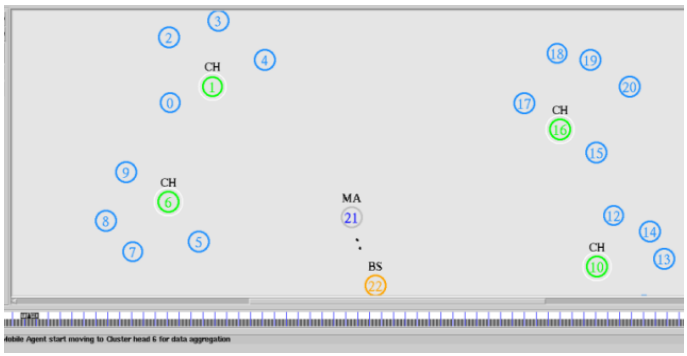


Fig.8.Embedding a mobile agent in WSN

Step 4: Migration of a mobile agent in clustered WSN

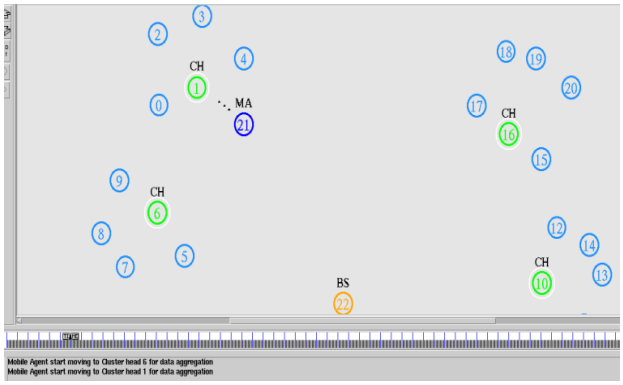


Fig.9.A mobile agent is moving to cluster head 1

A mobile agent uses two types of migrations weak and strong. In the weak migration mobile agent will move with its executable code and in strong it also execution state.before migration route for the mobile agent must be decided by base station .

VI. SIMULATION RESULTS

A mobile agent moves across the whole network and it can select the next node in routing table according their fewer loads which are near to present node to remove congestion control. By simulation of result shows to attain high throughput with reduced delay.

- ***Throughput/Bandwidth***

Mobile agent migrates according to the itinerary planning to each CH to collect data, refine it and return back to the sink node with efficient data. It defines the throughput on which the communication is performed. The throughput is defined in terms of a bit rate.This rate is also defined with delay parameters also. The throughput will vary over the communication over the network.

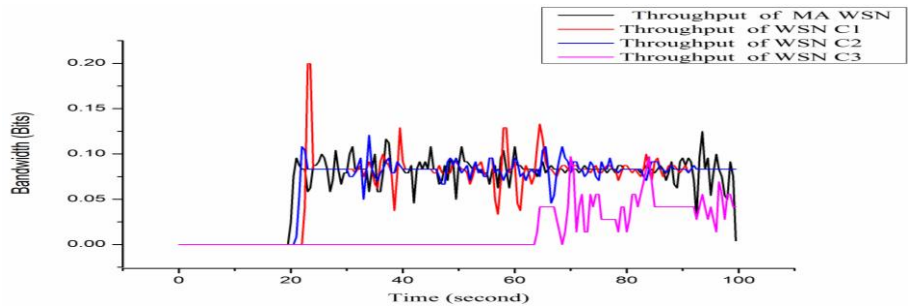


Fig.10. Compare Throughputs of network using mobile agent enabled WSN and Traditional WSN

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.512|

|| Volume 9, Issue 9, September 2020 ||

Figure 10 shows the throughput of Mobile Agent while it communicates with Sink node. In above graph x-axis denotes time and Y axis denote the number of packets over the network.The throughput of the network is being increased after using mobile agent technology and the redundant data is also removed by a mobile agent. So mobile agent increases the efficiency up to 30% of the network.

- ***Packet Loss***

The performance of a wireless sensor network can be calculated using packet loss rate. It defines how many numbers of data packets are lost during network communication. Here we can see that mobile agent technology reduce the possibility of packet lost in the communication of mobile agent and Base station. In figure 11 shows the packet loss between mobile agent and Sink node communication over the network. Graph shows x-axis represents time and y-axis represents the number of packet loss.

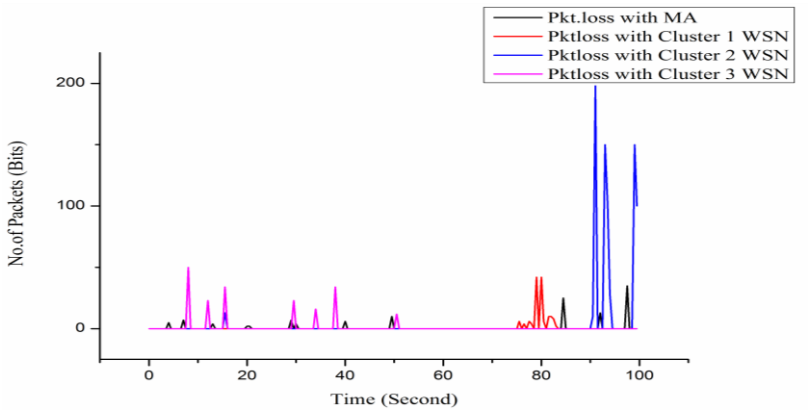


Fig.11. Compare Packet loss of network using mobile agent enabled WSN and Traditional WSN

- ***End to End Delay***

Delay rate will be different according to the topologies of the network. If the delay rate increases, it affects the overall performance of the network such as slow network communication, packet loss. Here the work is presented in sort of delay analysis over the network.

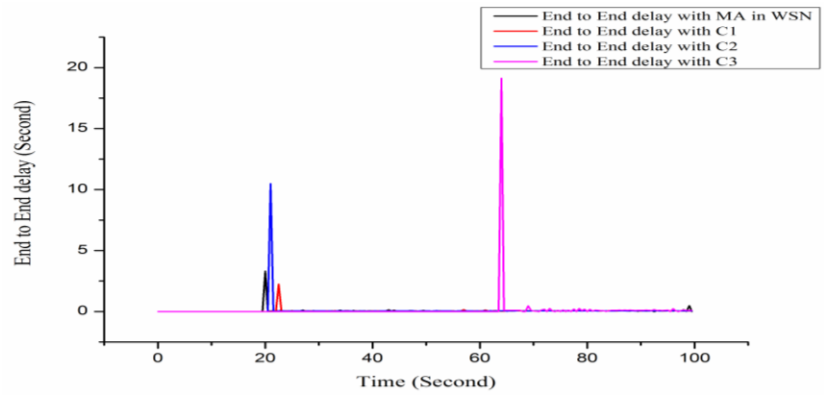


Fig.12. Compare end to end delay of network using mobile agent enabled WSN and Traditional WSN

VII. CONCLUSION

There are some problems in the traditional wireless sensor network such as bandwidth constraints, energy constraints, packet loss, data redundancy, lifetime of network, data security etc. MA technology improves the performance of WSN. Instead of collecting data from CHs, Host sent mobile agent in the network to collect data from each CHs. Mobile agent is a software code which has migrated within the network from node to node constant with to predefined static itinerary planning . Static itinerary planning decided by sink node,before transmitting data to sink node. It is pre-

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.512|

|| Volume 9, Issue 9, September 2020 ||

processed by Mobile Agent, it removed unnecessary or duplicate data and then transmits it to Host. A mobile agent deployed in such a way that the impact on the energy of the wireless sensor network minimized and it provides a high degree of flexibility, robustness, and load balancing. The performance of a mobile agent based wireless sensor network depend on various network parameters like network coverage, bandwidth, network security, energy utilization, as well as agent parameters like agent's code size and data size, execution environment etc.

The analysis of proposed work shows that A mobile Agent based Wireless Sensor Network improve network performance over without Mobile Agent Wireless Sensor Networks in the term of throughput, packet loss, end to end delay. Simulation result shows that Mobile Agent technology improves up to 30% bandwidth utilization, decreases the chance of packet loss and reduces end to end time delay and also helps in congestion control by increasing throughput of wireless sensor network.

REFERENCES

[1] Raheleh Hashemzehi, Reza Nourmandipour "Congestion in Wireless Sensor Networks and Mechanisms for Controlling Congestion" Indian Journal of Computer Science and Engineering (IJCSE) ISSN : 0976-5166 Vol. 4 No.3,Jun 2013

[2] Pang, Q., Wong, V.W.S. and Leung, V.C.M. "Reliable data transport and congestion control in wireless sensor networks", Int. J. Sensor Networks, Vol. 3, No. 1, pp.16–24, 2008.

[3] Justin Jones , and Mohammed Atiquzzaman "Transport Protocols for Wireless Sensor Networks:State-of-the-Art and Future Directions" International journal of distributed sensor network Vol. 3 issue 1, page(s): 119-133 Issue published: February 1, 2007

[4] Heikalabad S. R, Ghaffari A, Hadian M. A., Rasouli H. "DPCC: Dynamic Predictive Congestion Control in Wireless Sensor Networks" International Journal of Computer Science (IJCSI), page No.1694-0814, 2011

[5] Wei-wei Fang, Ji-ming Chen, Lei Shu, Tian-shu Chu, De-pei Qian. "Congestion avoidance, detection and alleviation in wireless sensor networks" Journal of University-Sciencevol, PP.No.63-73. 2009

[6] Cheng T.E., Bajcsy, R. "Congestion Control and Fairness for Many-to-One Routing in Sensor Networks." Proc. 2nd Int. Conf. On Embedded Networked Sensor Systems, p.148-161. 2004.

[7] Wan C -Y, Eisenman S B, Campbell A T, CODA: "Congestion detection and avoidance in sensor networks" In the Proceedings of the First International Conference on Embedded Networked Sensor Systems (SenSys'03), Los Angeles, CA, USA,pp. 266–279, 2003.

[8] A. Woo, D. Culler, "A Transmission Control Scheme for Media Access in Sensor Networks" Seventh Annual International Conference on Mobile Computing and Networking, pp. 221-235, July 2001.

[9] Kamal Deep, S Niranjan,Yashpal Singh "Effective Clustering Algorithm of Wireless sensor network through clustered Mobile agents" Journal of Computer Sciences and Applications, Vol. 3, No. 6,154-161, 2015

[10] Divya Lohani, Shirshu Varma, "Dynamic Mobile Agent Itinerary Planning for Collaborative Processing in Wireless Sensor Networks", IEEE INDICON , 2015.

[11] Huthiafa Q Qadori, Zuriati A Zulkarnain "Multi-mobile agent itinerary planning algorithms for data gathering in wireless sensor networks: A review paper", *International Journal of Distributed Sensor Networks* Vol. 13(2)(2017)

[12] "Network Animator",Available at ww.isi.edu/nsnam/nam/ accessed on 17 may 2020

INNO SPACE
SJIF Scientific Journal Impact Factor

Impact Factor:
7.512

ISSN INTERNATIONAL STANDARD SERIAL NUMBER INDIA

निस्केयर
NISCAIR

INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH

IN SCIENCE | ENGINEERING | TECHNOLOGY

9940 572 462 6381 907 438 ijirset@gmail.com

www.ijirset.com

Scan to save the contact details

International Journal of Advanced Technology in Engineering and Science
Vol. No. 10, Issue No. 11, November 2022
www.ijates.com
ijates
ISSN 2348 - 7550

Wastewater Treatment by using Bio-Enzymes Extracted from Fruits and Vegetables Waste

Anshal Kumar[1], Himanshu Kumar Sadhya[2]

ABSTRACT

There is urgent need to reclaim the water which gets polluted due to overexploitation and negligence of the human kind to check the water scarcity problem. Many efforts have been made to recycle that water by the help of technologies based on physical, chemical and biological processes. Out of these technologies, Bio-enzyme is the cost effective, eco-friendly and environmentally sustainable option. For the treatment of a sample of domestic wastewater in this investigation, bio-enzyme produced through the fermentation of vegetable and fruit waste was employed. The wastewater samples were mixed with a 5, 10, and 15% bio-enzyme solution and digested for 5, 15, and 25 days. The results demonstrated that bio-enzyme may significantly reduce the TDS, BOD5, and COD characteristics of wastewater, while 100% removal of ammoniacal nitrogen and phosphate was shown at low concentrations of bio-enzyme solution. The pH showed no significant fluctuation and it remains acidic. Low pH of the wastewater sample bio-enzyme makes it suitable for reducing salinity of the soil caused due to excessive use of fertilizers and pesticides. Bio-Enzyme extracted from fruit and vegetable waste gave almost similar results; No large variation was observed. With the help of bio-enzymes, wastewater may be improved and made suitable for a variety of uses. Additionally, using bio-enzymes can aid in reducing greenhouse gas emissions and the disposal of chemicals used in wastewater treatment operations, making it environmentally sustainable. Also reduces the burden on landfill sites by utilizing the waste as resource.

Keywords— Bio-Enzyme; Environmental Sustainability; Fruit Waste; Vegetable Waste; Waste Enzyme; Wastewater Treatment; Water Pollution

I. INTRODUCTION

Water is one of the most vital natural resources for all life on Earth. Most of the evolution theories state that life started with water. The availability and quality of water always have played an important part in determining not only where people can live, but also their quality of life [1]. As we know that about 60% of our body is water and in some organisms, it's as high as 90%. Nearly 97% of the world's water is salty or otherwise undrinkable [2]. Due to the increase in world population, rapid industrialization and ongoing development activities wastewater generation rate become many fold. The problem of management and disposal of the wastewater so generated has become serious threat [3]. Nearly 70-80% of water bodies are carrying polluted water. Large amount of domestic sewage is drained in to river and most of the sewage is untreated. Domestic sewage contains toxicants, solid waste, plastic litters and bacterial contaminants and these toxic materials causes water pollution. About

25% pollution of water is caused by the industries and is more harmful [4]. Hazardous material discharged from the industries is responsible for surface water and ground water contamination. Contaminant depends upon the nature of industries. Toxic metals enter in to water and reduced the quality of water [5]. Different industrial effluent that is drained in to river without treatment is the major cause of water pollution [6]. Municipal waste water generate from different sources, the major source is domestic i.e. waste water originated from residential sources (50-90%) while commercial waste water (5-30%) and industrial waste water (5-20%) are secondary sources. The removal of biological organic pollutants and nutrients is the main priority in domestic waste water treatment [7]. The strength and composition of the domestic wastewater changes on hourly, daily and seasonal basis, with the average strength dependent on per capita water usage, habits, diet, living standard and life style. The main reason is variation in water usage in households. Households in developed countries use more water than those in developing countries [8]. In present study, emphasis is given to domestic wastewater as it contains contain only 0.1% of solid material so there are wide scope to reuse this water for various purpose by giving some degree of treatment [9]. The main purpose for treatment of wastewater is to counterfeit the precious drinking water in applications which do not require the drinking water quality. It is used for various non-portable reuse application include industrial, irrigation, toilet flushing and laundry washing dependent on the degree of treatment of water [10]. By recycling the grey water, it is possible to reduce the amount of fresh water consumption as well as reduction in waste water generation, in addition to reducing the water bill. Use of grey water increases the supply for irrigation, which will lead to increase in agricultural productivity [11]. Various treatment and purification technologies have been developed to reclaim the usefulness of wastewater. Many researchers are working to find new techniques for reclamation of water focusing on biological or physical wastewater treatment methods rather than chemical ones [12]. The use of waste/garbage/bio-enzymes is investigated by researchers as an alternative solution for treatment of waste water. Bio-Enzyme used for treatment of waste water is a very eco-friendly and sustainable way of waste water treatment because organic wastes are used in the making of garbage/waste enzyme which catalyze the rate of chemical reaction in waste water [13].

Enzymes are basically protein molecules that catalyses the chemical reaction. They act as biological catalysts and catalyses only specific molecules (substrates). Enzymes are selective for their substrates and catalyses only one or a small number of chemical reactions among many possibilities. However they are physiologically important because they speed up, by at least 1000-fold, the rates of reactions by decreasing the amount of energy required to form a complex of reactant, known as the transition state complex, that is competent to produce reaction product [14]. Enzymes produced under anaerobic conditions from fermentation of organic waste material such as fruit/ vegetable waste along with brown sugar and water in a fixed proportion are called as Bio-Enzymes or Waste Enzyme or Garbage Enzymes [15]. These are the biocatalysts produced by living cell to lead specific biochemical reaction by forming the various metabolic processes of the cell and essential to maintain the activity of life. Enzymes are effective in their action on substrates and usually many different enzymes are required to create chain of metabolic reaction performed by a living cell. Each strain of a microorganism produces a large number of enzymes which can be hydrolyzing, oxidizing or reducing and metabolic in nature. Microbial enzymes are noted to play essential role as metabolic catalysts, resulting in their

use in various industrial applications [16]. In order to improve the properties of enzyme i.e. stability, substrate specificity and specific activity, it can be selected on the basis of genetic, and chemically-modified [17]. Garbage/Waste enzyme is different from fruit enzyme and is not for human consumption. It is a nutritious drink prepared through proper fermentation of fruits/vegetable wastes [18]. It is dark brown and has a strong sweet sour fermented scent. It is a complex organic substance of protein chains and mineral salts and juvenile hormones. The functions of bio-enzyme is to resolve (decompose), transform (change), and catalyze the reactions [7].

It is claimed as a multi-use solution for domestic and agricultural applications [19]. Due to low PH and high acetic acid concentration bio enzymes are used for many purposes. It contains traces of ethanol and propionic acid, ethanol has antiseptic properties and propionic acid is used for food preservation. Bio enzyme is used as a natural household cleaner, car care, air purifier, deodorizer, insecticide, detergent, body care, organic fertilizer, etc. It removes odour and dissolve toxic air released from smoking, car exhaust, chemical resides from household products, etc. It is natural antiseptic for your home and it also prevents drainpipe blockages [18].

Bio-Enzyme can be used as an anti-microbial agent, insecticide and pesticide. When diluted, it could provide nutrients to plants in the form of growth hormones, minerals, enzymes and/or other organic compounds extracted directly or converted from the waste materials. Rather than to be disposed and incinerated, these waste materials can further serve additional purposes through garbage enzyme, and subsequently be composted into organic fertilizer. This will surely help in preventing or reducing all forms of pollutions from the improper solid waste management and incineration, as well as to "close the waste loop" and promote recycling of waste back into the earth [18]. For the treatment of domestic wastewater with advanced level of degradation in a shorter span of time, bio-enzyme performs the same task as done by enzymes. In Malaysia, many researchers have performed investigation to check the bio-enzyme as viable solution for wastewater treatment [7]. In India, bio-enzyme is not much known and practiced at very low level [17]. Usage of bio-enzyme not only provides an alternative solution to biological recovery from organic waste it will also help in minimization and reduction of waste; since municipal solid waste mainly consists of organic waste. It also puts a check on greenhouse emissions; lessen the burden on landfills [20].

This paper presents the results from digestion of domestic wastewater using bio-enzymes produced from flower waste at three different concentrations i.e. 5%, 10% and 15% after 5, 10 and 25 days of digestion period. An attempt has been made to understand the effectiveness of bio-enzymes produced from organic waste material in treating domestic wastewater.

II. METHODOLOGY

Based on the objectives of this study the methodology adopted for the present investigation is presented below:

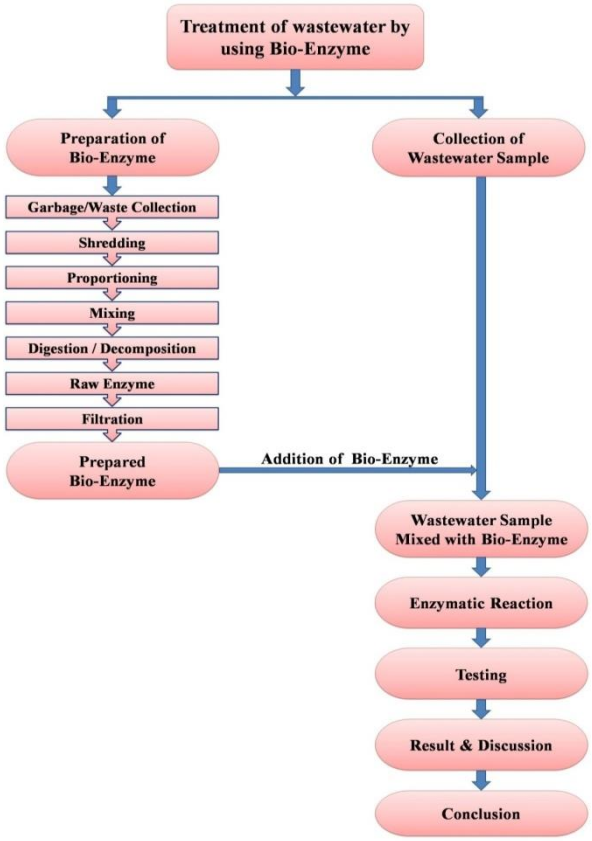


Fig. 1: Flow diagram of the work plan

A. Bio-Enzyme Preparation

Fruits and vegetables waste are collected from kitchens, vegetables shops, fruit & vegetable markets and fresh juice corners. After the collection of raw garbage separation is done on the basis of their chemical properties (citrus/garbage) and then shredding is done to reduce the size of garbage or fruits and vegetables waste into small size so that it can be decomposed easily After shredding the waste in to small pieces all the materials i.e. Jaggery, fruit/vegetable/flower waste and water were taken in proportion of 1: 3: 10 to mix them together for preparing bio-enzymes. All ingredients were mixed in a plastic container that has screw bottle caps to release the gases produced during the process. So, plastic container is the best option; with bottles having screw caps it is easier to manage the release of gases; don't screw the bottle too tight it could explode because of the gases formed inside and kept it at a dark place for digestion.

Then the lid of container was open to release the gases once in a day repeat this procedure to release the gases for first one month. In the second month the lid was opened once in a week and again kept in the dark. After the fermentation of three months the solutions which we get in raw form with undigested material and pulp. It was needed to separate out undigested or solid matter from liquid portion using filtration to enhance the properties of bio-enzyme and was stored in air tight container. To know the maturity of enzymatic solution, the different parameters were checked after filtration at 0, 30 and 60 days. [21].

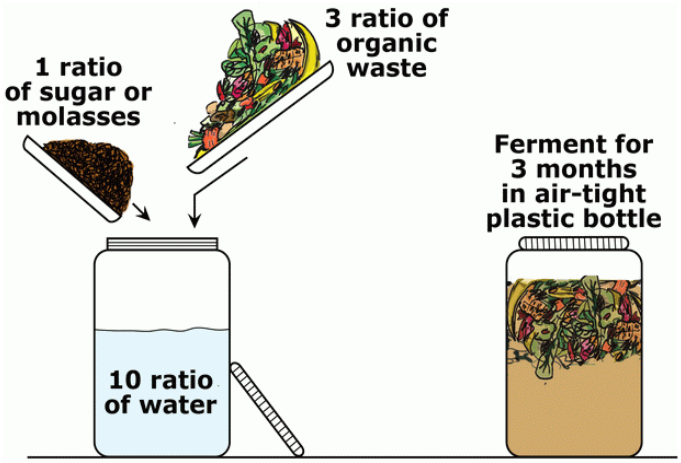


Fig. 2: Bio-Enzyme Production

B. Wastewater Treatment

Sample for testing should be collected from sewage treatment plant or drains which carry waste water from kitchens, washrooms, food producing and other industries. Bio-enzymes were added to the wastewater in different proportion i.e. 5%, 10%, and 15% [17]. Each three beakers having wastewater sample mixed same concentration of bio-enzyme was prepared for 5, 10, 15 days digestion.

III. Results & Discussion

To determine the effective dosage of bio-enzymes extracted from fruits and vegetables waste, to treat domestic wastewater sample various test were performed. In this study, parameters like pH, TDS, BOD_5, COD, Ammonia Nitrogen and Phosphate were analyzed as per procedures discussed in standard methods [22]. To understand the effect of bio-enzymes for treatment of waste water, characteristics of enzymes produced from vegetable waste and fruit waste are also determined. For treatment of the wastewater, 5%, 10% and 15%, of each enzyme solution was mixed. The variations in characteristics of the wastewater sample after 5, 15 and 25 days of digestion were observed and analyzed.

A. Characteristics of Bio-Enzymes

The characteristics of vegetable waste enzyme and fruit waste enzyme solutions were analyzed immediately after filtration, 30 days after filtration and 60 days after filtration. The parameters like pH, TDS, BOD_5, COD, Ammonia Nitrogen and Phosphate were observed. The characteristics of vegetable waste enzyme, fruit waste enzyme and flower waste enzyme solutions immediately after filtration of the enzyme solution, 30 days after filtration and 60 days after filtration are shown in Table 1 and 2. The pH of both enzyme solutions shows acidic character. The BOD_5 and COD values were high when the enzyme solution was analyzed immediately after filtration of the enzyme solution. But after 60 days of filtration BOD5 reduced to half and COD was reduced to 99% of its initial value. The enzyme solutions obtained from vegetable, fruit and flower were rich in organic content.

TABLE 1: Characteristics of Vegetable Waste Enzyme

Parameter	Just after filtration	30 Days of filtration	60 days of filtration
pH	3.01	3.5	4.18
TDS (mg/L)	2230	1505	1130
BOD_5(mg/L)	1311	570	94
COD (mg/L)	47900	2230	161
Ammonical Nitrogen (mg/L)	0	0	0
Phosphate (mg/L)	0	0	0

TABLE 2: Characteristics of Fruit Waste Enzyme

Parameter	Just after filtration	30 Days of filtration	60 days of filtration
pH	3.14	3.53	4.1
TDS (mg/L)	1963	1250	941
BOD_5(mg/L)	1270	553	90.1
COD (mg/L)	42310	2328	149
Ammonical Nitrogen (mg/L)	0	0	0
Phosphate (mg/L)	0	0	0

B. Characteristics of Domestic Wastewater (Raw) Sample

Before treating the wastewater sample with bio-enzyme, it is important to know the characteristics of the raw wastewater sample before treatment. The wastewater characteristics like pH, TDS, BOD5, COD, Ammonia nitrogen and Phosphates were determined and tabulated in Table 3.

TABLE 3: Raw Wastewater Characteristics

Parameter	Units	Value
PH	--	6.16

TDS (mg/L)	mg/L	563
BOD5(mg/L)	mg/L	192
COD(mg/L)	mg/L	290
Ammonical Nitrogen (mg/L)	mg/L	9.6
Phosphate (mg/L)	mg/L	110

C. Characteristics of Treated Wastewater Sample

5%, 10% and 15% solution of bio-enzymes extracted from fruits and vegetables waste, was used for the treatment of domestic wastewater. The treated wastewater sample characteristics like pH, TDS, BOD5 COD, Ammonia nitrogen and Phosphates were analyzed after 5, 15 and 25 days of digestion.

➢ *pH*

The corresponding variations observed in pH value of the effluent after 5, 15 & 25 days of digestion are shown in the figure 3.

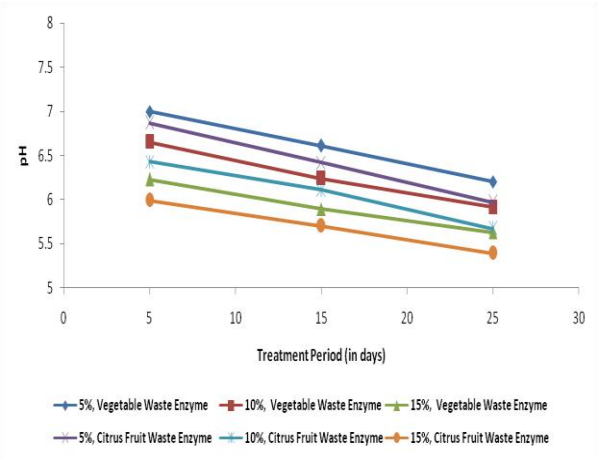


Fig. 3: Variation in pH characteristic of the treated wastewater sample

The filtered bio-enzyme obtained from garbage enzyme and citrus enzyme was found acidic in nature as indicated by low its pH value (Table 4.1 and 4.2). When it get mixed with domestic wastewater, the pH of wastewater sample having 5% bio-enzyme for digestion of 5 days, increased to nearly neutral range due to enzymatic reactions but slowly get reduced at constant rate with increase in digestion period as indicated in figure 4.1. Similar variation is also noted for wastewater samples having 10% and 15% bio-enzyme mixed..

➢ *TDS*

After treatment with bio-enzyme the variations was observed in TDS content of the effluent and the corresponding variation in the characteristic of treated wastewater sample after 5, 15 & 25 days of digestion are shown in figure 4.2. TDS characteristic of wastewater sample mixed with 5% bio-enzyme for digestion of 5 days, 15 days and 25 days was noted with decrement at constant rate; When compared with initial TDS of raw

wastewater sample (see Table 4.2), more than 50% TDS got removed after 25 days of digestion due to enzymatic reactions. Similar, variation is also noted for wastewater samples having 10% and 15% bio-enzyme mixed.

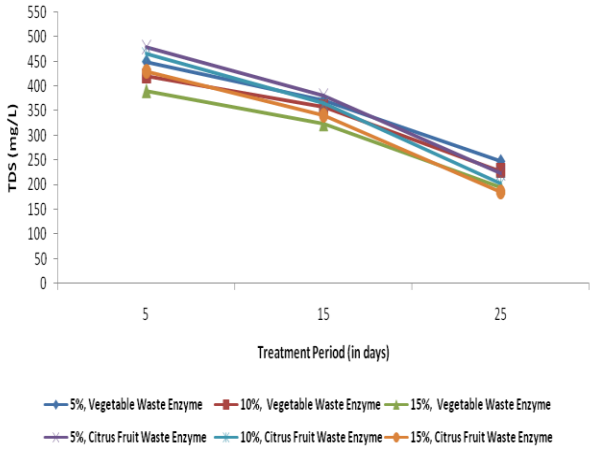


Fig.4: Variation in TDS characteristic of the treated wastewater sample

➢ *BOD_5*

The BOD_5 characteristic of treated wastewater sample after 5, 15 & 25 days of digestion with all three concentrations (i.e. 5%, 10% and 15%) of bio-enzyme solution, a constant rate of reduction in BOD_5 was observed for digestion of 5 days, 15 days and 25 days (see figure 5). For first 5 days of digestion period reduction was more than 50% but for next 10 and 20 days this rate got reduced to less than 10%.

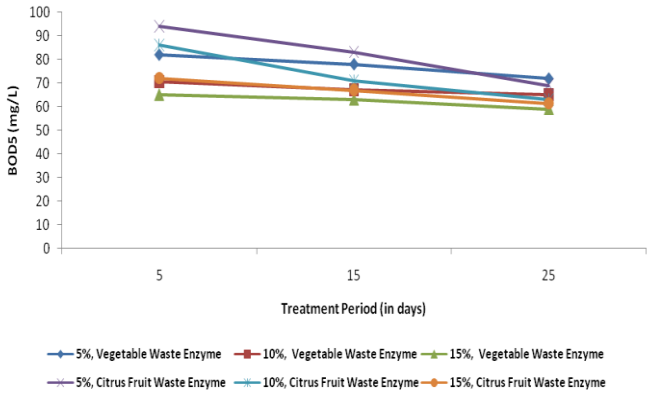


Fig. 5: Variation in BOD_5 characteristic of the treated wastewater sample

➢ *COD*

A decrease of about 20% can be observed in COD characteristic of wastewater sample (see Figure 5) mixed with 5% of bio-enzyme for 5, 15 and 25 days of digestion. When 10% and 15% bio-enzyme solution was mixed with wastewater a very good removal rate was noted.

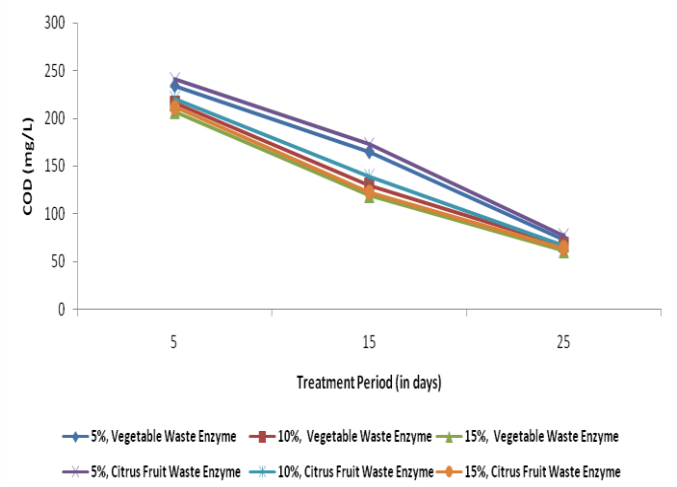


Fig. 6: Variation in COD characteristic of the treated wastewater sample

➢ *Ammonical Nitrogen*

A sharp reduction in the ammonical nitrogen characteristic of the treated wastewater sample after 5, 15 & 25 days of digestion with bio-enzyme was observed (see figure 7). More than 70% of the ammonical nitrogen was removed with 5% bio-enzyme for digestion of first 5 days. While 100% removal rate was observed for wastewater sample mixed with 10% and 15% bio-enzyme solution for first 5 days of digestion.

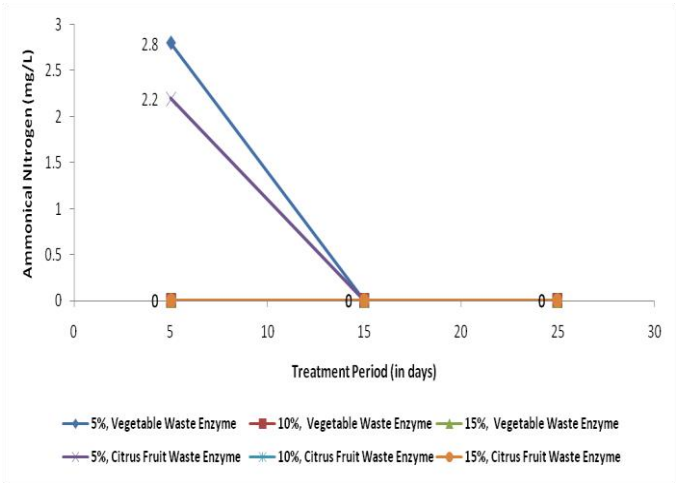


Fig. 7: Variation in ammonical nitrogen characteristic of the treated wastewater sample

➢ *Phosphate*

When compared with ammonical nitrogen a similar trend was observed in the phosphate characteristic of the treated wastewater sample after 5, 15 & 25 days of digestion with bio-enzyme. The variations in phosphate characteristic of the treated wastewater sample after 5, 15 & 25 days of digestion with bio-enzyme are shown in figure 8.

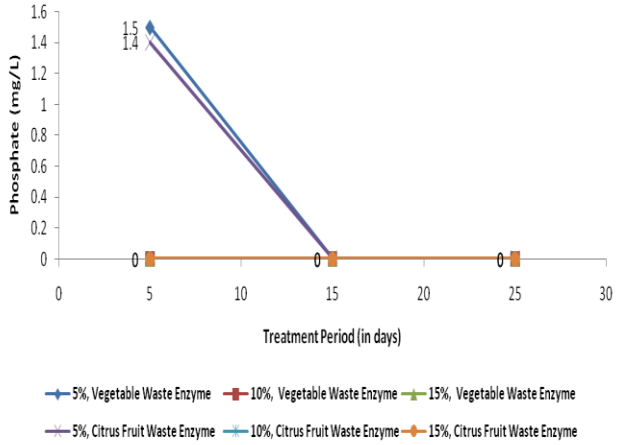


Fig. 8: Variation in phosphate characteristic of the treated wastewater sample

In case of phosphate characteristic, more than 95% removal was observed for wastewater sample mixed with 5% bio-enzyme solution for digestion of first 5 days. While 100% removal was observed for wastewater sample mixed with 10% and 15% bio-enzyme solution for the first 5 days of digestion.

IV. CONCLUSION

Bio-Enzymes are organic compounds extracted from fresh vegetable/fruit waste in presence of water and brown sugar/jaggery. Bio-Enzymes are powerful waste digesting enzymes, essential nutrients and breaks down the complex organic material into water-soluble nutrients. Bio-enzymes can be used for improving the efficacy and odor control in all facilities which generate organic contaminated wastewater treatment facilities. In this investigation, the treatment of wastewater using bio-enzymes has been examined along with the characteristics of bio-enzymes exteracted from different raw materials.

Due to the presensce of high organic content the bio-enzyme extracted from fruit/ vegetable waste exhibited high initial BOD. Acidic charcter exhibited by bio-enzymes helps in lowering the pH of the wastewater sample; makes the treated wastewater suitable for utilized as soil salinity reduction option. The results it can also be inferred that ammonical nitrogen, phosphate, TDS, BOD5 and COD characteristics of domestic wastewater can be removed effectively by using 10% bio-enzyme solution. The results obtained for the effluent showed similar trend when wastewater sample was treated with both type of enzyme solution i.e. fruit waste enzyme and vegetable waste enzyme. Because it is made from waste, bio-enzyme is inexpensive and cost-effective.Additionally, by making use of waste as resources, it helps to lessen the impact on the planet.As a result, Bio-Enzyme can be utilized as a cost-effective option to improve the characteristics of wastewater to make it suitable for further use.

ABBREVIATIONS

Acronyms	Full form
TDS	Total Dissolve Solid
BOD	Bio-chemical Oxygen Demand
COD	Chemical Oxygen Demand

REFERENCES

[1] H. A. Solley, W. B., Pierce, R. R., and Perlman, "The Water-Use Cycle," *water encyclopedia*, 1995. http://ga.water.usgs.gov/edu/wateruse.html.

[2] Toppr.com, "Water and its Importance," 2020. https://www.toppr.com/guides/evs/every-drop-counts/water-importance/ (accessed Feb. 21, 2020).

[3] M. Haseena, M. F. Malik, A. Javed, S. Arshad, and N. Asif, "Water pollution and human health .," *alliedacademies*, vol. 1, no. 3, pp. 16–19, 2017.

[4] P. Poonam and S. Ankita, "Effects of Water Pollution on Human Health: a Review," *Int. J. Adv. resarch Sci. Eng.*, vol. 7, no. 03, p. 504, 2018, doi: 10.20959/wjpps20181-10816.

[5] -Galvan, F. R., V. Barranco, J. C. Galvan, S. Batlle, Sebastian FeliuFajardo, and García, "We are IntechOpen , the world ' s leading publisher of Open Access books Built by scientists , for scientists TOP 1 %," *Intech open*, vol. i, no. tourism, p. 13, 2016, doi: http://dx.doi.org/10.5772/57353.

[6] S. M. Kamble, "Water Pollution and Public Health Issues in Kolhapur City in Maharashtra," *Int. J. Sci. Res. Publ.*, vol. 4, no. 1, pp. 1–6, 2014.

[7] F. E. Tang and C. W. Tong, "A Study of the Garbage Enzyme ' s Effects in Domestic Wastewater," *Int. J. Environ. Ecol. Eng.*, vol. 5, no. 12, pp. 887–892, 2011, [Online]. Available: https://zenodo.org/record/1332982#.Xr0S2G5Fz4g.

[8] Samwel, "Domestic wastewater sources and its characteristics," *TUHH interactive Web Server*, 2017. .

[9] Dr. Yavuz Özoguz (m-haditec GmbH & Co kG), "Efficient Management of Wastewater. Its Treatment and Reuse," 2008, p. 51.

[10] S. Manna, "Treatment of Gray Water for Reusing in Non-potable Purpose to Conserve Water in India," *Int. J. Appl. Environ. Sci.*, vol. 13, no. 8, pp. 703–716, 2018, [Online]. Available: http://www.ripublication.com.

[11] O. A. Al-Mashaqbeh, A. M. Ghrair, and S. B. Megdal, "Grey water reuse for agricultural purposes in the Jordan valley: Household survey results in Deir Alla," *Water (Switzerland)*, vol. 4, no. 3, pp. 580–596, 2012, doi: 10.3390/w4030580.

[12] N. J. A., "Environmental applications of enzymes Jim A. Nicell, Ph.D., P.Eng. Department of Civil Engineering and Applied Mechanics, mcgill University, 817 Sherbrooke Street West, Montreal, Quebec, Canada, H3A 2K6."

[13] K. Pandey, B. Singh, A. K. Pandey, and I. J. Badruddin, "Application of Microbial Enzymes in Industrial Waste Water Treatment," *Int. J. Curr. Microbiol. Appl. Sci.*, vol. 6, no. 8, pp. 1243–1254, 2017, [Online]. Available: https://doi.org/10.20546/ijcmas.2017.608.151.

[14] V. L. Schramm, "Enzymatic Transition States and Drug Design," *Chem. Rev.*, vol. 118, no. 22, pp. 11194–11258, 2018, doi: 10.1021/acs.chemrev.8b00369.

[15] K. Neupane and R. Khadka, "Production of Garbage Enzyme from Different Fruit and Vegetable Wastes and Evaluation of its Enzymatic and Antimicrobial Efficacy," *Tribhuvan Univ. J. Microbiol.*, vol. 6, no. 1, pp. 113–118, 2019, doi: 10.3126/tujm.v6i0.26594.

[16] J. L. Adrio and A. L. Demain, "Microbial Cells and Enzymes A Century of Progress," *resarch gate*, vol. 1, no. May, pp. 1–27, 2005, doi: 10.1385/1-59259-846-3:001.

[17] F. Nazim and V. Meera, "Treatment of Synthetic Greywater Using 5 % and 10 % Garbage Enzyme Solution," *Bonfring Int. J. Ind. Eng. Manag. Sci.*, vol. 3, no. 4, pp. 111–117, 2013, [Online]. Available: www.enzymesos.com/wp-content/uploads/2014/12/BIJ-47331.pdf%0D.

[18] F. Nazim and V. Meera, "Comparison of Treatment of Greywater Using," *Bonfring Int. J. Ind. Eng. Manag. Sci.*, vol. 6, no. 4, pp. 49–54, 2017.

[19] B. Penmatsa, D. C. Sekhar, B. S. Diwakar, and T. V Nagalakshmi, "Effect of Bio-Enzyme in the Treatment of Fresh Water Bodies," *Int. J. Recent Technol. Eng.*, vol. 8, no. June-1S3, p. 4, 2019.

[20] P. Rajasulochana and V. Preethy, "Comparison on efficiency of various techniques in treatment of waste and sewage water – A comprehensive review," *Resour. Technol.*, vol. 2, no. 4, pp. 175–184, 2016, doi: 10.1016/j.reffit.2016.09.004.

[21] B. Prakash, "How effective are Garbage Enzymes?," *Eco Walk the Talk, Asia's Global Green Community*, no. March, Mar. 2011.

[22] Apha, "APhA Committees for 1971 – 1972," *J. pf Am. Pharm. Assoc.*, vol. 11, no. 12, p. 669, 1971.

RESEARCH REVIEW JOURNALS
Volume-04
Issue-03
March-2019

ISSN: 2455-3085 (Online)
RESEARCH REVIEW International Journal of Multidisciplinary
www.rrjournals.com[UGC Listed Journal]

Context and Dictionary based Hybrid Encoding Method for Optimizing WIMAX Communication

[1]Mangal Sain, [2]Dr.Gulzar Ahmed & [3]Dr.Pawan Kumar

[1]Research Scholar, Mewar University, Chittorgarh, Raj (India)
[2]Associate Professor, Mewar University, Chittorgarh, Rajasthan (India)
[3]Principal, Ganga Technical Campus, Bahadurgarh (India)

ARTICLE DETAILS

Article History
Published Online: 13 March 2019

Keywords
WIMAX , WIMAX Layered Protocol Architecture , Dictionary Making Algorithm , Context-Based Coding Techniques, Dictionary-Based Coding Techniques, Research Challenges, Time Taken For Encryption-Decryption Process.

ABSTRACT

WIMAX is worldwide interoperability for microwave access technology used for long distance wireless communication with higher data rates. It can be used as an alternative broadband. There is significant interest worldwide in the development of technologies for broadband wireless access systems. In this paper the performance of reliable packet marking in such network. Here proposing the probabilistic packet marking algorithm with the adding of four other approaches are used. First one is to decide the transmission path, Random packet marking approach. Second one for identification of visited route approach to trace back the path. Third one verification of transmitted data approach of combination of Context based and Dictionary based encoding techniques and fourth onechecksum will be applied to vary the alteration of data. The result will be more reliable transmission on WIMAX using the proposed system.

1. Introduction

WIMAX (Worldwide Interoperability for Microwave Access) is one of the most developing advances for Broadband Wireless Access (BWA) in metropolitan territories by giving an energizing expansion to the current broadband systems for the last-mile get to. It is exhibited that WIMAX is a suitable option in contrast to the link modem and DSL advancements because of its high asset usage, simple execution and minimal effort. Moreover, WIMAX not just improves the current highlights of the focused cabled access systems, yet furnishes high information rate applications with an assortment of Quality of Service (QoS) requirements. We are arriving at the objective of understanding an extraordinary remote system to cover a major territory. In an enormous scale remote system, the radio asset must be shared among numerous clients.

The data transmission allotment calculations have been intended for the productive use of the rare radio asset. What's more, to help sight and sound deals, the Medium Access Control (MAC) conventions will co-ordinate the transmission of traffic streams. The channel qualities of clients and traffic stream necessities are to a great extent different, inspiring us to plan a productive MAC layer conventions that can improve the framework execution due to the channel and traffic elements.

WIMAX operates on both licensed and non-licensed frequencies, providing a regulated environment and viable economic model for wireless carriers. The average cell ranges for most WIMAX networks will likely boast 4-5 mile range (in NLOS capable frequencies) even through tree cover and building walls. Service ranges up to 10 miles (16 Kilometers) are very likely in line of sight (LOS) applications (once again depending upon frequency). Mobile WIMAX capabilities on a per customer basis are much better than competing 3G technologies. WIMAX is often cited to possess a spectral efficiency of 5 bps/Hz, which is very good in comparison to other broadband wireless technologies, especially 3G.

The rapid development of Internet and wireless communication with high speed connection become a boon for the world. Today in the world of high speed communication and fast data transmission, wireless technology becoming a boon for everyone. Many companies are focusing on developing wireless access systems on the basis of various variables, like bandwidth, distance and power and broadly classified Wireless Technologies as “Wireless Personal Area Network (WPAN)”, “Wireless Local Area Network (WLAN)” and “Wireless Metropolitan Area Network (WMAN)”, “Wireless Broadband Access (WBA)” but they mostly lacking the common protocol platform. WIMAX is developed to change the situation and provide Interoperability to broadband wireless products. In recent time, Worldwide Interoperability for Microwave Access (WIMAX) become hottest broadband wireless technologies which is based on a “Broadband Wireless Access Metropolitan Area Network (BWA-MAN)”.It allows one to many point broadband wireless access. WIMAX is not a standard, rather it is trademarked by the WIMAX Forum which certify the interoperability of WIMAX components. 802.16's predecessors were not very accommodative of the European standards. WIMAX technology uses OFDM (Orthogonal Frequency Division Multiplex), MIMO (Multiple Input Multiple Output), adaptive modulation for providing the high speed data rates.

A framework for the context based encoding of an info sign incorporates a space change module and a context based coding module. The area change module is operable to change over the info signal into a succession of change coefficients c[i]. The context based coding module incorporates somewhat plane filtering module, and context demonstrating module, and a measurable encoding module. The bit-plane checking module is operable to create somewhat plane image bps [i,bp] for each change coefficient c[i] and each piece plane [bp]. The context demonstrating module is operable to appoint at least one context esteems to every one of the got bit plane images bps [i,bp]. The factual coding module is operable to code every one of the bit plane images bps [i,bp] as a component of at

least one of the comparing context esteems to deliver a context based encoded image stream

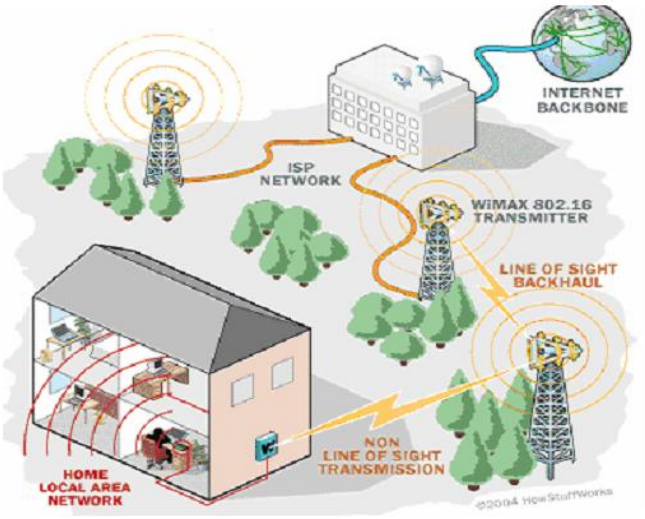


Figure1 OVERVIEW OF WIMAX TECHNOLOGY

2. WIMAX Layered Protocol Architecture

WIMAX network has primarily two topologies named as Point to Multi Point Base station for Subscriber station and Point to Point for backhaul. In this benchmark, multiple input multiple output antennas are utilized. IEEE 802.16 is Broadband wireless MAN protocol standard is mentioned below. WIMAX also provides numerous end user based applications and interfaces for examples ATM, IP, Ethernet, TDM, and VLAN.

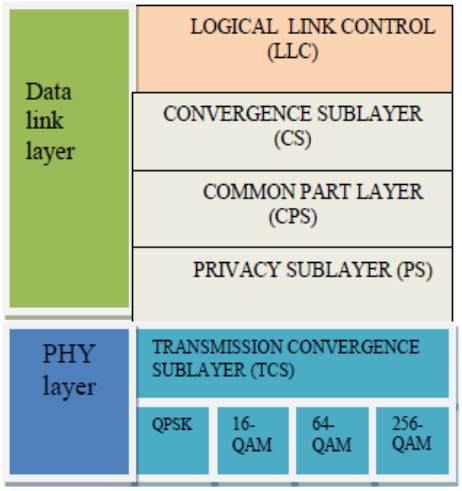


Figure 2 IEEE 802.16 Protocol layered architecture

To identify WIMAX protection troubles, we initial need to perceive WIMAX design and various characteristics of every components. In this section the background and various concerns regarding security and authorize exchange of data within the WIMAX network was discussed. IEEE 802.16 protocol architecture was designed as two layered architecture as:

1. Medium Access control (MAC) layer.
2. Physical (PHY) layer.

Logic link control is the communication protocol of OSI data link responsible for multiplexing and de-multiplexing protocols transmitted over MAC .PHY layer responsible for providing an electrical, mechanical, data transmission and reception. . It supports different digital modulation techniques like PSK, FSK, 16-QAM and 64-QAM". MAC sublayer is the responsible of determining which subscriber stations (SSs) have access to the network and is further divided in three more sublayers:

(1) Convergence Sublayer (CS): This layer maps data units of higher capacity into service units It allocate bandwidth and perform compress header part of data units. CS has two different services. ATM convergence sub layer and packet convergence sub layer. It suppresses the redundancy of headers at the sender side and restores those redundant headers at the receiver side.

(2) Common Part Sub-layer (CPS): This layer is personally integrated with the privacy sub-layer and responsible for establishing and maintaining the PMP (Point-to-multipoint) connection

(3) Privacy Sub-layer between the Common part sublayer of MAC and the PHY layer, dealing with the authentication, key swapping and cryptographic processing. It provides encryption and secure exchange of private key from the BS to SS.

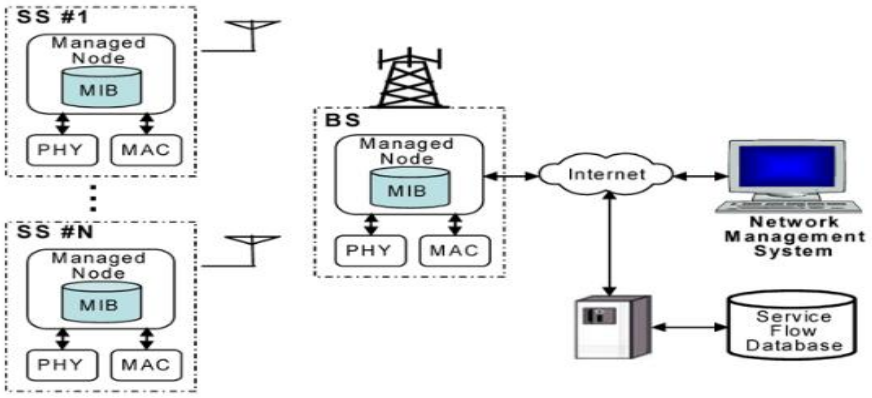


Figure 3 WIMAX Architecture

3. Dictionary Making Algorithm

Multiple sources files given as input to form a Dictionary.

1. Fetch the words from input files.
2. If a number is already present then increase this number by one else add this number and to the table and set the its occurrence to 1.
3. Arrange the table in descending order.
4. Assign the ASCII characters 33 to 250 to first 218 word of the table and then the remaining words.
5. Prepare a new table with words and code contained in it and store in dictionary 6. Stop.

4. Context-Based Coding

In this we encode by making some prediction by using some context based algorithm. So if the distribution or transformation is based on the history of sequence, it is predictive coding. We only work on history and we make some prediction for the sequence. There might not be need to send additional information to encoder and decoder. If we use that history to determine a sequence in a predictive manner, such scheme is known as predictive coding or context based coding. In this we only need to store that context that has occurred in the sequence being encoded. At the beginning of encoding we need to code letters that have not occurred previously in the context.

In this we utilize the restricted probabilistic replica to slant the allocation of the information the entropy employed the slanted allocation to instruct the novel information.

Utilize the conditional possibility to slant allocation unrestricted possibility:

P (‘h’) = 0.05, P(‘ u’) = 0.02.

Conditional probability:

P (‘h’ |‘t’) = 0.3, P (‘u’ | ‘q’) = 0.99.

Practical issues:

Can utilize lively or stationary facts? By means of higher-level context needs huge possibility table

Solutions:

Adaptive system

Using contexts of variable sizes

Prediction with Partial Match

Prediction with Partial Match (PPM) was proposed by Cleary and Witten in 1984. Instead of estimating these probabilities ahead of time, we estimate the probabilities as the coding proceeds Only need to store those contexts that have occurred in the sequence being encoded Need to code letters that have not occurred previously in this context ® using escape symbol.

Example

- Input sequence: probability
- Current symbol: a
- Check if P(a | prob) availble ® fourth-order context
- If yes, encode a, update P(a | prob)
- If not, send escape code, then check P(a | rob) ® third-order context
- . . . continue checking low-order contexts . . .
- If P(a | b) is not available, check P(a) ® zero-order context
- If ‘a’ has never happened before, use P(a) = 1/M, where M is the alphabet size, to encode a The equi-probable model is called ‘–1’ order context

5. Dictionary-Based Coding Techniques

The dictionary holds a list of strings of symbols and it may be static or dynamic (adaptive)

- Static dictionary – permanent, sometimes allowing the addition of strings but no deletions
- Dynamic dictionary – holding strings previously found in the input stream, allowing for additions and deletions of strings as new input symbols are being read

Basic Idea of Dictionary Coding

- Given an input source, we want to
- Identify frequent symbol patterns
- Encode those more efficiently
- Use a default (less efficient) encoding for the rest
- Hopefully, the average bits per symbol gets smaller
- In general, dictionary-based techniques works well for highly correlated data (e.g. Text), but less efficient for data with low correlation (e.g. i.i.d. Sources)

Example

- Consider an ‘English’ source with 26 letters & six punctuation marks
- Single-symbol FLC, fixed-length encoding: 5 bps
- Four-symbol FLC, fixed-length encoding: 20 bps (324)
- If we assume uneven distribution of the symbols

- Pick a dictionary which contains the 256 most-frequently
- Patterns (probability p) and encode them with 8 bits
- Encode the rest with 20 bits
- Use 1-bit prefix to distinguish the two cases
- Then, the average rate is 9p + 21 (1 – p) = 21 – 12p.
- If p > 0.084, 21 – 12p < 20.

Static Dictionary

- Using a static dictionary is less complex, but the probability p of a hit highly depends on the applications
- For student records at a university is probably ok.
- The key for success is that the most common patterns are a small subset of all possible messages
- Out of over 100,000 English words, only less than 2,000 words are used in most writings

Digram Coding

- The dictionary is composed of all letters from the alphabet
- As many digrams (pairs of letters) as possible
- For example, if we want to encode pure ASCII text documents, we can design a dictionary of size 256 entries, and Source alphabet: 95 printable ASCII symbols
- Digrams: 161 most common pairs

Simple Digram Coding Example

- The source alphabet A = {a, b, c, d, r}
- Dictionary:

Code	Entry	Code	Entry
000	*a*	100	*r*
001	*b*	101	*ab*
010	*c*	110	*ac*
011	*d*	111	*ad*

- Try to code the sequence abracadabra, the output is 101100110111101100000.

6. Research Challenges

Planning calculations fill in as a significant part in any correspondence arrange to fulfill the QoS necessities. The structure is particularly tested by the restricted limit and dynamic channel status that are natural in remote correspondence frameworks. To plan a MAC layer convention which can streamline the framework execution, the following highlights and criteria ought to be concerned.

• Bandwidth use

Effective transmission capacity usage is the most significant in the calculation structure. The calculation must use the channel effectively. This suggests the scheduler ought not dole out a transmission opening to an association with a right now awful connect.

• QoS necessities

The proposed calculation should bolster various applications to endeavor better QoS. To help delay-touchy applications, the calculation gives the postponement bound provisioning. The long haul throughput ought to be ensured for all associations when the adequate transfer speed is given.

• Fairness

The calculation should allocate accessible asset reasonably crosswise over associations. The decency ought to be accommodated both present moment and long haul.

• Implementation unpredictability

In a rapid system, the booking basic leadership procedure must be finished in all respects quickly, and the reconfiguration procedure in light of any system state variety. Consequently, the measure of time accessible to the scheduler is constrained. A low-unpredictability calculation is fundamental.

• Scalability

The calculation ought to work productively as the quantity of associations or clients sharing the channel increments.

7. Time Taken For Encryption-Decryption Process

We have performed 10 Simulations to get Time consumption in Encode-Decode process and to get accuracy of Process.

Table and figure shows the decoding time of the few Simulations which are encoded by proposed and existing approaches. It can be seen in the graph that binary data takes less time to decode.

Table 1: Decoding time

Sr. No.	Input Data	Validation	Context technique Time (S)	Dictionary technique Time (S)	Hybrid (Proposed technique) Time (S)
1	0100100011110	Success	0.0223685	0.0223683	0.0223682
2	Hello I LIVE IN INDIA I am Phd scholar Engineering	Success	0.175918	0.175917	0.175915
3	WELCOME TO INDIA	Success	0.087283	0.087283	0.087282
4	11101111	Success	0.0045889	0.0045888	0.0045887
5	TESTING	Success	0.069823	0.069823	0.069822
6	hybrid technique	Success	0.128476	0.128476	0.128475
7	Signal	Success	0.049350	0.049349	0.049347
8	Engineering	Success	0.052430	0.052429	0.052428

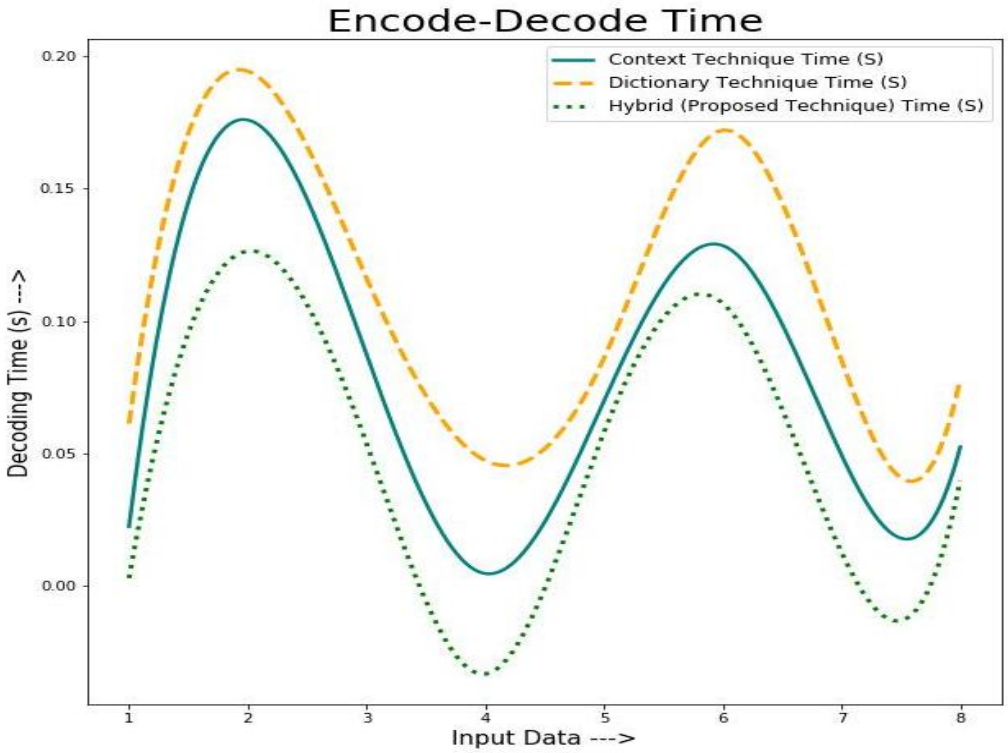


Figure 4: Encode-Decode time

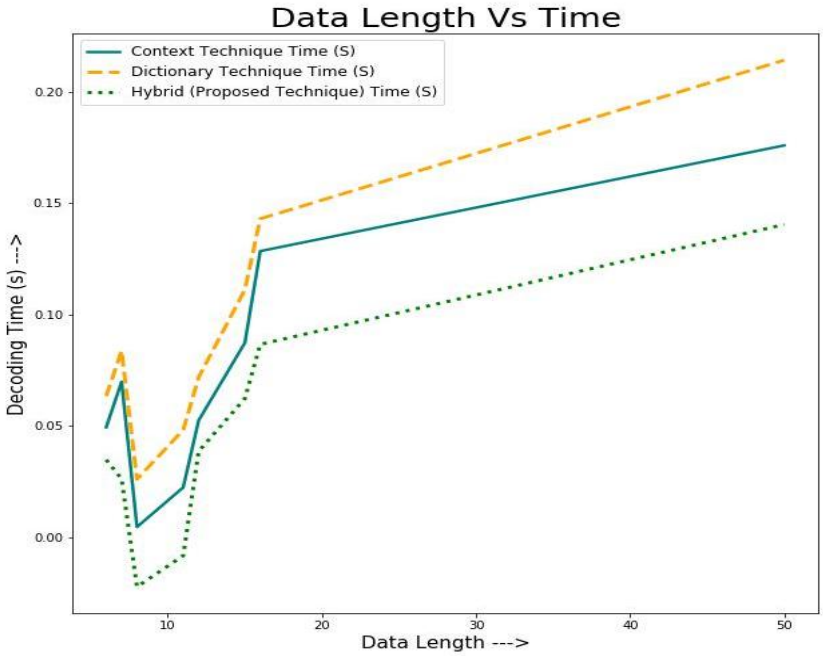


Figure 5: Length vs.time

As shown in figure 5 the decoding time increases as the length of the data increases, but the binary data takes lesser time to decode.

8. Conclusion and Future Scope

It is expected that WiMAX becomes the dominant standard for Wireless MAN networks in the world market, at least, in fixed broadband networks. A brief comparison between 802.16 and 802.16a has been provided and also it has been shown the advantage by using adaptive modulation. It has been explained that the key difference between the initial 802.16 standard and the 802.16a consists of the modulation scheme. The importance of OFDM has also been analyzed and this becomes an important feature that makes the difference between the 802.16 and 802.16a standard. More about this topic can be found in the literature provided. PHY and MAC layers of WiMAX have been Discussed Future possible applications have been discussed. WiMAX mobility standard is the next step. However, it will have its competition too with the 802.20 standard that in short is called Mobility-Fi. We will have to wait for the products and their performance in real environments in order to evaluate what the standard addresses

and the real performance of these products. There are already prototypes and also development kits using WiMAX standard that are used for education and mainly for research. Nowadays, there are also some products that have been introduced into the market that already contains the WiMAX standard presented here. Market is the key word to take into account. Products will have to be delivered according to the market needs and those for endusers will have to be extremely easy to install. Experience from DSL and cable modems services shows this drawback. Of course, in addition to be easy to install and provide good technical features, these products have to provide low-cost or at least a clear advantage over other technologies that are, at this moment, already matured in the market like xDSL and cable modem.

Communicating signals by using radio waves as the medium instead of wires is the method for utilized in remote. It has been offered an alternate way out for issues identified with the entrance the information. Today remote is extremely famous innovation that is offering shape to increasingly advantageous and practical world.

The projected way provides a trustworthy packet marking in wireless network which is based on Random packet marking approach with algorithm mentioned above. Also a combined approach of Context based and Dictionary based programming way implemented and executed to authenticate the communicated data along Checksum to check integrity for the information.

The primary goal of Packet Marking method is use IP address for routing path in the attack path and develops the attack path again to find out the source router of the intruder. Although it is not easy to deliver the IP address in a single packet, so the packet marking approach set length of marking node so that it can be easy to trace Node.

References

[1] IEEE Std. 802.16e: Draft IEEE std 802.16e/D9. IEEEStandard for local andmetropolitan area networks-Part 16: Air Interface for Fixed BroadbandWirelessAccessSystems. Amendment 2: Physical and Medium Access Control Layers for Combined Fixed and Mobile Operation inLicensed Bands, 2005.

[2] C. Cicconetti, L. Lenzini, E. Mingozzi, and C. Eklund,Quality of service support in IEEE 802.16 networks, IEEENetwork, 8(2), March 2006.

[3] K. Ramadas and R. Jain, WiMAX System EvaluationMethodology (Wimax Forum), January 2007.

[4] V. Singh and V. Sharma, Efficient and fair schedulingof uplink and downlink in IEEE 802.16 OFDMA Networks, IEEE WCNC, April 2006.

[5] www.wimaxforum.org

[6] T he Implications of WiMax for Competition andRegulation, OECD document [dated March 2,2006].

[7] http://electronicxtreme.blogspot.com/2006/12/wimax.html [dated December 11, 2006].

[8] http://news.techdirt.com/news/wirless/article/6929[dated October 26,2006].

[9]A. Lindgren, A. Doria, Probabilistic routing protocol for intermittently connected networks, in: IRTF Internet Draft, draft-irtf-dtnrg-prophet00.txt, 2008.

[10]. A. El Fawal, J.-Y. Le Boudec, K. Salamatian, Self-Limiting Epidemic Forwarding, Tech. rep., EPFL (2006). [11]. PreetKhandelwal, Surya PrakashAhirwar, AmitBhardwaj, Image Processing Based Quality Analyzer and Controller, International Journal of Enhanced Research in Science Technology & Engineering, Volume 2, Issue 7, 2013.

[12]. L. Lilien, Z. Kamal, V. Bhuse, A. Gupta, Opportunistic networks: The concept and research challenges in privacy and security, in: NSF Intl. Workshop on Research Challenges in Security and Privacy for Mobile and Wireless Networks (WSPWN 2006), Miami, 2006.

[13] D. Boneh, M. Franklin, Identity-based encryption from the weil pairing, in: CRYPTO, 2001, pp. 213–229.

[14] Vikram Kumar Kamboj, S.K. Bath, J. S. Dhillon, “Multiobjectivemultiarea unit commitment using hybrid differential evolution algorithm considering import/export and tie-line constraints”, Neural Computing and Applications (ISSN: 1433-3058), Vol.28, No.11, 2017, pp. 3521–3536, DOI 10.1007/s00521-016-2240-9.

[15] T. Spyropoulos, K. Psounis, C. S. Raghavendra, Spray and wait: an efficient routing scheme for intermittently connected mobile networks, in: ACM SIGCOMM workshop on Delay-tolerant networking (WDTN), 2005, pp. 252–259.

[16] D. Boneh, G. Crescenzo, R. Ostrovsky, G. Persiano, Public-key encryption with keyword search, in: Eurocrypt, 2004.

[17] Security in WiMAX 802.16-2009 networks, White Paper, 11Albentia Systems SA January 2011

[18] An Overview of Security Challenges of Next GenerationMobile Wimax IEEE 802.16m Technology, 3rd InternationalGraduate Conference on Engineering, Science andHumanities (IGCESH), Adnan Shahid Khan , N. Fisal ,Hashim E. A. Elshafie, Fath.E.I. Khalifa , M. Abbas,MasoumehShaneshin in Year 2010

[19] Dawn Xiaodong Song and Adrian Perrig ” Advanced andAuthenticated Marking Schemes for IP Traceback” PerrigIEEE INFOCOM 20011

[20] ”CERT Advisory CA-2000-01: Denial-of-ServiceDevelopments,”Computerhttp://www.cert.org/-advisories/-CA-2000-01. International Journal of Network Security & ItsApplications (IJNSA), Vol.2, No.3, July 2010

WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Covid-19: Different Approaches in Treatment

[1]Mohit soni, [2]Dr.Hariom Sharma, [3]Dr. Gaurav Kumar Sharma , [4]Dr. Kaushal Kishore Chandrul

[1] Student of Bpharmacy 4th Year , Mewar University Chittorgarh, India
[2] Professor, Department of Pharmacy, Mewar University Chittorgarh, India
[3]H.O.D, Department of Pharmacy, Mewar University Chittorgarh, India
[4]Principle, Department of Pharmacy, Mewar University Chittorgarh, India

ABSTRACT:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus strain that caused coronavirus disease 2019 (COVID-19).SARS-CoV-2, an emerging zoonotic coronavirus, identified in December 2019 in Wuhan, Hubei province, China, has spread rapidly across the whole world, causing disproportionately high morbidity and mortality, along with unprecedented disruptions in the global economy and society functioning .The World Health Organization declared the outbreak of the novel coronavirus (COVID-19) as a global health emergency on January 30, 2020, and as a pandemic disease on March 11, 2020. Although exploration for a specific drug required for the COVID-19 treatment is under extensive research worldwide and some of them are in clinical trial now. Virtual drug library screening is one of the current techniques for repurposing accessible compounds .This review highlights the current and new therapeutical approaches, risk factors, and related protections to be taken as prerequisite measures and probable treatment options for the COVID-19-infected population in the current scenario.

Keywords- COVID-19, SARS-CoV-2, therapeutic Approaches, Pandemic, Respiratory, Airborne, Treatment of COVID-19

Introduction: -

Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) is the coronavirus strain responsible for the novel coronavirus 2019 (COVID-19) infection. COVID-19 emerged in the Wuhan city of China in late 2019 and swiftly occupied many of the individuals across the city with symptoms of atypical pneumonia, resulting in an outbreak of epidemic phase (Zhu et al. 2020a, b). Later, World Health Organization (WHO) declared the outbreak as a pandemic after assessing the situation around the world on March 11, 2020 (Cucinotta and Vanelli 2020). By the end of July 2021, more than 192 million cases had been recorded worldwide, resulting in the deaths of more than 4.1 million individuals worldwide from the beginning of the pandemic (WHO 2022a). Exceptional measures were taken to slow down the spread of this respiratory pathogen, including lockdowns, restrictions on travel and gatherings, mask mandates, and closures of businesses and schools, all actions with a high economic and psychological burden.

Airborne transmission is a major concern of SARS-CoV-2 as the expiratory activities (i.e., coughing, sneezing) of an infected person can generate respiratory droplets and infect individuals within a radius of 6ft (Ghinai et al. 2020). The front portion of the mouth is where atomization of droplets occurs; thus, covering the mouth by the use of a surgical facemask is essential.

The incubation period of a virus is the period between the exposure and the potential earliest date of symptoms, and current research showed that the incubation period for COVID-19 ranges from 2 to 7 days while the median estimate is 4 days (Guan et al. 2020). Fever, dry cough, dyspnea, myalgia, tiredness, regular or reduced leukocyte counts, and radiographic indications of pneumonia are all common signs of COVID-19 infection. Symptoms of lung abnormalities, lymphopenia, and thrombocytopenia have also been observed in certain COVID-19 individuals. The pathophysiological feature of COVID-19 is governed by proliferative and exudative stages of alveolar damage, necrosis of pneumocytes, inflammatory infiltrates, and microvascular damage (Carsana et al. 2020). To successfully combat current and possible future pandemics, detailed investigations of this new coronavirus, its mode of infection, and replication are required. This review focuses on the therapeutic approaches, discussion, description, clinical manifestation, precautions to be taken as a precautionary measure, and various treatment approaches for COVID-19.

History and Classification

Coronaviruses are a family of hundreds of viruses, and it was seen that the majority of these viruses showed their harmful effect on different animals like bats, chickens, camels, and cats.

In the 1960s, human coronaviruses 229E and OC43 were first discovered that were able to infect humans (Andersen et al. 2020). Among human

coronaviruses, four are endemic (229E, OC43, NL63, and HKU1) and are well known for causing mild diseases (Kahn and McIntosh 2005; Saxena et al. 2020).

In November 2002, the first SARS-CoV virus was identified, resulting in severe acute respiratory syndrome (SARS) (Lau et al. 2020). In 2003, the members of Canada's National Microbiology Laboratory identified this virus's genome and confirmed the reason for this outbreak (Pal et al. 2020). Since 2005, several novel coronaviruses have been recognized from bats, and the evidence showed that human respiratory coronaviruses, SARS coronavirus, and MERS coronavirus were initially derived from bat viruses ancestral (Paden et al. 2018; Burrell et al.2017). Another deadlier coronavirus MERS-CoV (Middle East respiratory syndrome) was discovered in 2012. In MERS, the first case was from Saudi Arabia. Later another two MERS outbreak was identified in 2015 and 2018 in South Korea and Saudi Arabia, respectively. Then the first SARS-CoV-2 or COVID-19 infection was reported in December 2019 in Wuhan city of China.

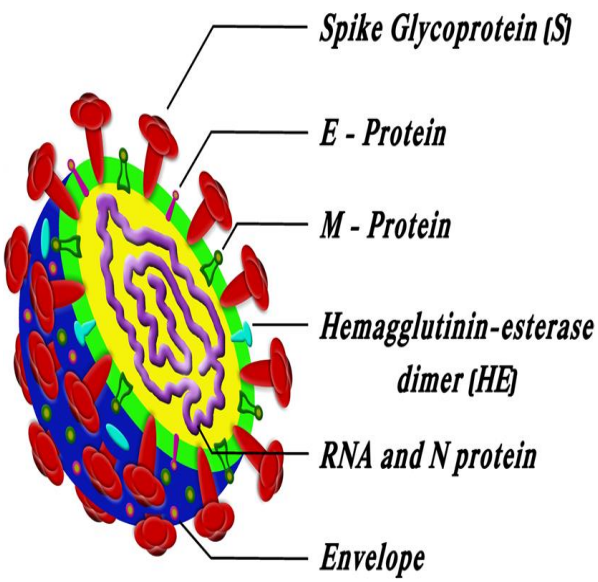
The virus was first discovered in bats and then pangolins (Panyod et al. 2020; Zhang et al. 2020). The genomic structure of virus SARS-CoV and SARS-CoV-2 bears many common characteristics and shows almost similar symptoms. This disease turns life-threatening if people are suffering from SARS. A total of 774 people was died from 2002 to 2014, according to the last reported case (Abdul-Fattah et al. 2021).

On account of their genus, there are four main subgroups of coronaviruses, known as alpha (α), beta (β), gamma (γ), and delta (δ) coronaviruses. Among them α and β coronaviruses are known to infect mammals, and other two γ and coronaviruses are known to create infection on birds (Wertheim et al. 2013; Guo et al. 2020).

Structure of Coronavirus

Coronaviruses are large, roughly spherical, and consisting of particles with bulbous surface projections . It is a single-stranded RNA-enveloped virus with the largest genomes (26.4–31.7 kb) among all known RNA viruses belonging to the *Coronaviridae* family. Its genome comprises around 30,000 nucleotides and contains four genes, which codify the surface protein characteristic of coronaviruses

1. Glycoprotein S, which exists as a homotrimer and forms the characteristic spikes found in the viral surface. Acting as a fusion protein, it allows entry of the virus into the host cell following recognition by its ACE2 membrane protein.
2. Envelope protein (E), E-protein is a tiny membrane protein with 76–109 amino acids that is a minor component of the viral particle. It is involved in virus assembly, host cell membrane permeability, and virus–host cell contact .
3. Membrane protein (M), which forms the matrix that connects the cover with the inner part of the virus.
4. Nucleocapsid (N) phosphoprotein, which holds the viral genome, a piece of positivestrand RNA N-protein coats the viral RNA genome which plays a vital role in its replication and transcription. It is responsible for encapsulating and protecting (+)-RNA, which contains the virus genome
5. HE protein ,The HE protein may have a role in viral entrance; it is not necessary for virus replication, but it appears to be important for natural host cell infection



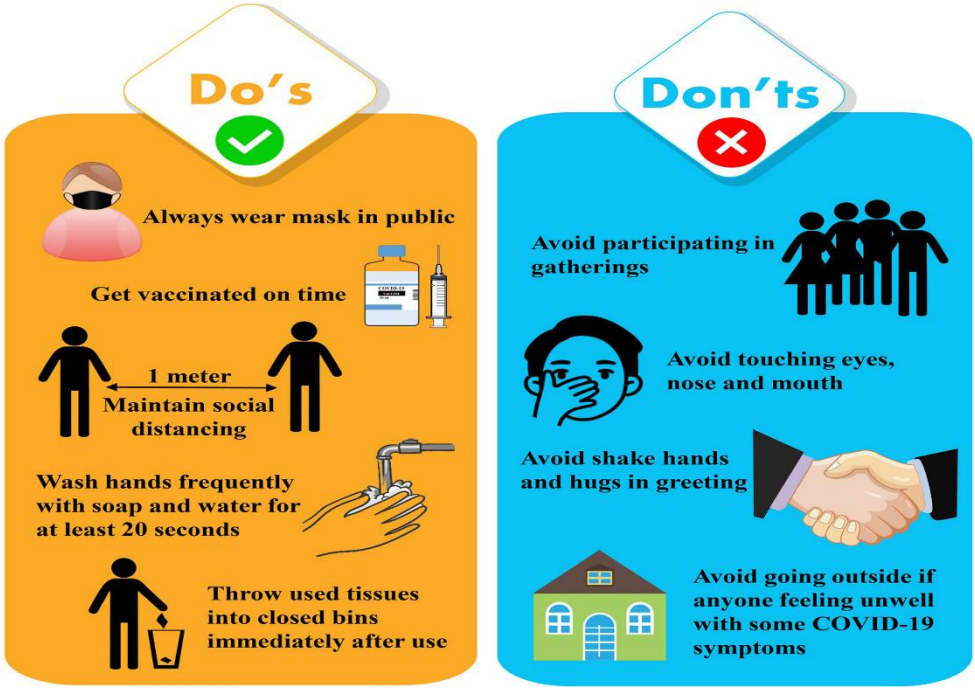
Preventions:

Prevention is better than cure; hence, the spread of this disease can be controlled by paying constant attention to some basic preventative measures given below.

- Get vaccine on time, and follow the local vaccination guideline.
- Maintain social distancing of at least 1-m space between yourself and others to reduce your threat of infection when others cough, sneeze,

or talk

- Use a face mask when being around other people .
- Frequently, in a proper manner, clean and rub your hands (at least 20 s.) with an alcohol-based hand wash or usage soap, followed by rinsing with water. If hand wash or soap is not available, use alcohol-based hand sanitizer (minimum 60% alcohol).
- Avoid going to crowded, congested, and/or involving close touch areas.
- Surfaces that are often handled, such as doorknobs, faucets, and phone displays, should be cleaned and disinfected regularly.
- Cover the nose and the mouth with the bent elbow or tissue during coughing or sneezing. After that, throw away the used tissue in a closed container and wash hands to maintain good respiratory hygiene.
- If anyone is feeling unwell with some COVID-19 mild symptoms, they should stay home and self-isolate until they recover
- If the person develops fever, cough, or difficulty breathing, get medical treatment, call the doctor ahead of time if possible, and follow your local health authority's instructions (WHO 2022c).



Feasible Therapeutic Approaches: -

Since the beginning of the COVID-19 pandemic, different measures have been taken to treat COVID-19infection. Still, there is no clinically validated and specific antiviral medication available to treat COVID-19 infection at this time Patients are usually provided medical treatment or supportive therapy, such as oxygen supplementation and mechanical ventilation, toalleviate symptoms For the treatment of COVID-19 infection, many strategies have been explored, and repurposing drugs is one of them. Some of the antivirals that have been repurposed include remdisivir, lopivir, lopinavir–ritonavir, ribavirin, baloxavirmarboxil, favipiravir, and arbidol/umifenovir. Other drugs that show potential action against COVID-19 but are not antivirals include chloroquine ,hydroxychloroquine, corticosteroids, losartan,statins, interferons, nitric oxide, and epoprostenol, which are instances for the repurposing strategy. Some medications have been suggested for treatment in critically sick patients. Tocilizumab, siltuximab, sarilumab, anakinra, and ruxolitinib were used to treat COVID-19 individuals who developed cytokine release syndrome (CRS). Antibiotics like azithromycin are frequently used to treat secondary infections (Ginsburg and Klugman 2020). The vaccine is another better approach for the prevention of COVID-19 infection. Though various vaccines against the SARS-CoV-2 virus have recently been approved, availability remains a major barrier, and public acceptance has become a contentious issue. But day by day, SARS-CoV-2 virus becomes more contagious and harmful due to their new mutants called variants. Recently the omicron variant's capacity to evade vaccine-elicited immunity is a major concern. So, there is a requirement for potential therapeutic molecules to treat the infection. Several antiviral drugs might be potentially repurposed or developed into viable treatments for this novel coronavirus. However, several clinical trials exploring possible therapies are now underway

Remdesivir-

Remdesivir is a nucleotide analog that competes with intracellular nucleosides for incorporation in the viral RNA and induces premature chain termination. Remdesivir is administered as a prodrug, metabolized intracellularly to an active metabolite, an analog of ATP. Its half-life of about 35 h

allows a single dose administration daily. Treatment is recommended for 5–10 days, with a higher initial loading dose (200 mg on the first day), followed by a maintenance daily dose of 100 mg to reach a stable plasma concentration .

Timing is essential for remdesivir efficacy. Initially recommended for hospitalized patients, remdesivir was proven to be more efficacious during the first 7 days of SARS-CoV-2infection. In high-risk outpatients (age > 60 years, diabetes, obesity, hypertension), an early,short, 3 days course of remdesivir significantly decreases the rates of hospitalization .Conversely, patients who are already symptomatic for more than 7 days and require oxygen support have no clinical benefit after remdesivir administration.

Remdesivir is EMA and FDA approved for the treatment of both hospitalized patients hospitalized ones (with mild to moderate forms of COVID-19, but at high risk for severe disease), aged _ 12 years and weighing _ 40 kg. The initial data on remdesivir efficacy came from the WHO SOLIDARITY study, that combined data from four clinical trials, showing a decrease in symptoms' severity in patients treated with remdesivir, and a significant increase in life expectancy in critically ill patients Among the side effects of remdesivir observed during clinical trials, and further reported during clinical use on the FDA or EMA websites, are gastrointestinal reactions (constipation, nausea, vomiting, diarrhea), increased prothrombin time, hypersensitivity reactions, hepato-, and renal toxicity .Therefore, monitoring of liver and kidney functions is recommended before and during remdesivir administration. Remdesivir is not administered if the glomerular filtration rate is less than 30 mL per minute, due to the presence of an excipient (sulfobutyl ether beta-cyclodextrin sodium) that accumulates in the kidney, causing renal toxicity . Remdesivir is not approved for the treatment of COVID-19 in pregnant women, but it was used off-label on a small number of patients, with good efficacy and minimal side effects. A large study on the safety of remdesivir administration in pregnant and breastfeeding women, conducted by the National Institute of Allergy and Infectious Diseases, US, is expected to be completed in 2022 . Treatment with remdesivir was available through an emergency authorization for patients younger than 12 years, due to insufficient data on the pharmacokinetics and safety of the drug in these patients. The evidence for remdesivir use in children is limited. A study done in early 2021 on 77 children (under 18 years old, with an average age of 14 years) with severe forms of COVID-19, showed improvement in the symptomatology, with good tolerance and few side effects [. In April 2022 FDA has approved remdesivir use in pediatric patients 28 days of age and older weighing at least 3 kg, based on the efficacy results in adults and on the data from a phase 2/3, single-arm, open-label clinical study of 53 pediatric patients

Favipiravir

Favipiravir is a broad-spectrum antiviral and antiinfluenza drug that restricts viral RNA replication by inhibition of RNA polymerase (Fang et al. 2020). Several studies have revealed that favipiravir can effectively treat COVID-19, particularly in patients with mild-to moderate disease. Favipiravir has been demonstrated in certain investigations to lower viral load in the upper respiratory tract and the lungs (Shirali and Daikoku 2020)
Favipiravir initially acts as a prodrug entering cells through endocytosis, and then after phosphoribosylation and phosphorylation, it is converted into an active favipiravir ribofuranosyl phosphates (Furuta et al. 2013). The antiviral activity is exhibited through selectively targeting the conservative catalytic domain of RNAdependent RNA polymerase (RdRp), interrupting the nucleotide incorporation process during viral RNA replication (Furuta et al. 2017). Favipiravir demonstrated 100% effectiveness in protecting mice against the Ebola virus, although its EC50 value in Vero E6 cells was high (Oestereich et al. 2014). Favipiravir has been used in the treatment of infectious diseases caused by RNA viruses such as influenza, Ebola, and norovirus (DeClercq 2019).

Lopinavir, Ritonavir

The antiretroviral drug, Lopinavir is widely used for treating HIV and is a potential candidate for the treatment of COVID-19.19 Ritonavir helps to stabilize Lopinavir and together they inhibit the replication of coronavirus *in vitro*.20 Cao *et al*. carried out an open-label trial for Lopinavir–Ritonavir in 199 hospitalized patients with severe COVID-19 and administered Lopinavir–Ritonavir (400 mg and 100 mg, orally every 12 h for 14 days). The authors found no benefit with Lopinavir–Ritonavir therapy in terms of time to clinical improvement beyond the standard of care.21 However, the analyses of secondary outcomes revealed that Lopinavir–Ritonavir may be associated with substantial lowering of overall mortality (19% in patients in Lopinavir–Ritonavir group vs. 25% in the standard-care group), reduced risk of severe adverse events (20% vs. 32%), and decreased risk of respiratory failure or acute respiratory distress syndrome(13% vs. 27%).22 Though this therapy has not shown meaningful clinical improvement, Lopinavir– Ritonavir may not be abandone d by clinicians in the current scenario of shortages of alternative drugs.

Arbidol

Arbidol is also known as umifenovir, a Russian antiviral drug that seems to be effective against many viruses, including influenza, respiratory syncytial virus (RSV), poliovirus, rhinovirus, Zika virus, hepatitis and SARSCoV, and MERS-CoV coronaviruses (Gao et al. 2020). The clinical evidence for using Arbidol in the treatment of COVID-19 is scarce.
A retrospective cohort study, case reports and case series revealed that Arbidol alone or combined with antiviral drugs produced certain benefits in the treatment of COVID-19.26 The dosing followed for Arbidol is 200mg every 8 h orally for 7-14 days. 4 The trimerization of SARS-CoV-2 spike glycoprotein, which is important for cell adhesion and penetration, may be effectively blocked or hampered by arbidol. When the trimerization of the SARS-CoV-2 spike glycoprotein is blocked, a bare or immature virus is formed, which is less infectious (Vankadari 2020). As a host-targeting drug, Arbidol also disrupts many steps of viral cycle replication, including entrance, attachment, internalization, and membrane fusion. Arbidol substantially improved the clinical state of hospitalized COVID-19 patients, including peripheral oxygen saturation, the need for ICU admissions, the length of hospitalization, chest computed tomography involvements, white blood cells, and erythrocyte sedimentation rate, according to a randomized controlled trial (Nojomi et al. 2020).

Ivermectin

Another natural product that has shown antiviral activity related to the blockade of a host cell target is ivermectin, which, together with the closely related avermectins, has an interesting history. The avermectins were discovered by Ōmura in *Streptomyces avermitilis* (currently *avermectinius*) isolated from soil samples and were studied as antiparasitic agents by Campbell in Merck. It was soon found that compounds lacking the double bond at the spirocyclic fragment of the molecule (ivermectins) were less toxic and had a broader antiparasitic spectrum. Commercially available ivermectin is an 8:2 mixture of ivermectins B1a and B1b (Figure 25). It has low toxicity and is widely employed as an antiparasitic medication for veterinary use; it has also been approved for a number of human parasitic diseases, most notably onchocerciasis (river blindness), and also filariasis, and pediculosis. Ōmura and Campbell shared half the 2015 Nobel Prize in Physiology/Medicine for their discovery.Regarding its use against COVID-19, in 2020, ivermectin was discovered to be antiviral in vitro. Its potency was moderate, with an IC50 = 2 _M, which is 15–30 times higher than the concentration that can be reached with a dose of 200_g/kg. Nevertheless, it seemed promising in early clinical testing [54] and it was later found to act on multiple targets, including the viral S protein and the host importins, which act as transporters of several viral proteins (ORF-3a, ORF-6, NSP-1) to the nucleus, where they block the production of the natural antiviral interferon. Moreover, ivermectin was found to act by other mechanisms not based on its viral action, since it is anti-inflammatory and antithrombotic. The clinical efficacy of ivermectin has become highly controversial; one meta-study showed a reduction of the risk of death in COVID-19 patients, especially for avoiding the progression of the disease towards the more severe stages but several problems with the data and the methodology have been pointed out by other authors and another meta-study concluded that the evidence available that can be considered reliable does not support the use of ivermectin for the treatment or prevention of COVID-19 outside of randomized trials . This is also the recommendation of the World Health Organization and of regulatory agencies such as FDA and EMA

Corticosteroids

Corticosteroids decrease the COVID-19-induced systemic inflammatory response, leading to an improvement in the clinical outcomes and a reduction in the 28-day mortality (8.7% in the critically ill and 6.7% in patients with severe COVID-19 who were not critically ill). Dexamethasone is the first-choice corticosteroid, widely used throughout the pandemic, with similar oral and intravenous bioavailability. Corticosteroids are highly effective in hospitalized patients in severe or critical conditions, requiring mechanical ventilation, while in those with mild forms of the diseases, their use is not recommended. Low-dose dexamethasone used in pregnant women requiring mechanical ventilation resulted in a decrease in COVID-19-induced complications, with a low risk of fatal adverse reactions. The international treatment guidelines do not recommend the use of corticosteroids in pediatric patients, as there are insufficient data to confirm extrapolation of corticosteroid doses used in adults for patients younger than 18 years .Inhaled administration of corticosteroids might be recommended in COVID-19 patients, due to an anti-inflammatory effect in the respiratory tract, that can decrease the innate immune inflammatory responses and the macrophages' infiltration in the lung tissue. In addition, inhaled corticosteroids can interfere with the replication of SARS-CoV-2, by downregulating ACE2 receptor expression, especially in patients with chronic obstructive pulmonary disease. Nevertheless, the COVID-19 EMA pandemic Task Force is advising that there is insufficient evidence on the benefits of inhaled corticosteroids for people with COVID-19 with normal levels of oxygen . The general safety profile of corticosteroids is well known, and the main side effects (including hyperglycemia, fluid retention, increased risk of opportunistic infections, and reactivations of latent infections) are manageable.

Chloroquine and Hydroxychloroquine

Chloroquine and hydroxychloroquine have a long history of use in the inhibition and treatment of malaria and the treatment of chronic inflammatory disorders such as rheumatoid arthritis. Hydroxychloroquine is derived from chloroquine, and initially, they have been proposed as an antiviral treatment for COVID-19 (Gasmi et al. 2021; Horby et al. 2020). Later on, a randomized controlled trial reported that hydroxychloroquine was administered as a postexposure prophylactic within 4 days of a high-risk or moderate-risk COVID-19 exposure, and hydroxychloroquine did not protect against COVID-19-related illness or infection (Boulware et al. 2020; Mitja et al. 2021). Another open-label randomized controlled trial reported that chloroquine/hydroxychloroquine treatment in patients brought to the hospital with severe COVID-19 resulted in clinical deterioration and increased rates of invasive mechanical ventilation and renal failure (Rea-Neto et al. 2021). The Food and Drug Administration (FDA) granted emergency use authorization (EUA) to chloroquine and hydroxychloroquine in May 2020 to treat severe cases of COVID-19 in hospital settings. Although additional mechanisms are involved, including clathrin interaction, their antiviral activity seems to be mainly due to their ability to alter endosomal pH . These compounds have two basic centers, namely the heterocyclic nitrogen belonging to the 4-aminoquinoline moiety, and the tertiary amine at the end of the side chain. As a consequence, at acidic pH values they can generate a monoprotonated species (CQH^+) and even small amounts of a diprotonated one (CQH_2^+), which, due to their low lipophilicity, become trapped in the acidic organelles, raising vesicle pH and hampering the membrane fusion process. . This property of CQ and HCQ renders them potentially useful for suppressing the immune system response characteristic of the severe forms of COVID19. Both chloroquine and its hydroxy derivative were broadly used in the clinic in many countries during the first wave of COVID-19. However, subsequent clinical studies have not shown evidence of clinical benefit and safety in their use for treating the SARS-CoV2 patients

Anakinra

Anakinra is a 17-kD recombinant human IL-1 receptor antagonist (blocking both IL-1α and IL-1β), with a short half-life of around 3–4 h and a favorable safety profile, authorized for the treatment of rheumatoid arthritis, gouty arthritis, and other uncommon auto-inflammatory disorders. Anakinra is a safe and effective treatment strategy for delaying mechanical ventilation, reducing the need for supplemental oxygen, and regulating SARSCoV- 2-triggered inflammation in patients with severe COVID-19 pneumonia and a high oxygen need (Balkhair et al. 2021). Later on, Tharaux et al. reported that the

patients with COVID-19 and mild-to-moderate pneumonia, a randomized clinical study found that anakinra was ineffective in lowering the requirement for noninvasive or mechanical ventilation or mortality. No major safety concerns were raised during anakinra use for the treatment of COVID-19. Reported side effects included neutropenia (particularly when given concomitantly with other drugs that decrease the number of leukocytes), headache, diarrhea, and flu-like symptoms . Data on pregnancy and breastfeeding are limited, and the efficacy in children under 18 years of age is not yet established .

Tocilizumab

Tocilizumab, a monoclonal anti-interleukin-6 (IL-6) antibody, has been identified as a possible therapeutic option for COVID-19 patients at risk of cytokine storms. IL-6 is an essential cytokine in inflammatory reaction and immune response and is one of the most significant cytokines involved in COVID-19-induced cytokine storms (Luo et al. 2020). However, a different study report showed that it is an effective treatment preference for critically ill COVID-19 patients, as it substantially reduces their oxygen requirements and their ICU stay, median hospital stay, and death. COVID-19-induced cytokine storms are effectively treated with this drug by decreasing the level of IL-6 (Chachar et al. 2021; Luoet al. 2020 Nevertheless, not enough data are presented yet to propose tocilizumab or sarilumab use as the standard treatment plan of COVID-19 patients (43)

Sotrovimab

Sotrovimab, a monoclonal antibody, has been developed to treat various types of coronaviruses, including COVID-19. It is primarily used to treat mild and moderate COVID-19 infection and prevent the progression of the disease condition from critical to severe. A retrospective study reported that the use of sotrovimab significantly improved symptom resolution, outcome, laboratory marker, and decreased hospitalization rate in individuals with mild and moderate COVID-19. This study suggests the use of sotrovimab in the early stages of COVID-19 treatment (Elesdoudy 2021). Later on, Guta and his group reported that the sotrovimab lowered the probability of disease progression in high-risk patients with mild-to-moderate COVID-19. And there were no threatening signs found during the study (Gupta et al.2021). The use of sotrovimab for treating mild or moderate COVID-19 in patients at high risk of hospitalization has also been conditionally recommended by the WHO (Kmietowicz 2022).

Janus Kinase Inhibitors;

Janus kinase (JAK) inhibitors interfere with one of the critical cellular pathways involved in the inflammatory response: the JAK/STAT signaling pathway, blocking phosphorylation of STAT proteins (signal transducer and activator of transcription) and preventing inflammation and immune activation . JAK inhibitors can be used as supplemental therapy in hospitalized patients receiving remdesivir and/or dexamethasone, who have signs of systemic inflammation and require rapid oxygen supplementation.

Baricitinib

Baricitinib , a clinically approved drug for rheumatoid arthritis, is a selective JAK1/JAK2 inhibitor with potent anti-inflammatory activity and a potential direct antiviral effect, by inhibition of the pivotal regulators of the ACE2 receptor that mediate the clathrin-dependent viral endocytosis . Three clinical trials (ACTT-2, COV-BARRIER, STOP-COVID) evaluated the efficacy of baricitinib for COVID-19 treatment, with positive results, demonstrating a decrease in hospitalization lengths, duration of mechanical ventilation, and mortality . Baricitinib was administered in monotherapy or in combination with other immunomodulatory and antiviral drugs. Co-administration of baricitinib and remdesivir improved the clinical outcome, compared to remdesivir alone, with a lower frequency of adverse effects . Coadministration of baricitinib and corticosteroids was associated with a significant decrease in the short and medium-term all-cause mortality, with a safety profile similar to the standard of care . No serious adverse reactions were reported and the drug can also be administered to children over 2 years of age .

Ruxolitinib

a selective JAK1/JAK2 inhibitor, and Tofacitinib (Xeljanz® Pfizer, Brooklyn, NY, USA),a JAK1/JAK3 inhibitor, are recommended in combination with corticosteroids, only if baricitinib or IL-6 inhibitors cannot be used. Currently, a beneficial effect on the clinical outcomes was not fully demonstrated, therefore their use in COVID-19 treatment remains limited

Convalescent plasma therapy

Convalescent plasma treatment is a type of adoptive immunotherapy that can treat a wide range of illnesses.Passive immunity can be created by using antiviral antibodies from recovered individuals to treat additional patients with a specific infectious illness. Other respiratory viral diseases, including SARS-CoV-1, H1N1 influenza, MERS-CoV, West Nile virus, and Ebola virus, have recently been treated with this technique (Marano et al. 2016). Hyperimmune immunoglobulin showed a statistically significant reduction in the risk of death among those treated with convalescent plasma or serum in all of the investigations (Al-Tawfiq and Arabi 2020). This treatment has played an essential role in treating COVID-19 patients when no effective antiviral drugs are available. In an initial uncontrolled case series, five critically sick patients with COVID-19 and acute respiratory distress syndrome underwent convalescent plasma treatment, and the result showed improvement in their clinical status (Shen et al. 2020). Later on, Duan et al. (2020) reported that a single dosage of CP (200 mL) was well tolerated and could considerably raise or sustain neutralizing antibodies at a high level, resulting in viremia disappearing in 7 days. However, clinical symptoms improved quickly over 3 days. This suggests that CP might be a viable rescue strategy for

severe COVID-19 and that a randomized study is necessary. Due to sample and experimental design constraints, a definitive conclusion on the potential efficacy of this form of treatment cannot be made, and further clinical observations will be required

Antibiotic

Azithromycin

Azithromycin is an antibiotic applied for the treatment of several different types of infections caused by susceptible bacteria (Perter et al. 1992). Azithromycin binds to the 50S subunit of the bacterial ribosome, inhibiting mRNA translation (Bulkley et al. 2010, Tu et al. 2005).
The use of Azithromycin together with other drugs has been successfully applied in the clinic for the treatment of viruses and to prevent severe respiratory tract infections for patients suffering from viral infection (Madrid et al. 2015, Retallack et al. 2016). As discussed before, the positive data for the use of its azithromycin along with hydroxychloroquine, in a COVID-19 clinical trial have been proposed (Gautret et al. 2020). In an open-label non-randomized study in France hydroxychloroquine + azithromycin presented with the highest virologic cure rate following 6-day treatment (Gautret et al. 2020). However, other studies affirm the data presented to date are insufficient to evaluate possible clinical benefits of azithromycin in patients with COVID-19 and repeated the experiments found patients had significant comorbidities (Molina et al. 2020).

Nitazoxanide

Nitazoxanide , an antiprotozoal, is an orally active nitrothiazolysalicylamide and antiviral prodrug that is converted rapidly to the active metabolites tizoxanide and nitazoxanide conjugates and unlike metronidazole (Rang et al. 2007, Rossignol 2016). Similarly, nitazoxanide is also known to potentiate interferon-alfa and interferon-beta production and it has been previously shown to exhibit an in vitro activity against MERS-CoV and other coronaviruses (Rossignol 2016). Nitazoxanide is hypothesized as a likely therapeutic approach and could have antiviral potential against Sars-CoV-2, as it works by interfering with host-regulated pathways in viral replication, amplifying the detection of cytoplasmic RNA and Interferon type 1. Some author suggests that nitazoxanide/azithromycin combination could have a potential that should be properly tested in clinical trials including randomized controlled trials

Serine Protease Inhibitor

Nafamostat

Nafamostat, a serine protease inhibitor that works as an anticoagulant, has demonstrated satisfactory results in inhibiting the action of MERS-CoV and has been shown to be effective against SARS-CoV-2 infection, preventing membrane fusion (Wang et al. 2020). Nafamostat mesylate inhibits TMPRSS2-dependent host cell entry of MERS-CoV (Yamamoto et al. 2016), and TMPRSS2 is responsible for cleaving and activate Sars-Cov-2 S protein.
However, the use of this anticoagulant in the treatment for COVID-19 is in a clinical trial, and the exact concentration of the compound to inhibit viral replication is not yet clear. In the deficiency of this information, other serial protease inhibitors were tested to inhibit the entry of Sars-Cov-2 into the cell, such as Naphthostat mesylate, which is already used for human use in Japan and the fact that this drug inhibits the action of TMPRSS2 in the host cell for infections caused by MERS-CoV (Hoffmann et al. 2020b). Nafamostat has FDA approval (unrelated to infections caused by coronavirus), and has been shown to inhibit the entry of Sars-Cov-2 mediated by protein S into the host cell with greater efficiency than Naphthostat mesylate, thus being considered the best option for the treatment of COVID-19.

New Therapeutical Approaches for COVID-19

- ***Broadly Neutralizing Antibodies***

Broadly neutralizing antibodies, active against different variants of SARS-CoV-2, including Omicron, were isolated from convalescent plasma donors or vaccinated individuals .Cryo-EM studies showed antibodies that were cross-reactive between sarbeco-,merbeco- and embecoviruses, and have flexible binding modes, targeting both the “up” and “down” conformations of the RBD. The development of such ultrapotent antibodiesvdirected towards conserved viral epitopes, with broad-spectrum activity against bothvwild-type and mutant virus strains, is an important strategy for COVID treatment and a step forward towards a pan-coronavirus vaccine. In addition, innovative antibody delivery techniques, such as inhaled antibodies, might offer a convenient, highly accessible method for COVID-19 prevention. Nanobodies (Nbs) are single-domain antibodies, similar to the heavy-chain-only antibodies initially isolated from camelids and cartilaginous fish . Nbs have a truncated structure, without any light chains and with a single variable domain in the two heavy chains (VHH), representing the antigen-binding region. Nbs exhibit ideal attributes for large-scale manufacture and have numerous advantages over classical human antibodies: ultra-high antigen-binding affinity, due to a very long CDR3, that can access otherwise inaccessible epitopes; recognition of a higher diversity of paratopes; good physicochemical qualities with increased solubility; good tissue penetration; and high stability, allowing for oral or inhalation administration. Bi- or multi-specific heavy chain antibodies and nanobody-drug conjugates are tested as antitumoral therapeutic strategies and can be used to prevent or treat inflammatory and infectious diseases .

Caplacizumab, a bivalent single-domain antibody, is the first nanobody-based medicine approved by the EMA and FDA in adults with thrombotic thrombocytopenic purpura and thrombosis in November 2018, and February 2019, respectively. Due to their high antigen affinity and stability, nanobodies can be administered in oral or inhaled versions and might be beneficial for COVID-19 non-hospitalized patients, during the early stages of the disease, acquiring high pulmonary concentrations with minimal systemic adverse effects. Nanobodies able to recognize the RBD of different variants of SARS-

CoV-2 were identified using phage display libraries derived from camels and llamas immunized with SARSCoV- 2 spike protein or receptor-binding domain . Engineered multivalent nanobodies constructs with superior neutralizing activity can block SARS-CoV-2 entry, either by inhibition of receptor binding or by inducing conformational modifications that prevent viral–cell fusion . In experimental mice models, prophylactically administered combinations of bivalent nanobody-Fc fusions, recognizing different epitopes in SARS-CoV-2 RBD, were able to decrease viral replication .Nanobodies that target chemokines or cytokines, can be customized to modify inflammatory responses in COVID-19 disease . Previously, several studies using the phage display method to elicit nanobodies directed towards cytokines were published, proving higher efficacy compared to the traditional cytokine blocking antibodies

- ***Novel Viral Entry Inhibitors***

Bemcentinib is a selective inhibitor of the AXL receptor tyrosine kinase, that mediates uptake of the apoptotic bodies, used by SARS-CoV-2 in a process of apoptotic mimicry, to adhere to and internalize into the host cells. Bemcentinib is currently tested in two phase 2b clinical trials in hospitalized COVID-19 patients. The first study recently reported the short-term efficacy results, with minor benefits in the primary trial endpoints (time to improvement by two points on the WHO ordinal scale or time to discharge), but with potentially significant clinical benefits in a key secondary endpoint (avoidance of clinical deterioration) .

Inhibitors of Host Transmembrane Surface Protease TMPRSS2

Camostat mesylate, an oral serine protease inhibitor, primarily used for symptomatic treatment in gastrointestinal tract disorders, is a potent inhibitor of the TMPRSS2 protease used by SARS-CoV-2 to prime and activate the spike protein. Randomized, double-blinded studies, with clinical endpoints including viral load, number of hospitalization days, and mortality, show that camostat mesylate might be a promising repurposed drug, with a very good safety profile in humans. N-0385 is a small peptidomimetic molecule, an inhibitor of TMPRSS2, that shows high efficacy in vitro on several SARS-CoV-2 variants (Alpha, Beta, Gamma, Delta) at low, nanomolar concentrations. The drug demonstrated a potential prophylactic and therapeutic effect during experimental intranasal infection in a transgenic mouse model, that expresses the human ACE2 receptor driven by a keratin promoter. Further studies are necessary to evaluate the efficacy of this compound on the Omicron variant, which was shown to have a decreased use of TMPRSS2 and a preference for endocytosis dependent cell entry, with altered spike processing and reduced fusogenicity

Interferons

A limited and delayed interferon (IFN) response might stimulate an uncontrolled viral replication and an aberrant immune response, leading to severe forms of SARS-CoV 2 infection. Patients with errors in the type I IFN activating pathways and those with auto antibodies neutralizing type I IFN are prone to a severe course of COVID-19. Systemic and inhaled IFN alpha and beta were administered in hospitalized patients, either alone or in combinations with antivirals, such as remdesivir or ribavirin, without major clinical benefits Interferon lambda has a limited inflammatory activity, due to a more restricted distribution of its IFNLR1/IL10R2 receptors, on epithelial and immune cells. Smallrandomized clinical trials with peginterferon lambda did not show significant clinical benefits for non-hospitalized patients , although an accelerated suppression of viral replication was demonstrated . Interferons can inhibit cell division, as such, treatment is associated with flu-like symptoms,nausea, fatigue, weight loss, hematological toxicities, alopecia, elevated transaminases, and psychiatric problems (e.g., depression, suicidal ideation) can most often occur. Concomitant treatment with immunomodulatory drugs or chemotherapeutic agents is not recommended, due to an increased risk of toxicity. Administration in pregnancy is not safe, as congenital anomalies in the fetus or spontaneous abortion may occur. There are insufficient data for interferons' administration in children

Immunonutrition

A healthy and 'well-fed' immune system is one of the most important weapons against COVID-19. Though an array of micronutrients is required, a large body of evidence is seen for Vitamin C and Zinc.

Vitamin C (Ascorbic Acid):

Vitamin C, a potent antioxidant agent is an effective anti-viral agent against influenza viruses. It helps to develop and mature T lymphocytes and NK (natural killer) cells. In 50 moderate to severe COVID-19 patients, intravenous vitamin C (between 10 g and 20 g per day given over a period of 8–10 h) improved oxygenation index. All patients were cured and discharged. 11 Though high dose vitamin C is safe, large clinical studies are needed for bedside use.

Zinc:

Zinc is a potential supportive therapy of COVID-19 owing to its immunomodulatory and antiviral effects. Zinc inhibits SARS-CoV RNA polymerase and decreases angiotensin-converting enzyme 2 (ACE2) (SARS-CoV-2 receptor). It also upregulates interferon α to improve antiviral immunity. In elderly individuals, 45 mg/day of oral zinc supplementation for a year has shown to lower the incidence of infections. It is hypothesized that Zinc

supplementation in HCQ-treated patients may lead to improved outcomes in COVID-19 patients. HCQ has Zinc ionophore characteristics, leading to increased intracellular levels of Zinc specifically in lysosomes. This elevated intracellular

Herbal Drugs used in COVID-19

For several years, medicinal plants have been used in different indigenous health schemes and traditional medicines for treating diseases. 21 Naturally occurring herbal medicine provides a wide variety of natural products, which can be used as an ancillary guide to unlocking many mysteries behind human illnesses. 22,23 According to a report by the WHO, 80% of people in developing countries rely on conventional plants for health needs. 23–25 With the enhanced resistance of microorganisms (bacteria, viruses, and parasites) to traditional anti-microbial therapy, alternative therapies are being re-explored at a growing rate, particularly from herbal sources. 25 Assessing the possible antiviral activity of various natural resources has gained remarkable attention with the emergence and re-emergence of new viruses, concerning the availability of advancing technological resources. 21,23,26 A variety of herbs have been investigated, and their effects against viral infections have been identified. 21 Amidst the mounting global concerns about the COVID19 outbreak, understanding the natural products with antiviral properties is essential for providing an alternative management option for COVID-19. The use of natural products and phytomedicine continues to grow fast around the world, with many people nowadays reverting to such remedies in different national healthcare settings for the treatment of various health challenges. 23 Herbal phytoconstituents effectively reduced infectious conditions, where they were the only treatments available before antibiotics were introduced. In particular, herbal medicinal products provide a rich tool for the production of novel antivirals. The use of these plants dates back to the beginning of civilization. 27,28 Traditional Chinese medicine includes treatments of herbal and acupuncture, where those aim to prevent and treat diseases by enhancing the immunity of the body. 29,30 Chinese medicine needs experience and knowledge; here, no adverse reactions could be identified if Chinese herbs are properly used, 30,31 Seven coronaviruses have been detected with an ability to spread among humans; three of them are harmful, namely, SARS (severe acute respiratory syndrome, China, 2002), MERS (Middle East respiratory syndrome, Saudi Arabia, 2012), and SARS-CoV-2 (COVID-19, 2019). These viruses are belonging to the coronaviridae family of the coronavirus genus. The genome sequence analysis concluded that SARS-CoV-2 belongs to the beta type genus, where this type also contains the Bat SARS-like coronavirus, SARS, and MERS. Furthermore, based on the nucleic acid structure similarity, COVID-19 is a betacoronavirus

Andrographolide

The andrographolide is a labdane diterpenoid that is mainly isolated from the Andrographis paniculate (green chiretta) herbaceous plant extract. This component was utilized in different medical functions due to its remarkable biological activity, such as immunity regulation, anti-hyperglycemia, anti-bacteria, anti-virus, anti-parasite, and anti-tumor. 32–34 Previous reports showed that andrographolide could treat multiple viruses such as influenza A virus (IAV), 35 human immunodeficiency virus (HIV), 36 Enterovirus D68 (EV-D68), 37 dengue virus (DENV), 38,39 and Chikungunya virus (CHIKV) 40 due to its wide range of antiviral properties. Recently, Enmozhi et al. found that andrographolide could be a good inhibitor for SARS-CoV-2 through in silico studies by influencing the viral 3-chymotrypsinlike cysteine protease (3CLpro). 41 In general, andrographolide is highly abundant and has low cost and cytotoxicity; though, its strong antiviral activity against different types of viruses needs to be further studied

Quercetin

It is a flavonoid compound that could commonly found in fruits and vegetables. In addition to its dietary property, quercetin owns multiple biological activities, including its anti-functions against inflammations, oxidants, viruses, allergies, cancer, and mood deterioration, similar to vasoprotective medication. 42–44 Previous studies showed that quercetin has antiviral activity against a group of viruses, including IAV, 44 Hepatitis C Virus (HCV), 45 Enterovirus 71 (EV-71), 46 SARS-CoV, etc. 47,48 Regarding the SARS viruses, quercetin showed a relatively high inhibition rate and half-maximal inhibitory concentration (IC50) values of 82% and 73 µM, respectively, against SARS-CoV 3CLpro in Pichia pastoris fungus.

Baicalin

It is another medicinal component found in Scutellaria baicalensis Georgi (Chinese name: Huang Qin) and has a wide window of curative applications as sensitizer and antiapoptosis. 49,50 Chen et al. reported the antiviral activity of baicalin versus SARS type viruses, with an effective concentration to reduce the virus forming unit by 50% (EC50) value of 12.5 µg/ml within two days. The activity was reduced as the incubation time continued more than two days. 51 The similarity between the current COVID-19 virus (SARSCoV-2) and SARS-CoV is anticipated to obtain an analogous antiviral effect from baicalin on the recent virus. Furthermore, Deng et al. utilized UV spectrophotometry to identify angiotensin-converting enzyme inhibition, where baicalin was found to be a good in vitro inhibitor angiotensin-converting enzyme (ACE), with an IC50 value of 2.24 mM. 52 Considering the low toxicity of baicalin, its usage as a drug or treatment agent could be promising against COVID-19

Curcumin

Its International Union of Pure and Applied Chemistry (IUPAC) name is (1,7-bis(4- hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione). It is an anti-cancer, antioxidant, anti-inflammatory, and amphipathic molecule that contains a polar center and a lipophilic methine segment surrounding it. 53 The β-dicarbonyl group in curcumin structure promoted the H-bond donating and accepting, where this group functions as a phenylic hydroxyl moiety and methoxy group. Also, curcumin can be used as a Michael reaction acceptor due to its affinity to multivalent metals and non-metals, which leads to a high polymerization around CC. 54 Here, two polyphenols, Catechin and Curcumin, were reported through computational approaches, which have a dual

binding affinity. Catechin binds to viral S-protein and ACE2 with a binding energy of -10.5 Kcal/mol and -8.9 Kcal/mol, respectively. As a result, it binds with a greater affinity than that of curcumin, which are -7.9 Kcal/mol and - 7.8 Kcal/mol for S-protein and ACE2, respectively. While curcumin gets bound directly to the receptorbinding domain (RBD) of viral S-protein, catechin binds to the proximity of S-protein's RBD sequence. A molecular simulation study demonstrated that curcumin directly binds with the RBD site of S-protein during 40-100ns. In contrast, catechin binds with S-protein near the RBD site and causes fluctuation in amino acid present in the RBD and its proximity. In conclusion, this computational study predicted the possible use of the above two polyphenols for therapeutic/preventive intervention.

LUTEOLIN

Luteolin (3′ ,4′ ,5′ ,7′ -tetrahydroxyflavone) is one of the flavonoids group that naturally exists in a massive number of plants and has multiple pharmaceutical functions, such as anti-diabetic, anti-inflammatory, anti-bacterial, anti-cancerogenic, antiviral, antioxidant, anti-proliferative, and heart protective. 65 This component is obtained from Chinese medicine herbs available almost everywhere and at a low price. 66 Hence, Luteolin is suggested as a potential therapy to treat COVID-19 pandemic

MYRICETIN

Myricetin is a common plant-derived flavonoid and has many types of nutrition. Moreover, it commonly enters the ingredients of different foods and beverages. Likewise, Myricetin's previous plants and herbs show a wide window of potentials and roles as anti-inflammatory, anti-cancer, anti-diabetic, and antioxidant. This component has a long history that dates back to more than a century. The first isolation was from Myrica nagi Thumb (Myricaceae) in the late 1800s in India and was finally obtained as pale-colored crystals. 67 Yu. et al. reported that myricetin in vitro inhibited SARS-CoV's helicase protein by influencing the ATPase action, but not the unwinding activity of nonstructural protein 13 (nsP13). Furthermore, it was observed that myricetin and scutellarein had no cytotoxicity versus normal breast epithelial MCF10A cells. It can be suggested that the naturally-existing flavonoids, including myricetin, might serve as a SARS-CoV 2 inhibitor. 68

Azadirachta Indica (Neem)

The main clinical symptom of COVID-19 is fever and to reduce it these plants have valuable outcomes. The leaves of neem are traditionally boiled and consumed for the management of fever-related with COVID-19, with reported anti-inflammatory effects in animal studies . The animal study and in-silico docking research confirmed that neem leaves extracts and their metabolic constituents such as flavonoids and polysaccharides have direct antiviral effects against different viruses including Hepatitis C Virus . Specific to SARS-CoV-2, molecular docking research has demonstrated that neem-derived compounds such as nimbolin, nimocin, and cycloartenol can bind to the SARS-CoV-2 envelope (E), membrane (M), glycoproteins, and also inhibitory role . Its leaves have positive effects on immunoregulatory effects to boost immune response in animals models . In mice vaccinated with Brucella Rev-1 vaccine, neem seed extract given subcutaneously boosted the production of IFN-γ post-vaccination neem seed extracts must be avoided in pregnant women as animal research its shown abortifacient effects . while clinical studies have reported its anti-human chorionic gonadotropin effects . Studies reported that the traditional purpose of neem for medicinal purposes mainly depends on leaves consumption, boiled the leaves in the water, and drank . One of the main concerns is about safety, a clinical trial should be done to establishing safe doses of neem leaves specific to the formulation intended for use are required before further investigations on efficacy. Although neem leaves have been used traditionally for a long time, the toxicity profile is not well-documented. clinical cases of acidosis and renal injury in the body system have also been reported on neem seed oil users [32]. The main challenges of ethnopharmacological study for therapeutic claims are quality control, identification, and standardization of biomolecules on herbal products.

Mentha Piperita

Peppermint (*M. Piperita*) is the oldest herbal remedy for different diseases condition in the world. Dry peppermint has been composed since 1000 BCE, and its importance has been described in ancient Egypt, Greece, and traditional Chinese medicine. Peppermint has essential oil and significant antibacterial and antifungal activity against Gram-negative and Gram-positive bacteria, yeast, and fungi, mainly as a result of the presence of the abundant phytochemicals menthol and menthone . However, to the best of our knowledge, a study done of Saudi Arabia stated that about 78% of non-hospitalized patients used peppermint, compared with only 22% of hospitalized patients without using peppermint supplement, due to COVID-pandemic so that use of peppermint during infection with COVID-19 was associated with lower odds of hospitalization

Glycyrrhiza Glabra

Glycyrrhizin, also called glycyrrhizic acid (GLR), is a triterpenoid saponin mainly isolated from the roots (Glycyrrhizae Radix) of the plant Glycyrrhiza . GLR effectively inhibited the replication of two clinical isolates of SARS-associated coronavirus (FFM-1 and FFM-2). The drug was found to inhibit the cytopathic effect of the virus with an EC50 of 300 mg/ml while being non-cytotoxic to the host cells. GLR inhibited virus replication but also the penetration and adsorption of the virus into cells . The mechanism of action at the origin of this activity was not known at that time but a drug-induced production of nitrous oxide synthase was mentioned, signifying that nitrous oxide could be accountable for the inhibition of virus replication . GLR also showed active when it was tested against 10 clinical isolates of SARS coronavirus in infected Vero-E6 cells but the activity was limited in time. The rapid metabolism of the drug limits the drug exposure, not permitting it to reach an effective concentration . The modification of the GLR structures, particularly to make amino-acid conjugates and amide derivatives can rise significantly the activity against SARS-CoV-2 but it can be at the expense of elevated cytotoxicity

Psoralea Corylifolia

Psoralea corylifolia L is used in Chinese medicine and traditional Ayurveda against different types of skin diseases, such as leukoderma, psoriasis, and leprosy . This plant is also known for its antimicrobial and anti-inflammatory activities . In a while, 6 aromatic constituents were isolated from seeds of Psoralea corylifolia ; the isolated phytoconstituents inhibited the enzyme in a dose-dependent manner with IC50 ranging from 4.2 to 38.4 μM. Likewise, numerous natural products have revealed antiviral effects at nanomolar concentration against SARS-CoV (e.g., homoharringtonine, ouabain, lycorine, tylophorine, 7 methoxycryptopleurine, and Silvestro) . Clinical trials of a few herbal compounds against SARS-CoV-2-3CLPro aroused hope for plant-derived *anti*-SARS-CoV-2 drugs. Very recently, 3CL protease inhibitor NLC-001, a plant product administered orally as a dietary supplement, got US FDA approval

Coronil : An Ayurvedic Attempt

On 23rd June, Patanjali launched Coronil and Swasari as an Ayruvedic cure for treating coronavirus infections. The launch of Coronil kit was based on the company's claim that the results were based on placebo controlled clinical trials. The drug was given to 95 COVID 19 infected patients and the company claims that 69 % patients were cured in 3 days and 100 % recovered in 7 days. The company further claims that high sensitive C-reactive protein and IL-6 levels were reduced in patients who were given Coronil. The reduction in IL-6 level reduces the chances of cytokine storm which has created a disturbing impact on patients. The company claimed that Coronil can cure Covid 19 patients in 3-14 days and it has no side effects. Coronil is made of the extracts of pure Giloy, Tulsi and Ashwagandha. Giloy has its own benefits. It improves platelet count, removes toxins from body, purifies the blood and fights bacteria. It is said to make immune system stronger and makes respiratory system stronger. Tulsi has proved to be highly effective in fighting against infection. It also acts as a natural immune booster, reduces fever, pain, reduces stress, cold, cough and other respiratory disorders and considered to be good for heart. Ashwagandha is said to be very beneficial herb for health of human beings. It is a rich source of antibiotics and very helpful in reducing body stress. The other ingredients were Kakda Singi,, Rudanti and Powerful Minerals. Patanjali launches this Coronil kit at Rs 545. They have planned to launch e-commerce application for delivery of coronil medicine within 2 hours of order placement using its own network. The entire Coronil kit included the medicine for 30 days and was expected to available on Patanjali stores in a week's time of its launch. The company also claimed that Coronil can also be used not only to cure corona but can be used also to prevent a person from getting infected

Covid-19 Vaccines

The world has taken different significant actions to control the COVID-19 pandemic from its beginning. However, the disease spreads unabated, wreaking havoc on people's health, social lives, and economies. Therefore, the prevention and control of the COVID-19 pandemic were immediately needed. Several vaccines have been studied, produced, tested, and assessed at a breakneck speed, and in 2021 many vaccines have been approved.
According to the WHO, more than 9.8 billion vaccination doses had been delivered as of January 27, 2022 (WHO 2022a). The immune system is triggered by vaccination, resulting in the generation of neutralizing antibodies against SARS-CoV-2. But the variants of the virus are always a major cause of concern. Vaccines have longbeen known to lose their potency over time. As a result, various countries have authorized the administration of an additional dose of vaccine (known as a booster) to people 3–5 months after their vaccination cycle is completed. This method appears to be efficient in preserving SARS-CoV-2 immunity

Vaccines authorized in India:

Globally, many vaccines are available some of them are Covishield® (Oxford-AstraZeneca), mRNA-1273 (Moderna), Janssen (Johnson & Johnson), AZD1222 (Pfizer BioNTech), Sputnik V® (Gamaleya), Covaxin® (Bharat Biotech), CoronaVac (Sinovac), NVX-Cov2373 (Novavax), BBIBP-CorV (Sinopharm) etc. In India, DCGI has approved three vaccines for restricted use in emergency situation in the India: the Covishield®, Covaxin®, and SputnikV®.15,16 As on 25th April, around 140.91 million vaccine has been inoculated24 which is around 10% of total population

Covishield:

The ChAdOx1 nCoV-19 vaccine (AZD1222) is made up of the replication-deficient simian (Chimpanzee) adenovirus vector ChAdOx1, which carries the full-length structural surface glycoprotein of SARS-CoV-2 along with a tissue plasminogen activator leader sequence. ChAdOx1 nCoV-19 expression optimizes the coding sequences for the codon of the spike protein. Two doses are required to administer at a dose of 0.5ml, contain 3.5-6.5×1010 viral particles as a single intramuscular injection (IM) into the deltoid up to 12 weeks apart (target 4 weeks) which induced maximum humoral and cellular immune responses against SARS-CoV-2.25,26,27 It can be kept in the refrigerator at temperatures ranging from +2˚C to +8˚C. When opened, multi-portion vials should be used as soon as practically possible and within 6 hours if held between 2˚C to 25˚C.28 It has shown the general efficacy of 70.42% in primary analysis population (Licensing regimen + Exploratory analysis) in the trials carried out in the UK and Brazil.26,28 Same vaccine shows only 22% efficacy according to preliminary South African data. It might be the reason of new variant 501Y.V2 (B.1.351), which is resistant to both natural and vaccine-induced immunity.29 Due to the South Africa variant (B.1.351), Shabir AM *et al.* found just 10.4 percent vaccine effectiveness and vaccine did not provide defense against mild-moderate Covid-19. However, the vaccine's effectiveness against the UK strain (B.1.1.7) of SARS-CoV-2 is comparable to that of other lineages.30 So it may not be effective in new variants. It is available at rate Rs. 600/- (8.04$) for private hospital per dose.31 Injection site tenderness (>60%); injection site discomfort, headache, exhaustion (>50%); myalgia, malaise (>40%); pyrexia, chills (>30 %); and arthralgia, nausea (>20 %) were the most commonly recorded unfavorable reactions. The majority of adverse reactions were mild to moderate in intensity

and apparently went away after a few day. By day 7 the incidence of subjects with at least one local or systemic reaction was 4% and 13%, respectively. As compared to the first dose, the second dose's adverse reactions were milder and were recorded less frequently.25,27,28 In the case report reported by Marie S *et al.*, anti-PF4 antibodies were observed 6 to 24 days after receiving the first dose of Covishield, unrelated to the use of heparin therapy, in a case report of 23 mostly young, usually healthy patients who presented with atypical thrombosis, mainly involving cerebral veins, and thrombocytopenia..32 With the exception of one patient who presented with fatal intracranial haemorrhage, Andreas G *et al.* confirmed that 11 original patients starting 5 to 16 days after vaccination presented with one or more thrombotic events; nine had cerebral venous thrombosis, three had splanchnic-vein thrombosis, three had pulmonary embolism, and four had other thromboses; six of these patients died.33 Chatterjee S *et al*. has reported a case of myocardial infraction post vaccination after 2 days.34 National Adverse event following immunization (AEFI) has documented which include myocardial infraction, cardiac death, trigger pro-thrombotic state, cardiovascular event, hypertensive emergency and anaphylaxis as adverse events in 11 patients and among them 10 had loss their lives.35 Although a causal link has yet to be established, viral vector, a vaccine additive, or a flaw in the manufacturing process may all play a role.32,36

Covaxin

The virus strain (NIV-2020-770) with the Asp614Gly mutation, which was isolated and sequenced from a Covid-19 patient, was used to produce BBV152. It is an entire virion β-propiolactone-inactivated SARS-CoV-2 vaccine with a toll-like receptor (TLR) 7/8 agonist molecule absorbed to alum (Algel-IMDG). To induce full cell mediate response, it injects intramuscularly in to deltoid muscle at a volume of 0.5ml/dose in two-dose regimen 28 days apart. It can be stored in the refrigerator at temperatures ranging from +2˚C to +8˚C, which is ideal for immunization cold chains. A Phase 3 clinical trial with 25,800 participants is ongoing, with interim analysis results indicating vaccine efficacy of 81 percent..37,38,39Sapkal GN *et al.* study shown that this vaccine is effective against B1.1.7 variant.40 It is available at the rate Rs. 1200/- (16.08$) for private hospital.41 Pain and swelling at the injection site were listed as local adverse effects, while fever, weakness or malaise, myalgia, body aches, headache, nausea or vomiting, anorexia, chills, generalised rash and diarrhoea were listed as systemic adverse events.37,38,39 AEFI had document 2 adverse event associated with vaccination which include sweeting, dizziness, anxiety, cold extremities, hypotension and anaphylaxis.35 Detail phase 3 clinical trial report will be revealed imminently, which will give more data with respect to the immunization efficacy and undesirable impact of it.

Sputnik:

Recombinant adenovirus type 26 (rAd26) and recombinant adenovirus type 5 (rAd5), both of which bear the gene for SARS-CoV-2 full-length glycoprotein S, are included in the vaccine (rAd26-s and rAd5-s).42,43 For both recombinant adenoviruses, a complete dose of the vaccine contain 1010 or 1011 viral particles44 and given intramuscularly one followed by another with 21 days apart. The antigen transmitted by adenoviral vectors is known to induce both cellular and humoral immunity after a single immunization, making it useful as an emergency pandemic prevention method. A long-lasting immune response can be achieved by combining two immunizations. It is available in two formulation, frozen and lyophilized dry powder vaccine. For injection per dose, frozen vaccine inoculated at a volume of 0.5 mL and lyophilized dry powder vaccine must be reconstituted in 1 mL of sterile water. Frozen vaccine required -18˚C and lyophilized dry powder vaccine can storage at +2 ˚C to +8˚C. It has shown 91.6% vaccine efficacy.42,43,44 It is equally effective in case of B1.1.7 variant and in case of B1.351 variant it has shown only minimal efficacy but better than other available vaccines.45,46,47 It is expected to be accessible in India by end of May 2021 at the rate less than 10$ per dose.48,49 Immunization with this vaccine is linked to mild adverse events such as discomfort at the injection site (58%), hyperthermia (50%), headache (42%), asthenia (28%), muscle and joint pain (28%). There were no severe adverse events identified

Conclusion

Extensive research has been being carried out on SARSCoV-2 and its different variants to combat them with the new treatment strategies. With the continued enormously hard efforts to prevent the spread of SARSCoV-2 globally, Some strategies like vaccination, social distancing, self-quarantine, stay home, stay safe, night curfew, partial or complete lockdown, maintaining hygiene, wearing masks, and using hand sanitizer frequently have been imposed to control the transmission of COVID-19. Presently, multiple vaccines have been approved, which are significantly efficacious toward prevention of COVID-19. Some of them In the current review, we presented the latest advancements in the treatment of COVID-19 patients. Along with supportive therapies, no specific treatment has been introduced for COVID-19. The efficacy of some antivirals, convalescent plasma transfusion, and many similar cases need to bestudied in more clinical trials

References

1) Jebril N. World Health Organization declared a pandemic public health menace: a systematic review of the coronavirus disease 2019 “COVID-19”. 2020. Available at: SSRN 3566298.
2) Worldometer. COVID-19 Coronavirus pandemic. Available from: https://www.worldometers.info/coronavirus/?%3D%3D; 2021.
3) Chan KW, Wong VT, Tang SCW. COVID-19: an update on the epidemiological, clinical, preventive and therapeutic evidence and guidelines of integrative Chinese–Western medicine for the management of 2019 novel coronavirus disease. Am J Chin Med 2020;48:737–62. 03.
4) Vellingiri B, , et alRajagopalan K. COVID-19: a promising cure for the global panic. Sci Total Environ 2020:138277.
5) Shankar A, et al. Role of complementary and alternative medicine in prevention and treatment of COVID-19: an overhyped hope. Chin J Integr Med 2020;26:565–7.
6) Ni L, et al. Combination of western medicine and Chinese traditional patent medicine in treating a family case of COVID-19. Front Med

2020;14(2):210–4.
7) Luo L, et al. Analysis on herbal medicines utilized for treatment of COVID-19. Acta Pharm Sin B 2020;10(7):1192–204.
8) Aucoin M, et al. A systematic review on the effects of Echinacea supplementation on cytokine levels: Is there a role in COVID-19? Metabolism open. 2021. p. 100115
9) Kritis P, et al. The combination of bromelain and curcumin as an immune-boosting nutraceutical in the prevention of severe COVID-19. Metabolism Open 2020;8: 100066.
10) Vallianou NG, et al. Anti-viral treatment for SARS-CoV-2 infection: a race against time amidst the ongoing pandemic. Metabolism open 2021:100096.
11) Ang L, et al. Herbal medicine for the treatment of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis of randomized controlled trials. J Clin Med 2020;9(5):1583.
12) Panyod S, Ho C-T, Sheen L-Y. Dietary therapy and herbal medicine for COVID-19 prevention: a review and perspective. Journal of traditional and complementary medicine 2020;10(4):420–7.
13) Lam TT-Y, et al. Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins. Nature 2020;583(7815):282–5.
14) Wang D, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. Jama 2020;323(11):1061–9.
15) Xu J, Zhang Y. Traditional Chinese medicine treatment of COVID-19. Compl Ther Clin Pract 2020;39:101165.
16) Liu L-S, et al. The effects and mechanism of Yinqiao Powder on upper respiratory tract infection. Int J Biotechnol Wellness Ind 2015;4(2):57–60.
17) Aldwihi LA, et al. Patients' behavior regarding dietary or herbal supplements before and during COVID-19 in Saudi Arabia. Int J Environ Res Publ Health 2021; 18(10):5086.
18) Süntar I. Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. Phytochemistry Rev 2020;19(5):1199–209.
19) Zeng F, et al. Association of inflammatory markers with the severity of COVID-19: a meta-analysis. Int J Infect Dis 2020;96:467–74.
20) Dai L, Gao GF. Viral targets for vaccines against COVID-19. Nature Reviews Immunology. 2020 Dec 18:1-10
21) Everything we know about the Indian COVID-19 variant so far, 21 April 2021. https://www.weforum.org/agenda/2021/04/indian-coronavirus-variant-vaccines-contagious-questions
22) Dalerba P, Levin B, Thompson JL. A Trial of Lopinavir–Ritonavir in Covid-19. N Engl J Med 382; 21.
23) Khalili JS, Zhu H, Mak NSA, Yan Y. Novel coronavirus treatment with ribavirin: Groundwork for an evaluation concerning COVID-19. J Med Virol. 2020; 1–7.
24) Ríos DG, VA, Agudelo López, Ramírez-Malule H. Repurposing antivirals as potential treatments for SARSCoV-2: From SARS to COVID-19. Journal of Applied Pharmaceutical Science Vol.2020; 10(05):001-009.
25) Hung IFN, Lung KC, Tso EYK, Liu R et al. Triple combination of interferon beta-1b, lopinavir–ritonavir, nd ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trials. Lancet 2020; 395: 1695–704.
26) Li H, Liu SM, Yu XH, Tang SL et al. Coronavirus disease 2019 (COVID-19): current status and future perspectives. Int J Antimicrob Agents. 2020 May; 55(5): 105951.
27) Cunningham AC, Goh HP, Koh D. Treatment of COVID-19: old tricks for new challenges. Critical Care (2020) ;24(91):1-2.
28) Mair-Jenkins J, Saavedra-Campos M, Baillie JK, ClearyP. The Effectiveness of Convalescent Plasma and Hyperimmune Immunoglobulin for the Treatment of Severe Acute Respiratory Infections of Viral Etiology: A Systematic Review and Exploratory Meta-analysis. J Infect Dis 2015 Jan 1; 211(1):80-90.
29) Zeng QL, Yu ZJ, Gou JJ, Li GM. Effect of Convalescent Plasma Therapy on Viral Shedding and Survival in COVID-19Patients. J Infect Dis. 2020:1-16.
30) Luo P, Liu Yi, Qiu L, Liu X. Tocilizumab treatment in COVID-19: A single center experience. Tocilizumab treatment in COVID-19: A single center experience. J Med Virol. 2020; 1–5.
31) Le TT, Andreadakis, Z, Kumar A, Roman GR. The COVID-19 vaccine development landscape. Nature Reviews Drug Discovery. 2020; 19: 305-306.
32) Retrieved from http://www.pharmabiz.com/NewsDetails. aspx?aid=126573&sid=1 on June 5, 2020.
33) Derbyshire E, Delange J. bmjnph 2020;0:1–6. doi:10.1136/ bmjnph-2020-000071
34) R. Derwand, M. Scholz. Does zinc supplementation enhance the clinical efficacy of chloroquine/hydroxychloroquine to in today's battle against COVID-19? Medical Hypotheses 142(2020) 109815.
35) Westendorf, K.; Žentelis, S.; Wang, L.; Foster, D.; Vaillancourt, P.; Wiggin, M.; Lovett, E.; van der Lee, R.; Hendle, J.; Pustilnik, A.; et al. LY-CoV1404 (bebtelovimab) potently neutralizes SARS-CoV-2 variants. BioRxiv 2022, preprint. [CrossRef]
36) Humeniuk, R.; Mathias, A.; Cao, H.; Osinusi, A.; Shen, G.; Chng, E.; Ling, J.; Vu, A.; German, P. Safety, Tolerability, and Pharmacokinetics of Remdesivir, An Antiviral for Treatment of COVID-19, in Healthy Subjects. Clin. Transl. Sci. 2020, 13, 896–906. [CrossRef]
37) EMA Veklury RCP. Available online: https://www.ema.europa.eu/en/documents/product-information/veklury-epar productinformation_ro.pdf (accessed on 15 March 2022).
38) Gottlieb, R.L.; Vaca, C.E.; Paredes, R.; Mera, J.;Webb, B.J.; Perez, G.; Oguchi, G.; Ryan, P.; Nielsen, B.U.; Brown, M.; et al. Early Remdesivir to Prevent Progression to Severe COVID-19 in Outpatients. N. Engl. J. Med. 2022, 386, 305–315. [CrossRef]
39) Ader, F.; Bouscambert-Duchamp, M.; Hites, M.; Peiffer-Smadja, N.; Pissy, J.; Belhadi, D. Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): A phase 3, randomized, controlled, open-label trial. Lancet Infect. Dis. 2022, 22, 209–221. [CrossRef]
40) Vermillion, M.S.; Murakami, E.; Ma, B.; Pitts, J.; Tomkinson, A.; Rautiola, D.; Babusis, D.; Irshad, H.; Siegel, D.; Kim, C.; et al. Inhaled

remdesivir reduces viral burden in a nonhuman primate model of SARS-CoV-2 infection. Sci. Transl. Med. 2021, 14, eabl828. [CrossRef]

41) Coronavirus (COVID-19) Update: FDA Approves First COVID-19 Treatment for Young Children. Available online: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-approves-first-covid-19 -treatment-young-children (accessed on 1 May 2022).
42) Patanjali Ayurved (2020) Swasari Coronil Kit. Retrieved from https://www.patanjaliayurved.net/product/ayurvedic-medicine/packages-for diseases/swasaricoronil- kit/3262
43) Awasthi, P. (2020, July) Coronil controversy the latest to embroil Patanjali. Retrieved from https://www.thehindubusinessline.com/news/national/patanjalis-coronil-to-be-sold-asimmunity- booster-not-cure/article31968666.ece
44) Bharat biotech. COVAXIN®® - India's First Indigenous COVID-19 Vaccine. Covid fact sheet. https://www.bharatbiotech.com/images/Covaxin®/Covaxin®-fact-sheet.pdf
45) PTI (2020, August) Coronavirus | Coronil demand at 10 lakh packs a day, says Baba Ramdev, Retrieved from https://www.thehindu.com/business/Industry/coronavirus-coronil-demand-atmany- lakh-packs-a-day-says-baba-ramdev/article32282831.ece
46) Shukla. R (2020, June 25) Coronil: All You Need To Know About Controversy Around Baba Ramdev's Ayurvedic Medicine For COVID-19. Retrieved from https://www.healthwire.co/coronilall- you-need-to-know-about-controversy-around-baba-ramdevs-ayurvedic-medicine-for-covid-19

World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

CURRENT SCENARIO OF HIV/AIDS, TREATMENT OPTIONS, AND MAJOR CHALLENGES WITH COMPLIANCE TO ANTIRETROVIRAL THERAPY

***[1]Jackson Kom, [2]Dr. Gaurav Kumar Sharma, [3]Ankita Sharma, [4]Dr. Kaushal K. Chandrul**

[1]Student of B.Pharma 4th Yr., [2]H.O.D, [3]Assistant Professor, [4]Principal
Department of Pharmacy, MEWAR UNIVERSITY, Chittaurgarh, India.

Corresponding Author: Jackson Kom
Student of B.Pharma 4th Yr., Department of Pharmacy, MEWAR UNIVERSITY, Chittaurgarh, India

Article Received on 13/06/2020 **Article Revised on 03/07/2020** **Article Accepted on 24/07/2020**

ABSTRACT

The discovery of the human immunodeficiency virus (HIV) as the causative organism of acquired immunodeficiency syndrome (AIDS) and the inability of modern medicine to find a cure for it has placed HIV as one of the most dreaded pathogens of the 21st century. With millions of people infected with HIV, it was once thought to result in "medical apocalypse". However, with the advent of antiretroviral therapy (ART), it is now possible to control HIV. Adherence to ART helps to keep the viral load under control and prolong the time of progression to AIDS, resulting in near normal life expectancy. Even with the introduction of ART, a substantial number of patients fail to adhere due to a variety of reasons, including adverse side effects, drug abuse, mental disorders, socioeconomic status, literacy, and social stigma. With the availability of so many options for HIV treatment at each stage of the disease progression, physicians can switch between the treatment regimens to avoid and/or minimize the adverse effects of drugs. Close monitoring, major social reforms, and adequate counselling should also be implemented to circumvent other challenges.

KEYWORDS: hiv, aids, drug adverse effects, hiv/aids, highly active antiretroviral therapy (haart), antiretroviral therapy, clinical managment

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is a medical condition caused by the human immunodeficiency virus (HIV). HIV infection is a very current threat and can easily be termed as a curse upon the human race. The scientific community first noticed and recognized the presence of AIDS as an actual disease following an increase in the incidence of very rare opportunistic infections and cancers among otherwise healthy homosexual men.[1] HIV-1 was identified as the causative organism soon after the first official recognition of HIV patients in the USA.[2] HIV-2 was reported first in Africa in 1985 and is markedly different from HIV1.[3] It closely resembles a simian virus that infects macaques in captivity. Simian viruses that naturally infect African primates are suspected to reach humans via multiple cross-species transmissions resulting in the spread of HIV-1 and HIV-2.[2] The global prevalence of HIV has expanded since its discovery and has now spread across the globe despite advances in antiretroviral treatments (ART). The mortality and morbidity rates related to HIV infections remain high in developing countries largely due to food insecurity and malnutrition.[4] Longterm concomitant sexual relationships and high infectivity during the early phase of HIV infections are other factors behind the extensive spread of HIV in the general population.[5]

The infection

The main site of the attack is the immune system, especially the CD4 T-lymphocytes (CD4 cells). Once infected, the virus gradually and silently overpowers the host's defense mechanisms, resulting in opportunistic infections and cancers that are otherwise rare. Activated and differentiated CD4 cells have a pivotal role in the activation of cell-mediated and humoral immune systems.[7] HIV infection results in the depletion of CD4 cells in the peripheral blood.[8] Among untreated patients, the depletion continues over a course of several years until the patient succumbs to AIDS. It is the last stage of the HIV infection, and it presents itself anywhere between two and 15 years post-infection.[9] The following figure represents the timeline of HIV infection from the initial infection to the expression of AIDSdefining symptoms (Figure 2).[10]

HIV subgroups HIV -1

HIV-1 is well-known for its extensive genetic diversity. There are four different lineages coming under HIV-1: M, N, O, and P. The most commonly reported HIV virus

across the globe is group M.[2] Group N less prevalent, reported only from Cameroon.[11] Group O is accountable for 1% of the total HIV-1 cases and is mainly found Cameroon and Gabon.[12] Group P is the rarest of all and has been identified in Cameroonian pregnant woman in France.[13] It has a prevalence of 0.06% of total HIV infections.[14]

HIV-2

HIV-2 is most commonly reported in West Africa, with Guinea-Bissau and Senegal having the highest incidence. Eight different types of HIV-2 exist, labeled HIV-A to HIV-H. Group A is reported throughout the sub-Saharan region.[15] Group B is reported more commonly in the Ivory Coast.[16] Due to the sporadic nature of the infection and incidence, C to H are categorized as "dead-end" transmissions that produce no subsequent infections.[2]

Current status of HIV infection and mortality rate

Western, Central Europe, and North America

Approximately 2.4 million individuals are HIV-positive in this region. An estimated 85,000 new HIV infections were reported in 2014, and more than 50% of infections were from the United States of America. About 26,000 AIDS-related deaths were also reported in the same period.[17]

Asia and Pacific

As of 2014, approximately five million individuals were previously infected in Asia and the Pacific, with as many as 340,000 new HIV infections arising that year. China, Indonesia, and India contribute to about 78% of the total new disease burden in Asia and the Pacific with about 240,000 deaths. Patients receiving ART are approximately 36%, with 3.2 million active HIV patients having no access to ART.[17]

Pakistan

In Pakistan, the index case of HIV infections was reported in 1987.[18] As per the annual report of Pakistan National AIDS Control Program, the incidence of HIV has been increasing since first reported. According to UNAIDS, the joint United Nations program on HIV/AIDS, the total number of individuals with an active HIV infection is approximately 94,000. The prevalence rate among adults is between < 0.1% and 0.2%. Currently, there are as many as 26,000 women, age 15 and older, and approximately 2,100 children, up to age 14, currently living with HIV. The total number of AIDS-related deaths in this region was 2,800 in the year 2014.[19]

Treatments options for HIV

HIV infection has a very complex pathogenesis and varies substantially in different patients. Therefore, it can easily be considered as a very host-specific infection. The specificity of pathogenesis often complicates treatment options that are currently available for HIV infection.[20] Effective management of HIV infection is possible using different combinations of available drugs. This method of treatment is collectively known as antiretroviral therapy (ART). Standard ART is comprised of a concoction of at least three medicines (termed as "highly active antiretroviral therapy" or HAART).[21] Effective ART often helps control the multiplication of HIV in infected patients and increases the count of CD4 cells, thus, prolonging the asymptomatic phase of infection, slowing the progression of the disease, and also helps in reducing the risk of transmission. Figure 3 demonstrates the percentage of HIV patients under ART.[22]

FDA-approved HIV drug classes Reverse Transcriptase Inhibitors

Reverse transcriptase inhibitors are a group of drugs, which can bind and inhibit the reverse transcriptase enzyme to intercept the multiplication of HIV. There are two types of inhibitors: non-nucleoside reverse transcriptase inhibitors (NNRTIs)[23] and nucleoside reverse transcriptase inhibitors (NRTI).[24] Examples of this group of drugs include zidovudine, didanosine, abacavir, tenofovir, and Combivir.

Protease Inhibitor

Regulation of HIV protease is of high importance for the correct assembly and production of HIV. Protease inhibitors effectively block the functioning of protease enzymes in acutely and chronically HIV-infected CD4 cells. Inhibition of HIV protease enzymes results in the liberation of immature and noninfectious viral particles.[25] Examples of this group of drugs include lopinavir/ritonavir, indinavir, ritonavir, nelfinavir, and amprenavir.

Fusion Inhibitors

This class of drugs acts by blocking HIV from entering the CD4 cells of infected patients. They inhibit the fusion of HIV particles with the CD4 cells.[26] Enfuvirtide is an example of a fusion inhibitor used in HIV treatment.

Chemokine Receptor 5 Antagonist

This group of drugs prevents the infection by blocking the chemokine receptor 5 (CCR5) antagonist receptor present on CD4 cells. In the absence of vacant CCR5 receptors, HIV fails to gain entry and infect the cell.[27] Maraviroc is an example of a CCR5 antagonist used in HIV treatment.

Integrase Strand Transfer Inhibitors

Strand transfer inhibitors prevent the integration of viral DNA into the host genome of CD4 cells by an integrase enzyme. Blocking integrase prevents HIV from replicating.[28] Raltegravir, elvitegravir, and dolutegravir are some medications in this category.

Treatment regimen for HIV

Present HIV treatment guidelines recommend ART treatment for all patients, irrespective of the CD4 cell count, to improve and prolong the progression of disease

to AIDS.[29] Adherence to treatment is of paramount importance in order to achieve the full efficacy of treatment and also to prevent the incidence of drug resistance.[30]

Latest WHO recommendations for ART A concise form of first, second, and third line treatment options recommended by the World Health Organization (WHO) is given below.[29]

First-line ART

Adults: First-line ART treatment for adults consists of two NRTIs and one NNRTI. Tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) or emtricitabine (FTC) + efavirenz (EFV) as a fixed dose is the favored choice for this type of ART. When this drug combination is contraindicated or is unavailable, 1) zidovudine (AZT) + 3TC + EFV, 2) AZT + 3TC + nevirapine (NVP), or 3) TDF + 3TC (or FTC) + NVP is used.

Contraindications

1. Creatinine clearance is less than 50 ml per minute: Tenofovir. 2. Patients on psychoactive drug treatment: Efavirenz. 3. Patients who are pregnant or who are trying to conceive: Efavirenz. 4. ALT elevation: Nevirapine.

Pregnant and breastfeeding patients: First-line ART in this subpopulation is comprised of a single daily dose of TDF + 3TC (or FTC) + NVP. Breastfeeding infants of mothers who are receiving ART must receive six weeks of infant prophylaxis with a daily dose of NVP. The preventive medication should commence immediately post-delivery or when HIV exposure is identified.

Pediatric patients: Patients below three years of age should be given Lopinavir/Ritonavir (LPV/r)-based treatment, even under NNRTI exposure. When LPV/r is not a viable option, NVPbased treatment should be used. For infected children who are over age three, EFV is the ideal NNRTI while NVP has been identified as the second option. For infected children younger than three years of age, who develop TB while on the Lopinavir/Ritonavir (LPV/r)-based treatment, the NRTI regimen should be switched to abacavir (ABC) + 3TC or AZT + 3TC until the TB infection is cleared. NRTI regimens similar to that of adults (TDF + 3TC (or FTC)) or (AZT + 3TC) or (ABC + 3TC) are preferred for patients between 10 and 19 years of age who weigh 35 kg or more.

Second-line ART

Adults, including pregnant and breastfeeding patients: When a first-line treatment of ART fails, a second-line ART should be utilized. The second-line ART is comprised primarily of two NRTIs and a ritonavir-boosted PI. The recommended option for second-line ART includes AZT and 3TC as the NRTI. After the failure of AZT or stavudine (d4T) + 3TC-based first-line regimen, TDF + 3TC (or FTC) as the NRTI should be considered. When first-line NNRTI-based treatment fails, two NRTIs + a boosted PI are suggested

Pediatric patients: For children below three years of age, first-line ART is continued even when it fails. No change itreatment is recommended; instead, adequate steps should be taken to improve adherence to the ART regimen. If first-line ART fails in children ages three and up, a second-line treatment consisting of one NNRTI and two NRTIs should be given. If ABC or TDF + 3TC (or FTC) fails, the recommended option is AZT + 3TC. After a failure of AZT or d4T + 3TC (or FTC) in first-line treatment, the preferred NRTI option is ABC or TDF + 3TC (or FTC).

Third-line ART

If first- and second-line ART fails, the WHO recommends inclusion of new medicines with the least amount of risk for development of cross-resistance towards previously used drugs (e.g. integrase inhibitors and second-generation NNRTIs and PIs).

Factors to consider when selecting ART

The major factors that deserve thorough consideration while choosing an ART for a patient include the viral load and CD4 cell count before the treatment, the result of HIV genotypic drug resistance test, HLA-B*5701 status, patient preferences, and anticipated adherence. Comorbid conditions to screen prior to ART include cardiovascular disease, hyperlipidemia, renal disease, osteoporosis, psychiatric illness, neurologic disease, drug abuse or dependency requiring narcotic replacement therapy, pregnancy, coinfections with hepatitis C (HCV), hepatitis B (HBV), and tuberculosis (TB).[31]

CD4 count monitoring for therapeutic response

Monitoring patients' viral load is critical to identify ART response (WHO 2015). When the viral load analysis is not practical via polymerase chain reaction (PCR), branched chained DNA (bDNA), and nucleic acid sequence-based amplification (NASBA), the CD4 count is used as an indicator of HIV treatment response. During the first year of treatment, increases in CD4 count from 50 to 150 cells/mm3 with an increased response in the first trimester are considered as a positive response. CD4 count rises steadily ranging from 50 to 100 cells/mm3 per year until equilibrium is reached in the subsequent years (normal range: 500 cells/mm3 to 1200 cells/mm3).[32] Periodic monitoring of CD4 count is required during and even after the patient achieves normal CD4 count under ART. A number of treatment independent factors like age, viral load, genetic make-up, lifestyle, quality of health care, etc., negatively influence the CD4 counts and HIV disease progression. Under such circumstances, a change in ART medication might be required.

Major factors for ART non-adherence

Adverse Effects of ART

One of the major challenges that patients and physicians face with ART is the incidence of adverse drug reactions (ADR). ADR is defined as "a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for modification of physiological function".[33] ADR often persuades patients from continuing treatment, thus resulting in suboptimal efficacy. A serious consequence of treatment discontinuation is the emergence of drug resistance, making future therapeutic interventions ineffective.[30]

The major adverse effects of ART can be grouped into the following categories:

1. Gastrointestinal: Nausea, diarrhea, vomiting, taste perversion, constipation, dyspepsia, abdominal pain, hepatotoxicity, and pancreatitis.[34-35] 2. Central nervous system: Headache, vision problems, dizziness, tinnitus, insomnia, paresthesia, pain/numbness/tingling in extremities, peripheral neuropathy, somnolence, excessive sleep at night, memory problems, loss of olfactory function, and hearing impairment.[34] 3. Hematological: Anemia, bilirubinemia, increased urate, and blood in the urine,[35] 4. Psychological: Anxiety, confusion, depression, nightmares, elation, and delusions.[35] 5. Metabolic: Abnormal fat distribution (lipodystrophy), anorexia, dyspnea, fatigue, lethargy, and weight gain.[34-35]

6. Dermatological: Skin rash, facial discoloration, and pruritus.[35] 7. Musculoskeletal: Body aches and vague chest pain.[34] 8. Miscellaneous: Hypersensitive reactions, oral ulcerations, fever, and irregular menstrual cycles.[34]

Drug Abuse

Continuous drug abuse is an important risk factor in HIV/AIDS patients' ART, nonadherence, and mortality.[36] In a study conducted on HIV-positive drug addicts in Canada, heroin and cocaine injections were reported to adversely affect adherence to ART.[37] In a separate sixmonth long longitudinal study, which examined the effect of drug use and abuse on ART among 150 HIV positive patients, it was discovered that acute effects of intoxication negatively influence ART adherence. The major mechanisms by which drug abuse results in ART nonadherence include drug abuse induced neurocognitive/psychosocial impairment and psychiatric dysfunctions.[38]

Mental Disorders

The prevalence of psychiatric disorders is reported to be very high among HIV-infected individuals.[36] In a longitudinal study investigating the mental health, substance abuse, and psychosocial predictors among HIV-positive mothers, the presence of psychiatric disorders, stressful lifestyles, suboptimal living conditions, and parenting stress were associated significantly with ART nonadherence.[39] Childhood sexual violence-induced anxiety and depression may also result in ART nonadherence.[40] Hazardous drinking is another significant precipitator of anxiety and depression among HIV patients that results in ART nonadherence.[41]

Socioeconomic Status

Socioeconomic status is strongly associated with HIV-related mortality in the contemporary universal healthcare system because opportunities for patients of lower socioeconomic status to receive ART are meager. In a study conducted among HIV-positive Cambodian women, 80% of those who discontinued ART were of low socioeconomic status. The estimated risk for low adherence in this population was reported to be five times higher for women than those in a medium or high social position.[42] Poverty-induced stress is an important aspect that has to be addressed in issues regarding ART nonadherence.[43] The quality of housing and access to food are the two most important factors that prevent the poverty-ridden population from ART adherence.[43]

Poor Literacy

Literacy is another major factor closely associated with ART nonadherence with people of lower health literacy experiencing higher illness severity than people with better health literacy.[44] Health literacy has been defined by the WHO as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand, and use information in ways which promote and maintain good health".[45] Many reports suggested that the inability to comprehend medication instructions by illiterate HIV-positive patients is an important factor resulting in failure to follow accurate daily medication therapy.[46]

Social Stigma

The stigma of HIV and AIDS is assumed to have a negative influence on ART 2016 Bhatti et al. Cureus 8(3): e515. DOI 10.7759/cureus.515 8 of 12 adherence.[47] Stigma can be defined as an "attribute that is deeply discrediting" imposed by society that reduces someone "from a whole and usual person to a tainted, discounted one".[48] In a cohort study conducted in five African countries (Lesotho, Malawi, South Africa, Swaziland, and Tanzania) among 1,457 HIV-positive patients over a period of 12 months, individuals perceiving a high HIV stigma reported greater nonadherence to ART. Symptom intensity is also high when compared to those who did not experience such a stigma.[49] One study conducted in South Africa reported that internalized stigma is responsible for 4.8% of the variance in cognitive-affective depression leading to ART nonadherence. Furthermore, the researchers urge the medical community to introduce social reform efforts to reduce stigma and assist people living with HIV/AIDS in adjusting and adapting.[50]

Clinical management

Diagnosis

The diagnosis of HIV-1 infection is based on the detection of specific antibodies, antigens, or both, and many commercial kits are available. Serological tests are generally used for screening. A major advance has been the availability of rapid HIV-1 antibody tests. These assays are easy to do and provide results in as little as 20 minutes,[51] enabling specimen collection and proper diagnosis at the same visit. Rapid tests are important tools for surveillance, screening, and diagnosis, and can be reliably done on plasma, serum, whole blood, or saliva by health-care providers with little laboratory expertise. The two limitations of these serological tests are detection of infection during primary infection when antibodies are absent, and in infants younger than 18 months who might bear maternal HIV-1 antibodies. In these instances direct virus detection is the only option (eg, quantification of viral RNA [standard] or p24 antigen in heat denatured serum [less expensive]).

For staging purposes, measurement of CD4+ cells and viraemia is required. Plasma viral load is widely used to monitor therapeutic success on antiretroviral treatment. Several commercially available tests provide sensitive quantification of plasma HIV-1 RNA copies. The newer versions of the Amplicor and Quantiplex (Roche, Indianapolis, IN, USA, and Bayer Diagnostics, Walpole, MA, USA, respectively) assays have overcome initial suboptimum performance for non-B subtypes.102 While the viral load determines the rate of destruction of the immune system, the number of CD4+ cells reveals the degree of immunodeficiency and is, therefore, used to assess the stage of infection. CD4+ cell counts together with clinical manifestations (eg, occurrence of opportunistic infections) are key criteria for HIV-1 disease classification. Flow cytometry analysis is the standard method for CD4+ cells quantification.

Standard methods for quantifying viral load and CD4+ cell counts need advanced laboratory infrastructures, and assays require a specimen to be tested within a short time of collection. These requirements pose challenges for resource-constrained settings. The use of dried blood spot specimen has resolved some of the difficulties associated with transportation of samples needed for virological assessments.[53] Measurement of reverse transcriptase activity in plasma samples, simplification of gene amplification methods (eg, Taqman technology), and paper-strip quantification (dipstick assays) might provide cost-effective alternatives for the future.[54–56] Similarly microcapilliary flow-based systems, CD4+ chips, or total white counts (panleucocyte gating) provide alternatives for establishment of the level of immunodeficiency in resource-limited settings.[57–60]

Drug treatment

Antiretroviral compounds

Antiretroviral treatment is the best option for longlasting viral suppression and, subsequently, for reduction of morbidity and mortality. However, current drugs do not eradicate HIV-1 infection and lifelong treatment might be needed. 20 of the 21 antiretroviral dr+ugs currently approved by the US Food and Drug Administration target the viral reverse transcriptase or protease (table 2). Eight nucleoside/ nucleotide analogues and three non-nucleoside reverse transcriptase inhibitors inhibit viral replication after cell entry but before integration. Fixed-dose combination tablets simplify treatment regimens by reducing the daily pill burden, and drugs with long half-lives allow once or twice daily dosing. Eight protease inhibitors prevent the maturation of virions resulting in production of non-infectious particles. The recently approved darunavir (June, 2006) is the first of its class that retains activity against viruses with reduced susceptibility to protease inhibitors. Enfuvirtide targets a gp41 region of the viral envelope and stops the fusion process before the cell is infected. This drug needs to be injected twice daily and its use is reserved for treatment of heavily drug-experienced patients since it can help overcome existing drug resistance.[61,62] Development of new antiretrovirals focuses on molecules that target entry, reverse transcription, integration, or maturation. Compounds that have been designed to inhibit resistant viruses are urgently needed since many patients treated during the past decades harbour viral strains with reduced susceptibilities to many if not all available drugs.

The goal of antiretroviral treatment is to decrease the morbidity and mortality that is generally associated with HIV-1 infection. A combination of three or more active drugs is needed to achieve this aim in most patients. Effective treatment returns to near normal the turnover rates of both CD4+ and CD8+ T-cell populations.[63] Potent but well tolerated drugs with long half-lives and simplified regimens improve the options for first-line and secondline chemotherapeutic interventions.

Combination antiretroviral treatment

High rate of viral replication, low fidelity of reverse transcription, and the ability to recombine are the viral characteristics that lead to the diversity of HIV-1 species (quasispecies) in chronically infected individuals. This high genetic variability provided the rationale for highly active antiretroviral treatments (HAART). By combination of several potent antiretroviral agents, viral replication is suppressed to such low levels that emergence of drug resistant HIV-1 variants was, if not prevented, at least delayed. By doing so, CD4+ T-lymphocyte numbers increase, leading to a degree of immune reconstitution that is sufficient to reverse clinically apparent immunodeficiency. Widespread introduction of HAART in industrialised countries resulted in a striking decrease in morbidity and mortality, putting forward the hope that HIV-1 infection can be transformed into a treatable chronic disease.[64-66]

A set of criteria composed of plasma viraemia concentration, absolute or relative CD4+ cell counts, and

clinical manifestations, is used to recommend initiation of HAART. The benefits of treatment clearly outweigh the potential side-effects in patients with clinical signs of immunodeficiency (eg, AIDS defining illnesses) or with CD4+ numbers less than 200 per μL (recommendation of US Department of Health and Human Services, October, 2005). However, the best time point to begin treatment remains controversial in asymptomatic patients with modest depletion of CD4+ T cells (eg, more than 350 per μL) and modest levels of viraemia (eg, less than 100 000 copies per mL).[67] Studies with clinical endpoints supporting the validity of early versus late interventions in asymptomatic patients are difficult to do and insufficient clinical data are currently available. Early depletion of gut CD4+ T lymphocytes,[68] increasing viral diversity, and the poor regenerative abilities of key populations of the immune system provide arguments for beginning treatment as early as possible. The wide application of this principle is restricted by long-term drug toxicities that lead to reduction of quality of life, and by treatment costs. Toxicities (eg, renal, hepato, mitochondrial), metabolic changes (eg, lipodystrophy, diabetes mellitus), and immune reconstitution disease are some of the long-term problems that complicate decade-long HAART.[69-72]

One strategy addressing life-long daily compliance to HAART has been structured treatment interruptions. The rationale for this approach was based on the premise that the body's own immune system could keep the virus in check if exposed to a very modest level of viral replication. If successful, this strategy could limit drug toxicity and reduce treatment costs.[73] Although preliminary findings for this strategy were mixed in terms of benefits,[74-76] the recent early closure of the SMART trial was based on increased morbidity and mortality in the treatment interruption arm.[77] Thus, in the absence of clinical benefits, most investigators strongly discourage treatment interruptions except as needed to address treatment intolerance.

HAART in resource-constrained settings

The transformation of AIDS into a chronic disease in industrialised countries has yet to be realised in resource-constrained settings. Access to HAART is an absolute humanitarian necessity to avert mortality in people who are central to the future survival of their countries.[78] Despite restricted health infrastructures and diverse co-morbidities in these regions, remarkable therapeutic success rates have been shown, with adherence rates at least comparable with those reported in industrialised countries.[79-82] WHO and UNAIDS treatment guidelines focusing on resource-limited settings suggest use of standard first-line regimen followed by a set of more expensive second-line options.[83] and proposes the use of standardised decision-making steps (eg, when to start, to substitute for side-effects, to switch for virological failure).[83,84] In many countries, treatment options are limited not only by the costs of HAART but also by restrictive licensing policies, and current estimates suggest that 80% of people infected with HIV-1 with a clinical need for treatment do not yet have access to antiretroviral drugs.1 Thus, efforts and strategies to further scale up treatment access are crucial,[85-88] since antiretroviral treatment is also an effective intervention for prevention.[89]

Drug resistance

Emergence of drug resistance is the most common reason for treatment failure. Insufficient compliance, drug side-effects, or drug-drug interactions can lead to suboptimum drug concentrations, resulting in viral rebound. Viral resistance has been described to every antiretroviral drug and therefore poses a serious clinical as well as public-health problem.[90] HIV-1 subtypes differ in the sequence of mutations leading to drug resistance, and some naturally occurring polymorphisms might actually modulate resistance.[91,92] Drug-resistant HIV-1 is transmissible and can be detected in up to 20% of newly infected individuals in countries with broad access to antiretrovirals.34 The prevalence of drug resistance in the untreated population remains low in regions with poor access to treatment.[93]

Short-term antiretroviral-based interventions are effective in prevention of mother-to-child transmission. However, these interventions could result in drug resistant viral variants in the mother, baby, or both.[94] Around half the women who received one dose of nevirapine to prevent mother-to-child transmission harbour viruses resistant to non-nucleoside reverse transcriptase inhibitors (NNRTI).[95,96] These resistant viruses replicate efficiently and canbe transmitted by breast milk,[97] and minor resistant populations present long after the intervention can possibly decrease the effectiveness of subsequent NNRTI-based treatment regimens.[98] The combination of short-course zidovudine, lamivudine, and nevirapine prevents peripartum transmission while reducing the risk of nevirapine resistant viruses.[99]

CONCLUSIONS

Recent advances in HIV treatments have dramatically altered the nature and progression of HIV/AIDS. It can be safely considered as a "chronic" disease, provided the infected patients receive proper ART. Unfortunately, current statistics of the worldwide HIV burden tells another story: one with a steady rate of HIV-related deaths. More people die of complications and the progression of HIV to AIDS than should be when ART is used properly. The major hurdle a physician faces with ART is the incidence of adverse side effects of the treatment, which persuade patients to discontinue the treatment. Poverty, lack of awareness, and the social stigma associated with the infection complicate an already complicated situation. Appropriate changes in treatment regimens and medications can help patients overcome such adverse effects and potential complications inherent to the disease. Additionally, it is highly advisable to provide patients and their immediate

family members with appropriate counseling for treatment compliance and psychological support.

REFERENCE

1. Friedman-Kien A, Laubenstein L, Marmor M, Hymes K, Green J, Ragaz A, Gottleib J, Muggia F, Demopoulos R, Weintraub M: Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men--New York City and California. MMWR Morb Mortal Wkly Rep., 1981; 30: 305–308.
2. Sharp PM, Hahn BH : Origins of HIV and the AIDS pandemic. Cold Spring Harb Perspect Med. 2011, 1:a006841. Accessed: December 28, 2015. http://perspectivesinmedicine.cshlp.org/content/1/1/a006841.full.pdf+html. 10.1101/cshperspect.a006841.
3. Barin F, M'Boup S, Denis F, Kanki P, Allan JS, Lee TH, Essex M: Serological evidence for virus related to simian T-lymphotropic retrovirus III in residents of west Africa. Lancet., 1985; 2: 1387–89. 10.1016/S0140-6736(85): 92556-5.
4. Dellar R, Karim QA: HIV/AIDS food insecurity, and undernourishment: amplifying cycles of risk in vulnerable populations. Handbook of Public Health in Natural Disasters: Nutrition, Food, Remediation and Preparation, 1st edition. Watson RR, Tabor JA, Ehiri JE, Preedy VR (ed): Wageningen Academic Publishers, Wageningen, Netherlands; 2015; 10: 537–562. 10.3920/978-90-8686-806-3_31.
5. Eaton JW, Hallett TB, Garnett GP: Concurrent sexual partnerships and primary HIV infection: A critical interaction. AIDS Behav, 2011, 15: 687–92. 10.1007/s10461-010-9787-8.
6. WHO: Global summary of the HIV/AIDS epidemic, December 2014. (2015). Accessed: December 6, 2015. http://www.who.int/hiv/data/epi_core_july2015.png?ua=1.
7. Luckheeram RV, Zhou R, Verma AD, Xia B: CD4+T cells: Differentiation and functions. Clin Dev Immunol. 2012, 2012 :925135. Accessed: December 28, 2015.
8. Brenchley JM, Schacker TW, Ruff LE, Price DA, Taylor JH, Beilman GJ, Nguyen PL, Khoruts A, Larson M, Haase AT, Douek DC: CD4+ T cell depletion during all stages of HIV disease occurs predominantly in the gastrointestinal tract. J Exp Med, 2004, 200: 749–59. 10.1084/jem.20040874
9. Moss AR, Bacchetti P, Osmond D, Krampf W, Chaisson RE, Stites D, Wilber J, Allain JP, Carlson J: Seropositivity for HIV and the development of AIDS or AIDS related condition: three year follow up of the San Francisco General Hospital cohort. Br Med J (Clin Res Ed), 1988; 296: 745–50. 10.1136/bmj.296.6624.745
10. HIV/AIDS. Accessed: December 6, 2015: https://en.wikipedia.org/wiki/HIV/AIDS, 2015.
11. Vallari A, Bodelle P, Ngansop C, Makamche F, Ndembi N, Mbanya D, Kaptué L, Gürtler LG, McArthur CP, Devare SG, Brennan CA.: Four new HIV-1 group N isolates from Cameroon: Prevalence continues to be low. AIDS Res Hum Retroviruses, 2010; 26: 109–15. 10.1089/aid.2009.0178.
12. Peeters M, Gueye A, Mboup S, Bibollet-Ruche F, Ekaza E, Mulanga C, Ouedrago R, Gandji R, Mpele P, Dibanga G, Koumare B, Saidou M, Esu-Williams E, Lombart JP, Badombena W, Luo N, Vanden Haesevelde M, Delaporte E: Geographical distribution of HIV-1 group O viruses in Africa. AIDS, 1997; 11: 493–98. 10.1097/00002030-199704000-00013
13. Plantier JC, Leoz M, Dickerson JE, De Oliveira F, Cordonnier F, Lemée V, Damond F, Robertson DL, Simon F: A new human immunodeficiency virus derived from gorillas. Nat Med, 2009; 15: 871–72. 10.1038/nm.2016
14. Vallari A, Holzmayer V, Harris B, Yamaguchi J, Ngansop C, Makamche F, Mbanya D, Kaptué L, Ndembi N, Gürtler L, Devare S, Brennan CA: Confirmation of putative HIV-1 group P in Cameroon. J Virol, 2011; 85: 1403-1407. 10.1128/JVI.02005-10.
15. de Silva TI, Cotten M, Rowland-Jones SL: HIV- 2: The forgotten AIDS virus. Trends Microbiol, 2008; 16: 588–95. 10.1016/j.tim.2008.09.003.
16. Ishikawa K, Janssens W, Banor JS, Shinno T, Piedade J, Sata T, Ampofo WK, Brandful JA, Koyanagi Y, Yamamoto N, Canas-Ferreira WF, Adu-Sarkodie Y, Kurata T: Genetic analysis of HIV type 2 from Ghana and Guinea-Bissau, West Africa. AIDS Res Hum Retroviruses, 2001; 17: 1661–63. 10.1089/088922201753342077
17. UNAIDS: Fact sheet 2015. (2015). Accessed: December 28, 2015. http://www.unaids.org/en/resources/documents/2015/20150714_factsheet.
18. Khanani RM, Hafeez A, Rab SM, Rasheed S: Human immunodeficiency virus-associated disorders in Pakistan. AIDS Res Hum Retroviruses, 1988; 4: 149–54. 10.1089/aid.1988.4.149.
19. UNAIDS: Pakistan. (2014). Accessed: December 28, 2015. http://www.unaids.org/en/regionscountries/countries/pakistan.
20. Brass AL, Dykxhoorn DM, Benita Y, Yan N, Engelman A, Xavier RJ, Lieberman J, Elledge SJ: Identification of host proteins required for HIV infection through a functional genomic screen. Science, 2008; 319: 921–26. 10.1126/science.1152725.
21. WHO: Antiretroviral therapy. (2015). Accessed: December 28, 2015. http://www.who.int/topics/antiretroviral_therapy/en/.
21. Number of people receiving antiviral therapy (ART) and percentage of all people living with HIV receiving ART in low- and middle-income countries overall and by WHO region, 2013. (2013). Accessed: December 28, 2015. http://www.who.int/hiv/data/artmap2014.png?ua=1.

22. de Béthune MP: Non-nucleoside reverse transcriptase inhibitors (NNRTIs), their discovery, development, and use in the treatment of HIV-1 infection: a review of the last 20 years (19892009). Antiviral Res., 2010; 85: 75–90. 10.1016/j.antiviral.2009.09.008
23. Whitcomb JM, Parkin NT, Chappey C, Hellmann NS, Petropoulos CJ: Broad nucleoside reverse-transcriptase inhibitor cross-resistance in human immunodeficiency virus type 1 clinical isolates. J Infect Dis., 2003; 188: 992–1000. 10.1086/378281.
24. Hughes PJ, Cretton-Scott E, Teague A, Wensel TM: Protease inhibitors for patients with HIV1 infection: A comparative overview. P T., 2011; 36: 332–45.
25. Greenberg ML, Cammack N: Resistance to enfuvirtide, the first HIV fusion inhibitor. J Antimicrob Chemother, 2004; 54: 333–40. 10.1093/jac/dkh330
26. Rao PKS: CCR5 inhibitors: Emerging promising HIV therapeutic strategy. Indian J Sex Transm Dis., 2009; 30: 1–9. 10.4103/0253-7184.55471
27. Pandey KK, Grandgenett DP: HIV-1 Integrase strand transfer inhibitors: Novel insights into their mechanism of action. Retrovirology (Auckl), 2008; 2: 11–16.
28. WHO:Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. (2015). Accessed: December 28, 2015. http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/.
29. Olem D, Sharp KM, Taylor JM, Johnson MO: Overcoming barriers to HIV treatment adherence: A brief cognitive behavioral intervention for HIV-positive adults on antiretroviral treatment. Cogn Behav Pract., 2014; 21: 206–23. 10.1016/j.cbpra.2013.09.003.
30. AIDS Info: Clinical guidelines Portal. Guidelines for the use of antiretroviral agents in HIV-1infected adults and adolescents. (2015). Accessed: December 6, 2015. http://aidsinfo.nih.gov/guidelines.
31. Kaufmann GR, Perrin L, Pantaleo G, Opravil M, Furrer H, Telenti A, Hirschel B, Ledergerber B, Vernazza P, Bernasconi E, Rickenbach M, Egger M, Battegay M; Swiss HIV Cohort Study Group: CD4 T-lymphocyte recovery in individuals with advanced HIV-1 infection receiving potent antiretroviral therapy for 4 years: the Swiss HIV Cohort Study. Arch Intern Med, 2003; 163: 2187–95. 10.1001/archinte.163.18.2187.
32. WHO: International drug monitoring: The role of national centers. Report of a WHO meeting . (1972). Accessed: December 28, 2015. http://apps.who.int/iris/bitstream/10665/40968/1/WHO_TRS_498.pdf.
33. Nagpal M, Tayal V, Kumar S, Gupta U: Adverse drug reactions to antiretroviral therapy in AIDS patients at a tertiary care hospital in India: A prospective observational study. Indian J Med Sci., 2010; 64: 245–52. 10.4103/0019-5359.99597.
34. Tadesse WT, Mekonnen AB, Tesfaye WH, Tadesse YT: Self-reported adverse drug reactions and their influence on highly active antiretroviral therapy in HIV infected patients: a cross sectional study. BMC Pharmacol Toxicol. 2014, 15:32. Accessed: December 28, 2015. http://bmcpharmacoltoxicol.biomedcentral.com/articles/10.1186/2050-6511-15-32. 10.1186/2050-6511-15-32
35. Ingersoll K: The impact of psychiatric symptoms, drug use, and medication regimen on nonadherence to HIV treatment. AIDS Care. 2004, 16:199–211. 10.1080/09540120410001641048.
36. Azar P, Wood E, Nguyen P, Luma M, Montaner J, Kerr T, Milloy MJ: Drug use patterns associated with risk of non-adherence to antiretroviral therapy among HIV-positive illicit drug users in a Canadian setting: a longitudinal analysis. BMC Infect Dis., 2015; 15: 193. Accessed: December 28, 2015: http://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-015-0913-0. 10.1186/s12879015-0913-0
37. Chang L, Ernst T, Speck O, Patel H, DeSilva M, Leonido-Yee M, Miller EN: Perfusion MRI and computerized cognitive test abnormalities in abstinent methamphetamine users. Psychiatry Res., 2002; 114: 65–79. 10.1016/S0925-4927(02)00004-5.
38. Mellins CA, Kang E, Leu CS, Havens JF, Chesney MA: Longitudinal study of mental health and psychosocial predictors of medical treatment adherence in mothers living with HIV disease. AIDS Patient Care STDS, 2003; 17: 407–16. 10.1089/108729103322277420.
39. Willie TC, Overstreet NM, Sullivan TP, Sikkema KJ, Hansen NB: Barriers to HIV medication adherence: Examining distinct anxiety and depression symptoms among women living with HIV who experienced childhood sexual abuse. Behav Med, 2016; 42: 120-27. 10.1080/08964289.2015.1045823.
40. Garey L, Bakhshaie J, Sharp C, Neighbors C, Zvolensky MJ, Gonzalez A: Anxiety, depression, and HIV symptoms among persons living with HIV/AIDS: the role of hazardous drinking. AIDS Care, 2015; 27: 80–85. 10.1080/09540121.2014.956042.
41. Arrivillaga M, Ross M, Useche B, Alzate ML, Correa D: Social position, gender role, and treatment adherence among Colombian women living with HIV/AIDS: social determinants of health approach. Rev Panam Salud Publica, 2009; 26: 502–10. 10.1590/S10204989200900120005.
42. Kalichman SC, Grebler T: Stress and poverty predictors of treatment adherence among people with low-literacy living with HIV/AIDS. Psychosom Med, 2010; 72: 810–16. 10.1097/PSY.0b013e3181f01be3.
43. Kalichman SC, Rompa D: Functional health literacy is associated with health status and health-related knowledge in people living with HIV-AIDS. J

Acquir Immune Defic Syndr, 2000; 25: 337–44. 10.1097/00042560-200012010-00007.
44. Nutbeam D: Health promotion glossary. Health Promotion International, 1998; 13: 349–64.
45. Waldrop-Valverde D, Jones DL, Weiss S, Kumar M, Metsch L: The effects of low literacy andcognitive impairment on medication adherence in HIV-positive injecting drug users. AIDS Care, 2008; 20: 1202–10. 10.1080/09540120801927017.
46. Rintamaki LS, Davis TC, Skripkauskas S, Bennett CL, Wolf MS: Social stigma concerns and HIV medication adherence. AIDS Patient Care STDS, 2006; 20: 359–68. 10.1089/apc.2006.20.359.
47. Goffman E: Stigma and social identity. Stigma: Notes on the Management of Spoiled Identity. Goffman E (ed): Simon and Schuster, New York, 1963; 1–40.
48. Dlamini PS, Wantland D, Makoae LN, Chirwa M, Kohi TW, Greeff M, Naidoo J, Mullan J, Uys LR, Holzemer WL: HIV stigma and missed medications in HIV-positive people in five African countries. AIDS Patient Care STDS, 2009; 23: 377–87. 10.1089/apc.2008.0164.
49. Simbayi LC, Kalichman S, Strebel A, Cloete A, Henda N, Mqeketo A: Internalized stigma, discrimination, and depression among men and women living with HIV/AIDS in Cape Town, South Africa. Soc Sci Med, 2007; 64: 1823–31. 10.1016/j.socscimed.2007.01.006.
50. Greenwald JL, Burstein GR, Pincus J, Branson B. A rapid review of rapid HIV antibody tests. Curr Infect Dis Rep, 2006; 8: 125–31. [PubMed: 16524549]
51. Berger A, Scherzed L, Sturmer M, Preiser W, Doerr HW, Rabenau HF. Comparative evaluation of the Cobas Amplicor HIV-1 Monitor Ultrasensitive test, the new Cobas AmpliPrep/Cobas Amplicor HIV-1 Monitor Ultrasensitive test and the Versant HIV RNA 3.0 assays for quantitation of HIV-1 RNA in plasma samples. J Clin Virol, 2005; 33: 43–51. [PubMed: 15797364
52. Uttayamakul S, Likanonsakul S, Sunthornkachit R, et al. Usage of dried blood spots for molecular diagnosis and monitoring HIV-1 infection. J Virol Methods, 2005; 128: 128–34. [PubMed: 15913797]
53. Jennings C, Fiscus SA, Crowe SM, et al. Comparison of two human immunodeficiency virus (HIV) RNA surrogate assays to the standard HIV RNA assay. J Clin Microbiol, 2005; 43: 5950– 56. [PubMed: 16333081]
54. Lombart JP, Vray M, Kafando A, et al. Plasma virion reverse transcriptase activity and heat dissociation-boosted p24 assay for HIV load in Burkina Faso, West Africa. AIDS, 2005; 19: 1273–77. [PubMed: 16052082]
55. Tuaillon E, Gueudin M, Lemee V, et al. Phenotypic susceptibility to nonnucleoside inhibitors of virion-associated reverse transcriptase from different HIV types and groups. J Acquir Immune Defic Syndr, 2004; 37: 1543–49. [PubMed: 15577405
56. Rodriguez WR, Christodoulides N, Floriano PN, et al. A microchip CD4 counting method for HIV monitoring in resource-poor settings. PLoS Med, 2005; 2: e182. [PubMed: 16013921]
57. Spacek LA, Shihab HM, Lutwama F, et al. Evaluation of a low-cost method, the Guava EasyCD4 assay, to enumerate CD4-positive lymphocyte counts in HIV-infected patients in the United States and Uganda. J Acquir Immune Defic Syndr, 2006; 41: 607–10. [PubMed: 16652034]
58. Mofenson LM, Harris DR, Moye J, et al. Alternatives to HIV-1 RNA concentration and CD4 count to predict mortality in HIV-1-infected children in resource-poor settings. Lancet, 2003; 362: 1625–27. [PubMed: 14630444]
59. Ceffa S, Erba F, Assane M, Coelho E, Calgaro M, Brando B. Panleucogating as an accurate and affordable flow cytometric protocol to analyse lymphocyte subsets among HIV-positive patients on HAART treatment in Mozambique. J Biol Regul Homeost Agents, 2005; 19: 169–75. [PubMed: 16602633
60. Lazzarin A, Clotet B, Cooper D, et al. Efficacy of enfuvirtide in patients infected with drugresistant HIV-1 in Europe and Australia. N Engl J Med, 2003; 348: 2186–95. [PubMed: 12773645]
61. Lalezari JP, Henry K, O'Hearn M, et al. Enfuvirtide, an HIV-1 fusion inhibitor, for drug-resistant HIV infection in North and South America. N Engl J Med, 2003; 348: 2175–85. [PubMed: 12637625
62. Mohri H, Perelson AS, Tung K, et al. Increased turnover of T lymphocytes in HIV-1 infection and its reduction by antiretroviral therapy. J Exp Med, 2001; 194: 1277–87. [PubMed: 11696593
63. Mocroft A, Vella S, Benfield TL, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. Lancet, 1998; 352: 1725–30. [PubMed: 9848347]
64. Hogg RS, Heath KV, Yip B, et al. Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. JAMA, 1998; 279: 450–54. [PubMed: 9466638]
65. Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med, 1998; 338: 853–60. [PubMed: 9516219]
66. Mocroft A, Lundgren JD. Starting highly active antiretroviral therapy: why, when and response to HAART. J Antimicrob Chemother, 2004; 54: 10–03. [PubMed: 15163656]
67. Mehandru S, Tenner-Racz K, Racz P, Markowitz M. The gastrointestinal tract is critical to the pathogenesis of acute HIV-1 infection. J Allergy Clin Immunol, 2005; 116: 419–22. [PubMed: 16083799]
68. Nolan D, Mallal S. Antiretroviral-therapy-associated lipoatrophy: current status and future directions. Sex Health, 2005; 2: 153–63. [PubMed: 16335543]

69. French MA, Price P, Stone SF. Immune restoration disease after antiretroviral therapy. AIDS, 2004; 18: 1615–27. [PubMed: 15280772]
70. Wyatt CM, Klotman PE. Antiretroviral therapy and the kidney: balancing benefit and risk in patients with HIV infection. Expert Opin Drug Saf, 2006; 5: 275–87. [PubMed: 16503748]
71. Calza L, Manfredi R, Chiodo F. Dyslipidaemia associated with antiretroviral therapy in HIVinfected patients. J Antimicrob Chemother, 2004; 53: 10–14. [PubMed: 14645323]
72. Hirschel B. Planned interruptions of anti-HIV treatment. Lancet Infect Dis, 2001; 1: 53–59. [PubMed: 11871414]
73. Powers AE, Marden SF, McConnell R, et al. Effect of long-cycle structured intermittent versus continuous HAART on quality of life in patients with chronic HIV infection. Aids, 2006; 20: 837–45. [PubMed: 16549967]
74. Dybul M, Nies-Kraske E, Daucher M, et al. Long-cycle structured intermittent versus continuous highly active antiretroviral therapy for the treatment of chronic infection with human immunodeficiency virus: effects on drug toxicity and on immunologic and virologic parameters. J Infect Dis, 2003; 188: 388–96. [PubMed: 12870120]
75. Abbas UL, Mellors JW. Interruption of antiretroviral therapy to augment immune control of chronic HIV-1 infection: risk without reward. Proc Natl Acad Sci USA, 2002; 99: 13377–78. [PubMed: 12370421]
76. El-Sadr, W.; Neaton, J. Episodic CD4-guided use of ART is inferior to continuous therapy: results of the SMART study. 13th Conference on Retroviruses and Opportunitic Infections; Denver, CO, USA. Feb 6–9, 2006.
77. Kim JY, Gilks C. Scaling up treatment—why we can't wait. N Engl J Med, 2005; 353: 2392–94. [PubMed: 16319389]
78. Orrell C. Antiretroviral adherence in a resource-poor setting. Curr HIV/AIDS Rep, 2005; 2: 171– 76. [PubMed: 16343374]
79. Ferradini L, Jeannin A, Pinoges L, et al. Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment. Lancet, 2006; 367: 1335–42. [PubMed: 16631912]
80. Coetzee D, Hildebrand K, Boulle A, et al. Outcomes after two years of providing antiretroviral treatment in Khayelitsha, South Africa. AIDS, 2004; 18: 887–95. [PubMed: 15060436]
81. Levy NC, Miksad RA, Fein OT. From treatment to prevention: the interplay between HIV/AIDS treatment availability and HIV/AIDS prevention programming in Khayelitsha, South Africa. J Urban Health, 2005; 82: 498–509. [PubMed: 16049203]
82. WHO. Scaling up antiretroviral therapy in resource-limited settings: treatment guidelines for a public health approach: 2003 revision. Geneva, Switzerland: WHO, 2004.
83. Badri M, Bekker LG, Orrell C, Pitt J, Cilliers F, Wood R. Initiating highly active antiretroviral therapy in sub-Saharan Africa: an assessment of the revised World Health Organization scalingup guidelines. AIDS, 2004; 18: 1159–68. [PubMed: 15166531]
84. Calmy A, Klement E, Teck R, Berman D, Pecoul B, Ferradini L. Simplifying and adapting antiretroviral treatment in resource-poor settings: a necessary step to scaling-up. AIDS, 2004; 18: 2353–60. [PubMed: 15622311.
85. Kober K, Van Damme W. Scaling up access to antiretroviral treatment in southern Africa: who will do the job? Lancet, 2004; 364: 103–07. [PubMed: 15234864]
86. Libamba E, Makombe S, Harries AD, et al. Scaling up antiretroviral therapy in Africa: learning from tuberculosis control programmes—the case of Malawi. Int J Tuberc Lung Dis, 2005; 9: 1062– 71. [PubMed: 16229216]
87. Gupta R, Irwin A, Raviglione MC, Kim JY. Scaling-up treatment for HIV/AIDS: lessons learned from multidrug-resistant tuberculosis. Lancet, 2004; 363: 320–24. [PubMed: 14751708]
88. Bachmann MO. Effectiveness and cost effectiveness of early and late prevention of HIV/AIDS progression with antiretrovirals or antibiotics in Southern African adults. AIDS Care, 2006; 18: 109–20. [PubMed: 16338768]
89. Deeks SG. Treatment of antiretroviral-drug-resistant HIV-1 infection. Lancet, 2003; 362: 2002–11. [PubMed: 14683662]
90. Kantor R, Katzenstein DA, Efron B, et al. Impact of HIV-1 subtype and antiretroviral therapy on protease and reverse transcriptase genotype: results of a global collaboration. PLoS Med, 2005; 2: e112. [PubMed: 15839752]
91. Parkin NT, Schapiro JM. Antiretroviral drug resistance in non-subtype B HIV-1, HIV-2 and SIV. Antivir Ther, 2004; 9: 3–12. [PubMed: 15040531]
92. Wensing AM, Boucher CA. Worldwide transmission of drug-resistant HIV. AIDS Rev, 2003; 5: 140–55. [PubMed: 14598563]
93. Toni TD, Masquelier B, Lazaro E, et al. Characterization of nevirapine (NVP) resistance mutations and HIV type 1 subtype in women from Abidjan (Cote d'Ivoire) after NVP single-dose prophylaxis of HIV type 1 mother-to-child transmission. AIDS Res Hum Retroviruses, 2005; 21: 1031–34. [PubMed: 16379606]
94. Eshleman SH, Jackson JB. Nevirapine resistance after single dose prophylaxis. AIDS Rev, 2002; 4: 59–63. [PubMed: 12152519]
95. Flys TS, Chen S, Jones DC, et al. Quantitative analysis of HIV-1 variants with the K103N resistance mutation after single-dose nevirapine in women with HIV-1 subtypes A, C, and D. J Acquir Immune Defic Syndr. 2006 published online June 12, 2006. 10.1097/01.qai. 0000221686.67810.20.
96. Lee EJ, Kantor R, Zijenah L, et al. Breast-milk shedding of drug-resistant HIV-1 subtype C in

women exposed to single-dose nevirapine. J Infect Dis, 2005; 192: 1260–64. [PubMed: 16136470]
97. Palmer S, Boltz V, Martinson N, et al. Persistence of nevirapine-resistant HIV-1 in women after single-dose nevirapine therapy for prevention of maternal-to-fetal HIV-1 transmission. Proc Natl Acad Sci USA, 2006; 103: 7094–99. [PubMed: 16641095]
98. Chaix ML, Ekouevi DK, Rouet F, et al. Low risk of nevirapine resistance mutations in the prevention of mother-to-child transmission of HIV-1: Agence Nationale de Recherches sur le SIDA Ditrame Plus, Abidjan, Cote d'Ivoire. J Infect Dis, 2006; 193: 482–87. [PubMed: 16425126.

WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Dengue Fever

Ramanjeet Kumar Mandal[1], Dr.Himani Tiwari[2], Dr. Gaurav Kumar Sharma[3], Dr. Kaushal K Chandraul[4], Dr. Hariom Sharma[5]

[1]UG Student, [2] Supervisor, [3]HOD,[4] Principal, [5]Professor, Pharmacy Department, Mewar University, India

ABSTRACT

Dengue fever is the maximum not unusual place arthropod-borne self-proscribing viral disorder with medical spectrum ranging fromasymptomatic contamination to lifestyles threatening surprise. It is referred to as dengue surprise syndrome. Hemoconcentration andthrombocytopenia are the one-of-a-kind functions of dengue hemorrhagic fever. Supportive fluid substitute therapyand vigilant tracking for the a success control of the condition. Vector manage measures are the maximumcrucial preventive methods. As the outbreaks of Dengue fever growing in India, one country after different getting gaffected, it's miles very important to understand greater approximately this disorder and prevalence, any alternate withinside the viral strain, severityof the disorder pattern, early detection of the virus and early control of the disorder ensuing in correct recovery .Population growth, speedy urbanization, growth in global tour from endemic regions and international warming aregambling a chief position in disorder unfold. Measures ought to be taken to govern the aforementioned reasons to preventdisorder unfold and decrease epidemic flare up.

KEYWORD: Dengue, Flavivirus, Dengue Shock Syndrome, Mac-Elisa

Introduction

Dengue is an infectious ailment resulting from lady mosquito AEDES AEGYPTI. It is a mosquito-borne contamination determined in tropical and sub-tropical areas across the world.[1] Infection with dengue virus consequences in numerous situations like pathological starting from moderate asymptomatic dengue fever to excessive dengue hemorrhagic fever and dengue surprise syndrome that reasons to death.[2]Epidemiology: Dengue has emerge as one of the widestspreadable illnesses globally. In India, outbreak of dengue turned into recorded in 1812. A latest dengue distribution version has anticipated 390 million dengue infections annually, out of which ninety six million instances befell.

A double top hemorrhagic fever epidemic befell in India for the primary time in Calcutta among July 1963 and March 1964. Thus, there's an pressing want of development in surveillance to permit theauthorities to put together correctly for document of outbreak.[3]

Dengue Virus: This virus is likewise referred to as Flavivirus and they may be in round and 40-60 mm in diameter. It is RNA virus this is enveloped includes 3 structural polypeptides are glycosylated and replication in cytoplasm.[4]

Most robust vector having epidemic capacity A. aegypti and different species are Aedes albopictus, stegomyia, A. polnesiensis, A. scutellaris, A. finalaya however in India A. tigris may be very common. Four dengue viruses (sorts 1-4) in the genus flavivirus and own circle of relatives flaviviridae, are the causative agents.

[5] . All 4 subtypes are determined in India. Dengue virions are small debris with lipoprotein envelope and nucleocapsid of unmarried stranded RNA genome with wonderful polarity. There is a near antigenic similarity among the 4 serotypes however the move safety in human beings is at exceptional partial and transient.[6]

Symptoms

Many humans specifically youngsters and teenagers sense no symptoms and symptoms or signs and symptoms all through a slight case of dengue fever. When signs and symptoms do occur, they normally start four to 7 days when you are bitten through an inflamed mosquito.[7]

Dengue fever reasons a excessive fever 104 F and those are following signs and symptoms:

- Headache
- Muscle, bone and joint pain
- Nausea
- Vomiting
- Pain in the back of the eyes
- Swollen glands
- Rash

Most human beings get better inside a week. In a few cases, signs and symptoms get worse and may turn out to be life-threatening.Blood vessels regularly turn out to be harm and leaky and the quantity of clot-forming cells (platelets) to yourbloodstream drops. This can motive a intense shape of dengue fever, known as dengue hemorrhagic fever, intense dengue or dengue surprise syndrome.

Signs and signs and symptoms of dengue hemorrhagic fever or intense dengue a life-threatening emergency include:

- Severe belly pain
- Persistent vomiting
- Bleeding out of your gums or nose
- Blood to your urine, stools or vomit
- Bleeding below the skin, which would possibly appear like bruising
- Difficult or fast breathing
- Cold or clammy skin (surprise)
- Fatigue
- Irritability or restlessness

Diagnosis

Efficient and correct analysis of dengue is of number one significance for scientific care (i.e. early detection of excessive cases, case affirmation and differential analysis with different infectious diseases), surveillance activities, outbreak control, pathogenesis, instructional research, vaccine development, and scientific trials.[8]

A variety of laboratory diagnostic techniques has been advanced to guide affected person control and sickness control. The desire of diagnostic approach relies upon at the cause for which the checking out is done (e.g. scientific analysis, epidemiological survey, vaccine development), the form of laboratory centers and technical understanding available, costs, and the time of pattern collection.[9]

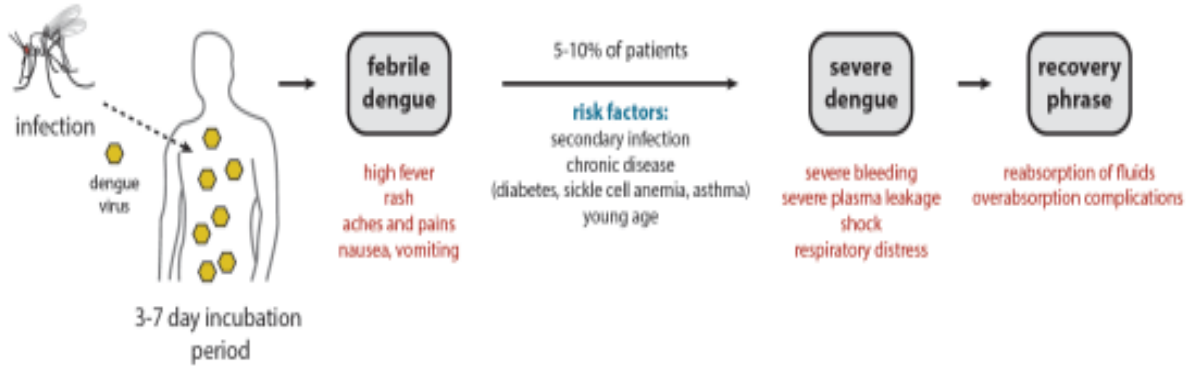
Considerations in The Choice of Diagnostic Methods

Clinical Management

Dengue virus contamination produces a huge spectrum of signs and symptoms, many this is non-specific. Thus, a analysis primarily based totally best on scientific signs and symptoms is unreliable. Early laboratory affirmation of scientific analysis can be treasured due to the fact a few sufferers development over a brief duration from slight to intense sickness and occasionally to death. Early intervention can be life-saving.[10]

Differential Diagnosis

Dengue fever can without difficulty be pressured with non-dengue illnesses, specially in nonepidemic situations.Depending at the geographical foundation of the patient, different etiologies together with non-dengue flavivirusinfections have to be dominated out[11] These consist of yellow fever, Japanese encephalitis, St Louis encephalitis, Zika, and West Nile, alphaviruses (including Sinbis and chikungunya), and different reasons of fever including malaria, leptospirosis, typhoid, Rickettsial diseases (Rickettsia prowazeki, R. mooseri, R. conori, R. rickettsi, Orientia tsutsugamushi, Coxiella burneti, etc.), measles, enteroviruses, influenza and influenza-like illnesses, haemorrhagic fevers (Arenaviridae: Junin, etc.; Filoviridae: Marburg, Ebola; Bunyaviridae: hantaviruses, Crimean-Congo haemorrhagic fever, etc.).



Outbreak Investigations

During outbreaks a few sufferers can be visible imparting with fever without or with rash throughout the extreme contamination stage. a few others can also additionally gift with symptoms and symptoms of plasmaLeakage even as nevertheless others can be found at some stage in the convalescent segment.[12]

One of the priorities in a suspected outbreak is to perceive the causative agent in order that suitable publichealth measures may be taken and physicians may be recommended to provoke suitable acute contamination management.[13] In such cases, the rapidity and specificity of diagnostic assessments is greater essential than take a look at sensitivity. Samples amassed from febrile sufferers might be examined through nucleic acid strategies in a well-ready laboratory or a broader spectrum of laboratories the use of an ELISA-primarily based totally dengue antigen detection kit. Serological assays can be used to decide the volume of outbreaks.[14]

Vaccine trials

Vaccine trials are completed on the way to degree vaccine protection and efficacy in vaccinated persons. The plaque discount and neutralization take a look at (PRNT) and the microneutralization assays are typically used to degree safety correlates.[15]
The assay is primarily based totally at the precept that neutralizing antibodies inactivate the virus in order that it's miles now no longer capable of infect and mirror in goal cells. After a 2d dengue virus infection, high-titre neutralizing antibodies are produced in opposition to as a minimum two, and frequently all 4, dengue viruses in addition to in opposition to non dengue flaviviruses.[16] During the early convalescent level following sequential dengue infections, the highest neutralizing antibody titre is frequently directed in opposition to the primary infecting virus and now no longer the maximum current one.[16]

Current Dengue Diagnostic Methods

Virus isolation

Specimens for virus isolation need to be amassed early withinside the direction of the infection, at some stage in the length of viremia (typically earlier than day 5). Virus can be recovered from serum, plasma and peripheral blood mononuclear cells and tries can be crafted from tissues amassed at (e.g. liver, lung, lymph nodes, thymus, bone marrow). Because dengue virus is heat-labile, specimens waiting for delivery to the laboratory need to be saved in a fridge or packed in moist ice. For garage as much as 24 hours, specimens need to be saved at between +4 °C and +8 °C.[17]

Nucleic acid detection

RNA is heat-labile and consequently specimens for nucleic acid detection should be treated and saved in line with the tactics defined for virus isolation.[18]

RT-PCR

Since the 1990s, numerous opposite transcriptasepolymerase chain response (RT-PCR) assays have beendeveloped. They provide higher sensitivity in comparison to virus isolation with a far greater speedy turnaround time. In situ RT-PCR gives the capacity to stumble on dengue RNA in paraffin-embedded tissues.[19] All nucleic acid detection assays contain 3 simple steps: nucleic acid extraction and purification, amplification of the nucleic acid, and detection and characterization of the amplified product. Extraction and purification of viral RNA from the specimen may be executed through conventional liquid segment separation strategies (e.g. phenol, chloroform) however has been regularly changed through silica-primarily based totally business kits (beads or columns) which can be greater reproducible and faster, mainly considering they may be automatic the use of robotics systems. A mixture of the 4 serotype-precise oligonucleotide primers in a unmarried response tube (onestep multiplex RT-PCR) is an thrilling opportunity tothe nested RT-PCR.[20]

Real-time RT-PCR

The actual-time RT-PCR assay is a one-step assay gadget used to quantitate viral RNA and the use of primer pairs and probes which can be unique to every dengue serotype. The use of a fluorescent probe allows the detection of the response merchandise in actual time, in a specialised PCR machine, with out the want for electrophoresis. Many actual-time RT-PCR assays were advanced using TaqMan or SYBR Green technologies.[21]
The TaqMan actual-time PCR is notably unique because of the collection-unique hybridization of the probe.Nevertheless, primers and probes mentioned in courses might not be capable of hit upon all dengue virusstrains: the sensitivity of the primers and probes relies upon on their homology with the centered gene collection of the unique virus analyzed. The SYBR inexperienced actual-time RTPCR has the gain of simplicity in primer layout and makes use of familiar RT-PCR protocols however is theoretically much less unique.[22]
Real-time RT-PCR assays are both ―singleplex‖ (i.e. detecting handiest one serotype at a time) or ―multiplex‖ (i.e. capable of pick out all 4 serotypes from a unmarried sample). The multiplex assays have the gain that a unmarried response can decide all 4 serotypes with out the cappotential for advent of infection at some stage in manipulation of the sample.[23] However the multiplex actual-time RT-PCR assays, even though faster, are presently much less touchy than nested RT-PCR assays. An gain of this approach is the capacity to decide viral titre in a scientific sample, which can be used to look at thepathogenesis of dengue disease.[24

Isothermal Amplification Methods

The NASBA (nucleic acid sequence-basedamplification) assay is an isothermal RNA particular amplification assay that doesn't require thermal biking instrumentation.[25] The preliminary level is a opposite transcription wherein the single-stranded RNA goal is copied right into a double-stranded DNA

molecule that serves as a template for RNA transcription.[26] Detection of the amplified RNA is finished both by electrochemiluminescence or in real-time with fluorescent-labelled molecular beacon probes. NASBAhas been tailored to dengue virus detection withSensitivity close to that of virus isolation in mobileular cultures and can be a beneficial approach for analyzing dengue infections in area studies.[27]

Detection of Antigens

Detection of dengue antigens in acute-segment serum become uncommon in sufferers with secondary infections due to the fact such sufferers had pre-present virus-IgG antibody immune complexes.[28] New trends in ELISA and dot blot assays directed to the envelop/membrane (E/M) antigen and the non-structural protein 1 (NS1) tested that excessive concentrations of those antigens withinside the shape of immune complexes can be detected in sufferers with each number one and secondary dengue infections as much as nine
days after the onset of illness.[29]

Serological Tests

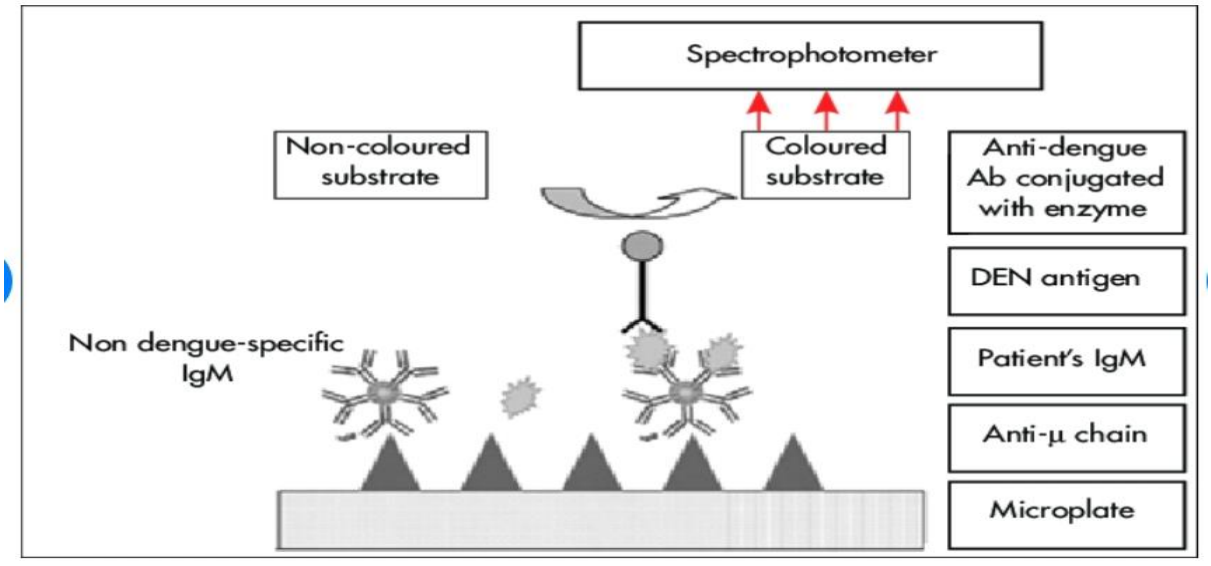
MAC-ELISA

For the IgM antibody-seize enzyme-related immunosorbent assay (MAC-ELISA) overall IgM in sufferers' sera is captured with the aid of using anti-μ chain precise antibodies (precise to human IgM) lined onto a microplate. Dengue-precise antigens, from one to 4 serotypes (DEN-1, -2, -3, and -4), are sure to thecaptured anti-dengue IgM antibodies and are detected with the aid of using monoclonal or polyclonal dengue antibodies without delay or in a roundabout way conjugated with an enzyme with a view to remodel a non-colored substrate into colored products. The optical density is measured with the aid of using spectrophotometer.[30]

IgG ELISA

The IgG ELISA is used for the detection of latest or beyond dengue infections. This assay makes use of the identical antigens because the MAC-ELISA. The use of E/M-unique seize IgG ELISA (GAC) lets in detection of IgG antibodies over a length of 10 months after the infection. IgG antibodies are lifelong as measured via way of means of E/M antigen-covered oblique IgG ELISA, however a fourfold or extra growth in IgG antibodies in acute and convalescent paired sera may be used to file current infections. Test consequences correlate properly with the haemagglutination-inhibition test.[31]
This approach may be used to come across IgG antibodies in serum or plasma and filter-paper saved blood samples and lets in identity of a case as a number one or secondary dengue infection. In general, IgG ELISA lacks specificity in the flavivirus sero complicated groups.

Principle of MAC-ELISA Test



IgM/IgG Ratio

A dengue virus E/M protein-precise IgM/IgG ratio may be used to differentiate number one from secondary dengue virus infections. IgM seize and IgG seize ELISAs are the maximum not unusualplace assays for this purpose.[32] In a few laboratories, dengue contamination is described as number one if the IgM/IgG OD ratio is extra than 1.2 (the use of patient's sera at 1/one hundred dilution) or 1.4 (the use of patient's sera at 1/20 dilutions). The contamination is secondary if the ratio is much less than 1.2 or 1.4. This set of rules has additionally been followed with the aid of using a few business vendors. However, ratios may also range among laboratories, accordingly indicating the want for betterstandardization of check performance.

IgA

Positive detection for serum anti-dengue IgA as measured with the aid of using anti-dengue virus IgA seize ELISA(AAC-ELISA) regularly takes place someday after that for IgM. The IgA titre peaks round day eight after onset of fever and reduces swiftly till it's far undetectable through day 40. No variations in IgA titres have been observed through authors among sufferers with number one or secondary infections. Even aleven though IgA values are normally decrease than IgM, each in serum and saliva, the 2 strategies will be done collectively to assist in deciphering dengue serology.[33] This method isn't used very regularly and calls for extra evaluation.

Haemagglutination-Inhibition Test

The haemagglutination-inhibition (HI) take a look at is primarily based totally at the capacity of dengue antigens to agglutinate purple blood cells (RBC). Anti-dengue antibodies in sera can inhibit this agglutination and the efficiency of this inhibition is measured in an HI take a look at. Serum samples are dealt with with acetone or kaolin to dispose of non-particular inhibitors of haemagglutination, after which adsorbed with gander to dispose of non-particular agglutinins.[34]

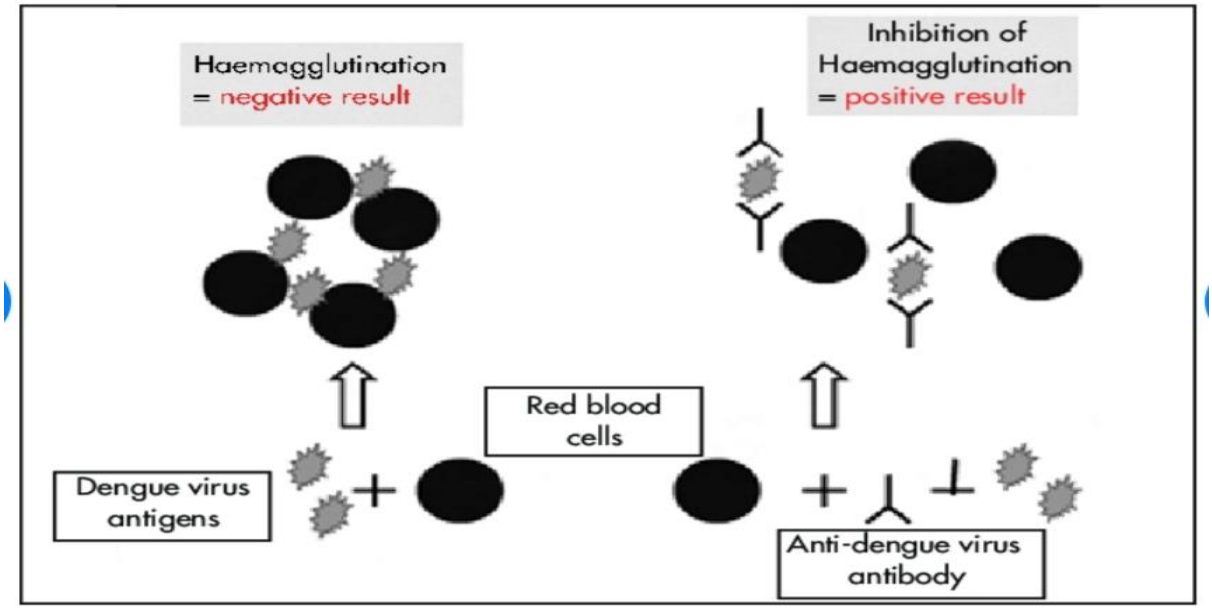


Figure: Haemagglutination-inhibition assay

Haematological Tests

Platelets and haematocrit values are typically measured for the duration of the extreme levels of dengue infection. These need to be achieved cautiously the usage of standardized protocols, reagents and equipment. A drop of the platelet matter underneath a thousand in step with µL can be found in dengue fever however it's miles a consistent function of dengue haemorrhagic fever.[35]
Thrombocytopaenia is normally found withinside the duration among day three and day eight following the onset of illness.Haemoconcentration, as predicted via way of means of an growth in haematocrit of 20% or greater as compared with convalescent values, is suggestive of hypovolaemia because of vascular permeability and plasma leakage.[36]

Treatment

There isn't anyt any precise remedy to be had for dengue virus infections.it's miles critical to exclude different treatable diagnoses. Patients at chance for dengue can collect different illnesses with comparable medical features, including malaria,typhoid fever, and leptospirosis.[37] Symptoms in sufferers with dengue virus infections clear up in 5 to seven days. Supportive remedies are to be had for the precise ailment manifestations of dengue virus infection.[38]
Dengue Fever: Patients with dengue fever need to be advised to preserve their consumption of oral fluid to keep away from dehydration.[39] Fever and myalgias may be controlled as wished with acetaminophen. Aspirin or nonsteroidal antiinflammatory marketers need to commonly be averted due to the chance of bleeding headaches and in kids due to the capability chance of Reye's syndrome.[40] The maximum critical degree to help the affected person with dengue fever is to cautiously compare theaffected person for approaching headaches.

Dengue virus contamination with massive Bleeding:

Gastrointestinal bleeding or menorrhagia in sufferers with DHF, and from time to time in sufferers with dengue fever as well, may be extreme sufficient to require blood transfusion.[41] Factors that make a contribution to bleeding encompass thrombocytopenia because of reduced platelet survival and, in extreme cases, frank disseminated intravascular coagulation. Platelet transfusions are hardly ever given, however can be warranted in sufferers with extreme thrombocytopenia (<10,000/mm3) and lively bleeding.[42]

Dengue Hemorrhagic Fever: Plasma leakage in DHF is crucial to manipulate with competitive intravascularquantity repletion to save you or opposite hypovolemicshock.[43] In moderate cases, specifically whilst medical interest is obtained early, oral rehydration can be sufficient.[44] However, in sufferers with establishedintravascular fluid loss, intravenous fluid management is recommended. Blood transfusion is suitable in sufferers with massive bleeding.[45]

Treatment of Shock: A protocol for intravenous fluid remedy has been evolved through the World Health Organization (WHO) primarily based totally upon medical enjoy in particular in youngsters from Southeast Asia.[46] For sufferers with shock, an preliminary bolus of 5 percentage dextrose in everyday saline or Ringer's lactate (10 to twenty mL according to kg of frame weight) infused swiftly is recommended, observed through non-stop infusion (10 to twenty mL/kg according to hour) till critical symptoms and symptoms and urine output normalize. The infusion rateCan then be regularly decreased till it fits plasma fluid losses.[47]

As a Herbal Treatment

Role of Papaya in Dengue fever

Botanical Name: Carica papaya
Family Name: Caricaceae
Common Name: Papaya, Paw Paw, Kates, Papaw
Part Used: Leaves, Fruits, bark
With the growing wide variety of human beings catching dengue fever, the call for for papaya leaf juice has soared.
Thrombocytopenia is one of the scientific manifestations in dengue fever and contributes to the plasma leakage and haemorrhage withinside the presence of greater vascular permeability.[48] Thrombocytopenia in dengue is taken into consideration to be an immune related, molecular mimicry concerning dengue viral debris and the platelet results in auto-destruction of the platelets with the aid of using immunoglobulin M(IgM) antibodies.[49] Interestingly, C. papaya leaves juice have proven a effective impact on growing platelet remember in healthful mice. C. papaya leaves extract organized in water has been examined in opposition to dengue fever.
After the management of aqueous extract in dengue inflamed patient, the platelet remember accelerated from55x103/µL to 168x103/µL, White blood cells from 3.7x103/µL to 7.7x103/µL and neutrophils from 46%to 78%. Carica papaya leaf juice confirmed a good sized inhibition of haemolysis invitro and will have a capability healing impact on disorder procedures inflicting destabilization of organic membranes may also correctly beautify the survival of platelets.[50] Thus, carica papya may be used to goal dengue fever.

Prevention

The best hazard for dengue virus contamination is in people living in endemic regions and now no longer intravelers.[51] Public fitness efforts in endemic regions: Control of the Aedes aegypti mosquito, which transmits dengue virus, and the improvement of vaccines are capability strategies in stopping dengue virus infections.[52]

Mosquito Control: Mosquito manage is the best technique to the prevention of denguetransmission. Programs focused on the Aedes aegypti mosquito as a way to get rid of city yellow fever withinside the Americas from the Nineteen Forties via Nineteen Seventies have been pretty successful.[53] These packages have been additionally powerful at lowering dengue transmission withinside the vicinity. These packages have been primarily based totally on a "pinnacle down" technique concerning competitive mosquito surveillance and insecticide use. However, loss of interest and investment of those packages withinside the Nineteen Seventies caused re-emergence of A. aegypti all through its former vicinity and the corresponding re-emergence of dengue.[54]Insecticide spraying, in reaction to dengue outbreaks, isn't always fantastically powerful in opposition to A. aegypti mosquitoes, which regularly breed internal houses. Community-primarily based totallyprocedures regarding schooling of the populace in efforts to lessen breeding sites, including discarded tyres and different boxes that gather status water.[55]In one study, a complete network and governmental manipulate strategy, along with the seeding ofwater vessels with Copepods (Fish) that feed on mosquito larvae, became a hit in doing away with A.aegypti and dengue transmission in 32 groups in rural regions of Vietnam.[56]

Vaccination: Infection with dengue gives lengthy-time period safety towards the precise serotype that precipitated the disease, helping the feasibility of a dengue vaccine. However, it gives simplest short-lived immunity to the alternative 3 dengue serotypes.[57] In view of the affiliation of DHF with preceding publicity to dengue viruses and the popularity that each one 4 serotypes are able to inducing DHF it's far the overall consensus withinside the medical and public fitness groups that any candidate vaccine ought to produce defensive immunity towards DEN 1-4. Since waning immunity may additionally boom the hazard for DHF in vaccines, vaccine-caused defensive immunity ought to additionally be lengthy-lived.[58]

Animal research suggest that defensive immunity towards dengue may be mediated through neutralizing antibodies, specifically the ones directed towards the envelope (E) glycoprotein. However, herbal dengue contamination induces low ranges of cross-reactive antibodies which can be detected in neutralization assays, however do now no longer save you contamination with the alternative dengue serotypes.[59]

Tetravalent vaccines that result in immunity towards all 4 serotypes are in development. In a rhesus monkey model, one tetravalent stay attenuated dengue virus vaccine established seroconversion charges of 100, 100, ninety and 70 percentage towards dengue serotypes 1, 2, 3, and 4. In addition, vaccination led to whole safety towards viremia from inoculation with serotype 2; mission with the alternative dengue serotypes established safety in 50 to eighty percentage of animals as compared to controls.[60]

Recommendations for vacationers: Most vacationers from non-endemic nations are at pretty low hazard for DHF due to the fact they lack preceding publicity to dengue viruses.[61] Avoidance of publicity to inflamed A. aegypti mosquitoes is the number one technique to prevention of dengue virus infections in vacationers. These mosquitoes predominantly stay in city regions in and round houses.[62]

There are following a few steps that taken as prevention of dengue virus infection

- Spray mosquito repellant in your pores and skin and clothes.
- Wear lengthy sleeves, lengthy pants, and socks sprayed with mosquito repellant.
- Avoid being outside at sunrise and nightfall while mosquitoes are maximum active.
- Take time to go searching your private home and backyard for mosquito-breeding places, mainly regions where
- there's status water. To keep away from status water round your private home:
- Drain kiddie swimming pools weekly.
- Change water in flower vases, hen baths, and animal watering pans two times a week.
- Get rid of antique tires, buckets, bottles, and cans, or make sure they're empty of water.
- Repair any leaky pipes and outdoor faucets, and flow air conditioner drain hoses frequently.

Conclusion

Though dengue fever is mostly a self-proscribing disorder, loss of right tracking and ok volumesubstitute may also result in deadly outcome. In view of rising outbreaks of dengue fever in numerous states of India, it will become vital for number one care physicians to have an up to date know-how approximately early prognosis and latest control guidelines.
Dengue has advanced as a international life-threatening public fitness concern, affecting round 2.five billion people in extra than a hundred countries. The health practitioner ought to be privy to the numerous scientific manifestations of this circumstance and make sure an early and ok remedy plan. Future guidelines to fight this dreadful disorder goal at techniques of mosquito control, improvement of vaccine, and antiviral drug regimen.

References

1. R. Chen and N. Vasilakis, ―Dengue-Quo Tu et QuoVadis? Viruses‖, 1993; 3(9).
2. B.R. Murphy and S.S. Whitehead, ―Immunereaction to dengue virus and potentialities for avaccine,‖ Annual Review of Immunology, 29.
3. World Health Organiazation, Dengue: Guideline forDiagnosis, Treatment, Prevention, and, Control,WHO, Geneva, 2009.
4. S. Bhatt, P. W. Gething, O. J. Brady et al., ―Thenternational distribution and burden of dengue,‖ Nature,2013; 496: 7446-504–507.
5. O. J. Brady, P. W. Gething, S. Bhatt et al., ―Refiningthe worldwide spatial limits of dengue virus transmissionwith the aid of using evidence-primarily based totally consensus,‖ PLoS Neglected Tropical Diseases, Article ID e1760, 2012; 6(8).
6. G. N. Malavige, S. Fernando, D. J. Fernando, and S.L. Seneviratne, ―Dengue viral infections,‖Postgraduate Medical Journal, 2004; 80: 948-588–601.
7. https://www.mayoclinic.org/diseasesconditions/dengue-fever/symptoms-causes/syc20353078.
8. Vorndam V, Kuno G. Laboratory prognosis ofdengue virus infections. In: Gubler DJ, Kuno G, eds. Dengue and dengue hemorrhagic fever. New York,CAB International, 1997; 313–333.
9. Chanama S et al. Analysis of unique IgM responsesin secondary dengue virus infections: stages andsuperb charges in evaluation with number one infections.Journal of Clinical Virology, 2004; 31: 185–189.
10. Shu PY et al. Comparison of a capturimmunoglobulin M (IgM) and IgG ELISA and nonstructural protein NS1 serotype-unique IgG ELISAfor differentiation of number one and secondary denguevirus infections. Clinical and Diagnostic LaboratoryImmunology, 2003; 10: 622–630.
11. Hunsperger EA et al. Evaluation of commerciallyto be had anti–dengue virus immunoglobulin M tests. Emerging Infectious Diseases (serial online),;March (date cited). Accessible athttp://www.cdc.gov/EID/content/15/3/436.htm.2009.
12. Morens DM et al. Simplified plaque discount neutralization assay for dengue viruses with the aid of using semimicro techniques in BHK-21 cells: evaluation of the BHK suspension check with preferred plaque discount neutralization. Journal of Clinical Microbiology, 1985; 22(2): 250–254.
13. Alvarez M et al. Improved dengue virus plaque formation on BHK21 and LLCMK2 cells: assessment of a few factors. Dengue Bulletin, 2005;29: 1–9.
14. Halstead SB, Rojanasuphot S, Sangkawibha N. Original antigenic sin in dengue. American Journal of Tropical Medicine and Hygiene, 1983, 32: 154–156.
15. Lanciotti RS et al. Rapid detection and typing of dengue viruses from scientific samples with the aid of using using opposite transcriptase-polymerase chain reaction. Journal of Clinical Microbiology, 1992; 30: 545–551.

16. Harris E et al. Typing of dengue viruses in scientific specimens and mosquitoes with the aid of using unmarried tube multiplex opposite transcriptase PCR. Journal of Clinical Microbiology, 1998; 36: 2634–2639.
17. Vaughn DW et al. Dengue viremia titer, antibody reaction sample and virus serotype correlate with sickness severity. Journal of Infectious Diseases, 2000; 181: 2–9.
18. Shu PY, Huang JH. Current advances in dengue prognosis. Clinical and Diagnostic Laboratory Immunology, 2004; 11(4): 642–650.
19. Parida MM et al. Rapid detection and differentiation of denguevirus serotypes with the aid of using a real-time opposite transcription-loop-mediated isothermal amplification assay. Journal of Clinical Microbiology, 2005; 43:2895–2903. (doi: 10.1128/JCM.43.6. 28952903.2005).
20. Vazquez S et al. Serological markers all through dengue three number one and secondary infections. Journal ofClinical Virology, 2005; 33(2): 132–137.
21. Fernandez RJ, Vazquez S. Serological prognosis of dengue with the aid of using an ELISA inhibition method (EIM). Memórias do Instituto Oswaldo Cruz, 1990; 85(three):347–351.
22. Vazquez S, Fernandez R, Llorente C. Usefulness of blood specimens on paper strips for serologic research with inhibition ELISA. Revista do Instituto deMedicina Tropical de São Paulo, 1991; 33(four): 309–311.
23. Vazquez S et al. Kinetics of antibodies in sera, saliva, and urine samples from grownup sufferers with number one or secondary dengue three virus infections. International Journal of Infectious Diseases, 2007;11: 256–262.
24. Nawa M. Immunoglobulin A antibody responses in dengue sufferers: a beneficial marker for serodiagnosis of dengue virus infection. Clinical and Vaccine Immunology, 2005; 12: 1235–1237.
25. Lemmer K et al. External fine manipulate exams in PCR diagnostics of dengue virus infections. Journal of Clinical Virology, 2004; 30:291–296.
26. WHO. Laboratory biosafety manual, third ed. Geneva, World Health Organization, 2004. (ISBN ninety two four 154650 6, WHO/CDS/CSR/LYO/2004.11.
27. http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf).
28. Ramos MM et al. Dengue Serosurvey Working Group. Epidemic dengue and dengue hemorrhagic fever on the Texas-Mexico border: consequences of a household-primarily based totally seroepidemiologic survey, December 2005. American Journal of Tropical Medicine and Hygiene, 2008; 78(three): 364--369.
29. Centers for Disease Control and Prevention. Dengue hemorrhagic fever -- U.S.Mexico border, 2005. Morbidity and Mortality Weekly Report, 2007;56(31): 785-789. Erratum in: Morbidity and Mortality Weekly Report, 2007; 56(32): 822.
30. PAHO. Dengue and dengue hemorrhagic fever. Regional Committee decision CD43.R4, followed on the 53rd consultation of the Regional Committee for the Americas, forty third Directing Council. Washington, DC, Pan American Health Organization, 2001(http://www.paho.org/english/hcp/hct/vbd/newgeneration-resolutions.pdf).
31. PAHO. Dengue. Regional Committee decision CD44.R9, followed on the fifty fifth consultation of the Regional Committee for the Americas, forty fourth Directing Council. Washington, DC, Pan American Health Organization, 2003.
32. (http://www.paho.org/english/gov/cd/cd44-r9-e.pdf).
33. PAHO. Grupo de Trabajo sobre Dengue. Estrategia de Gestión Integrada para l. a. prevención y manipulate del dengue en l. a. Región de las Américas. 2.ª versión. Santa Cruz de l. a. Sierra, Bolivia. Pan American Health Organization, (Document OPS/ HDM/CD/440.07, in Spanish), 2003.
34. PAHO. Pan American Health Organization. Prevención y manipulate del dengue en las Américas. Resolución CSP27.R15. 27. a Conferencia Sanitaria Panamericana CSP27. R15 (Esp.) 1--five de octubre de(in Spanish), 2007.
35. Nathan MB, Dayal-Drager R. Recent epidemiological trends, the worldwide method andpublic fitness advances in dengue. Working paper three.1 in: Report of the Scientific Working Groupassembly on Dengue, Geneva, 1–five October 2006.Geneva, World Health Organization, Special Programme for Research and Training in Tropical Diseases, 2007; 29—34. (Document TDR/SWG/07).
36. Kokernot RH, Smithburn KC, Weinbren MP. Neutralising antibodies to arthropodborne viruses inhuman and animals withinside the Union of South Africa. Journal of Immunology, 1956; 77: 313–322.
37. Blackburn NK, Rawal R. Dengue fever imported from India: a file of three cases. South African Medical Journal, 1987; 21: 386–287.
38. Boisier P et al. Dengue 1 epidemic withinside the Grand Comoro Island (Federal Islamic Republic of theComores), March-May 1993. Annales de l. a. Société Belge de Médecine Tropicale, 1993; 74: 217–229.
39. Gubler DJ et al. Dengue three Virus Transmission in Africa. American Journal of Tropical Medicine andHygiene, 1986; 35(6): 1280--1284.
40. Carey DE et al. Dengue virus from febrile sufferers in Nigeria 1964–68. Lancet, 1971; 1: 105–106.
41. Gonzalez JP et al. Dengue in Burkina Faso: seasonal epidemics withinside the city vicinity of Ouagadougu. Bulletin de l. a. Société de pathologie exotique et de ses filiales, 1985; 78: 7–14.
42. Diallo M et al. Amplification of the sylvatic cycle of dengue virus kind 2, Senegal, 1999--2000: entomologic findings and epidemiologic considerations. Emerging Infectious Diseases (serial online), 2003. March (date cited). Accessible at http:// www.cdc.gov/ncidod/EID/vol9no3/02-0219.htm.
43. WHO/EMRO. World Health Organization, Regional Office for the Eastern Mediterranean, Division of Communicable Disease Control, Newsletter, 2005;6: 7–8. (http://www.emro.who.int/pdf/ dcdnewsletter6.pdf).
44. Hyams KC et al. Evaluation of febrile sufferers in Port Sudan, Sudan: isolation of dengue virus.American Journal of Tropical Medicine and Hygiene, 1986; 35: 860– 865.
45. Rodier GR et al. Epidemic dengue 2 withinside the town of Djibouti 1991–1992. Transactions of the RoyalSociety of Tropical Medicine and Hygiene, 1996; 90:237–240.
46. Bushra J. Dengue Virus Serotype three, Karachi, Pakistan. Emerging Infectious Diseases, 2007;13(1).

47. European Centre for Disease Prevention and Control. Dengue worldwide: a top level view of the present day state of affairs and implications for Europe, Eurosurveillance, 2007; 12(25). (http://www.eurosurveillance.org/ViewArticle.aspx? PublicationType=W&Volume=12&Issue=25&OrderNumber=1).
48. WHO. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control, 2d ed. Geneva,World Health Organization, 1997.
49. Guha-Sapir D, Schimmer B. Dengue fever: new paradigms for a converting epidemiology. Emerging Themes in Epidemiology, 2005. (Open get admission to journal, http:// www.ete-online.com/content/2/1/1
50. L. Hermida, L. J. Bernardo, M. Mart´ın et al., ―A recombinant fusion protein containing the domain III of the dengue-2 envelope protein is immunogenic and protecting in nonhuman primates, 2006; 24(16): 3165–3171.
51. J. R. Danko, C. G. Beckett, and K. R. Porter, ―Development of dengue DNA vaccines,‖ Vaccine, 2011; 29(42): 7261–7266.
52. C. G. Beckett, J. Tjaden, T. Burgess et al., ―Evaluation of a prototype dengue-1 DNA vaccine in a Phase 1 scientific trial,‖ Vaccine, 2011; 29(5): 960–968.
53. K. R. Porter, D. Ewing, L. Chen et al., ―Immunogenicity and protecting efficacy of a vaxfectin-adjuvanted tetravalent dengue DNA vaccine,‖ Vaccine, 2012; 30(2): 336–341.
54. K. Raviprakash, T. Luke, J. Doukas et al., ―A dengue DNA vaccine formulated with Vaxfectin® is nicely tolerated, and elicits sturdy neutralizing antibody responses to all 4 dengue serotypes in New Zealand white rabbits,‖ Human Vaccines and Immunotherapeutics, 2012; 8(12): 1764–1768.
55. US Army Medical Research and Materiel Command, Evaluation of the Safety and the Ability of a DNA Vaccine to Protect Against Dengue Disease (TVDV), ClinicalTrials.gov, Bethesda, Md, USA, National Library of Medicine (US), NLM Identifier: NCT01502358, 2000.https://clinicaltrials.gov/ct2/show/ NCT01502358.
56. K. Raviprakash, D. Wang, D. Ewing et al., ―A tetravalent dengue vaccine primarily based totally on a complicated adenovirus vector affords massive safety in rhesus monkeys towards all 4 serotypes of dengue virus,‖ Journal of Virology, 2008; 82(14): 6927–6934.
57. L. J. White, M. M. Parsons, A. C. Whitmore, B. M. Williams, A. de Silva, and R. E. Johnston, ―An immunogenic and protecting alphavirus replicon particle-primarily based totally dengue vaccine overcomes maternal antibody interference in weanling mice,‖ Journal of Virology, 2007; 81(19): 10329–10339.
58. S. Brandler, M. Lucas-Hourani, A. Moris et al., ―Pediatric measles vaccine expressing a dengue antigen induces long lasting serotype-unique neutralizing antibodies to dengue virus,‖ PLoS Neglected Tropical Diseases, 2007; 1(3): article e96.
59. D. H. Holman, D. Wang, K. Raviprakash et al., ―Two complicated, adenovirus-primarily based totally vaccines that collectively result in immune responses to all 4 dengue virus serotypes,‖ Clinical and Vaccine Immunology,2007; 14(2): 182–189.
60. N. U. Raja, D. H. Holman, D. Wang et al., ―Induction of bivalent immuneresponses byex pression of denguevirustype 1andtype 2 antigens from a unmarried complicated adenoviral vector,‖ AmericanJournal of Tropical Medicine and Hygiene, 2007; 76(4): 743– 751.
61. WHO. Dengue hemorrhagic fever: diagnosis, treatment, prevention, and control. second ed. Geneva: World Health Organization, 2002.
62. Nimmannitya, S, Thisyakorn, U, Hemsrichart, V. Dengue haemorrhagic fever with unusual manifestations. Southeast Asian J Trop Med Public Health, 1987; 18: 398.

Journal of
Composites Science

MDPI

Article

Determination of Quantum Capacitance of Niobium Nitrides Nb_2N and Nb_4N_3 for Supercapacitor Applications

Bharti [1,2], Gulzar Ahmed [1], Yogesh Kumar [3,*], Patrizia Bocchetta [4] and Shatendra Sharma [5]

1 Department of Physics, Mewar University, Gangrar, Chittorgarh 312901, India; bhartibaniwal@shivaji.du.ac.in (B.); gulzarahmed61@gmail.com (G.A.)
2 Department of Physics, Shivaji College, University of Delhi, New Delhi 110027, India
3 Department of Physics, ARSD College, University of Delhi, New Delhi 110021, India
4 Dipartimento di Ingegneria dell'Innovazione, Università del Salento, Via Monteroni, 73100 Lecce, Italy; patrizia.bocchetta@unisalento.it
5 School of Engineering and USIC, Jawaharlal Nehru University, New Delhi 110067, India; shatendra@gmail.com
* Correspondence: ykumar@arsd.du.ac.in; Tel.: +91-999-925-4014

Abstract: The density of states and quantum capacitance of pure and doped Nb_2N and Nb_4N_3 single-layer and multi-layer bulk structures are investigated using density functional theory calculations. The calculated value of quantum capacitance is quite high for pristine Nb_2N and decent for Nb_4N_3 structures. However for cobalt-doped unpolarized structures, significant increase in quantum capacitance at Fermi level is observed in the case of Nb_4N_3 as compared to minor increase in case of Nb_2N. These results show that pristine and doped Nb_2N and Nb_4N_3 can be preferred over graphene as the electrode material for supercapacitors. The spin and temperature dependences of quantum capacitance for these structures are also investigated.

Keywords: niobium nitride; electrode; supercapacitors; quantum capacitance

Citation: Bharti; Ahmed, G.; Kumar, Y.; Bocchetta, P.; Sharma, S. Determination of Quantum Capacitance of Niobium Nitrides Nb_2N and Nb_4N_3 for Supercapacitor Applications. *J. Compos. Sci.* **2021**, *5*, 85. https://doi.org/10.3390/jcs5030085

Academic Editor: Wei Yuan

Received: 4 March 2021
Accepted: 17 March 2021
Published: 20 March 2021

1. Introduction

Efficient and environment friendly energy conversion and storage is a challenge to researchers, with increasing demand for energy sources in electric (or hybrid) vehicles and portable electronic devices [1]. Supercapacitors are considered as viable devices for storing electrical energy because of their high energy and power densities and excellent discharging/charging performance [2,3]. Supercapacitor's energy density depends on the specific capacitance of the electrolyte-electrode system and the operating voltage [4]. The specific capacitance of an electrode in supercapacitor is a resultant of two capacitances, namely EDLC capacitance (C_{EDL}) and Quantum capacitance (QC), as represented by Equation (1) [5–7].

$$\frac{1}{C} = \frac{1}{QC} + \frac{1}{C_{EDL}}. \quad (1)$$

It is clear from the above equation that a low value of quantum capacitance can significantly decrease the total electrode capacitance. Therefore, apart from looking for advanced electrolytes, finding electrode materials with a high QC is a good way to increase the capacitance.

Carbon, metal oxides and conducting polymers are the most used material for supercapacitor electrodes [3,8–10]. However, conducting polymers and metal oxide electrodes exhibit poor electrochemical stability and electrical conductivity, whereas carbon electrodes suffer from poor capacitance. The graphene has been widely investigated for supercapacitor electrodes, because of its large specific surface area and electronic properties, but graphene also has low capacitance performance near Fermi level [6,11,12].

In search for better options, transition metal nitrides are explored as supercapacitor electrodes. These nitrides exhibit good chemical stability along with fair conductivity. They

are cost effective and have excellent electrochemical property which makes them suitable material for supercapacitor electrodes [13,14]. Transition metal nitrides, like vanadium nitride, titanium nitride, tungsten nitride etc., have already been investigated [15–20] as electrode materials. Among them, vanadium nitride is reported to have quite a high value (1340 F g^{-1}) of capacitance [15]. Different nanostructures of titanium nitride are prepared [21–23] to see their effectiveness as high energy supercapacitor electrodes. Many studies have been done regarding the fabrication of niobium nitrides and their superconducting properties. Experimental studies have already reported superconductivity in polycrystalline hexagonal ε-NbN [24] and in the tetragonal phases of both Nb_4N_3 and Nb_4N_5 with long-range-ordered arrangement of vacancies [25]. Nanowires and nanoribbons of Nb_4N_5 and Nb_5N_6 have also been fabricated and studied for their superconducting properties [26]. Researchers have used porous NbN as anode material and activated carbon as the cathode for a Li-ion hybrid capacitor LIHC [27]. The device has a wide potential window and exhibits a high energy and power density. Experimental study has been done using niobium nitride electrodes for hybrid supercapacitors as well. Niobium titanium nitride TiNbN is studied as supercapacitor electrode material [28] and a high specific capacitance value of up to 59.3 mF cm^{-2} at 1.0 mA cm^{-2} is achieved. The study has opened up the possibility of fabrication of all nitride-based asymmetric supercapacitors. In another study, niobium nitride Nb_4N_5 is explored to be an excellent capacitive material for the first time with an areal capacitance of 225.8 mF cm^{-2} [29]. Faradaic pseudo capacitance is confirmed by the mechanistic studies, deriving from the proton incorporation/chemisorption reaction owing to the copious +5 valence Nb ions in Nb_4N_5 [29]. Such studies prove the importance of exploring niobium nitride for supercapacitor applications.

Despite several reports on niobium nitrides, not much work is reported for their quantum capacitance. A thorough theoretical investigation on the QC of several structures of niobium nitride is required to assess their potential as supercapacitor electrode. The present work is further important as Nb_2N and Nb_4N_3 also satisfy the theoretical definition of MXenes. MXenes, a new class of two-dimensional materials, are produced from the ternary layered compounds [30]. MXene sheets [31] are a family of transition metal nitrides or carbides. These provide a substitute for graphene electrodes. These MXenes are synthesized by using hydrofluoric acid for exfoliation of "A" elements from their crystals known as MAX [32,33]. The "A" in MAX generally represents IV A or III A element (Si, Al, Ga etc.). The representative formula of MXene is $M_{m+1}X_m$ (m = 1, 2, 3 and so on), where "M" is an early transition metal like Ti, Mo, V, Cr, Zr, Hf, Nb and Ta and "X" is nitrogen or/and carbon [34–36]. MXenes are gaining attention due to their novel electronic and physical properties [37] and excellent mechanical flexibility [38,39]. MXenes with many layers generally exhibit better conductivity due to availability of more channels for transport of electrons, but the details in the impact of multilayers should be investigated individually. MXenes have been demonstrated to be thermally, chemically and mechanically stable and resistant to light radiation damage [40–43]. Due to these features, MXenes are being considered as a good option for a wide range of applications [38], including catalysis [44], energy storage [45], mano electronics [46–48], rechargeable batteries [49] and modern electronic devices [50]. Many investigations related to MXenes are focused on their applications in metal-ion batteries [51–54]. Few studies done to explore Mxenes for their supercapacitor applications have mainly explored Titanium-based MXenes [55,56]. No experimental work has been reported on niobium nitride MXene.

In this paper, for the first time, the QC of Nb_2N and Nb_4N_3 structures are determined using DFT calculations for supercapacitor applications. Effect of doping on quantum capacitance of these niobium nitride structures is also investigated. In our work, cobalt is used as dopant because of a recent experimental study [57] where the cobalt doping has shown a rise in capacity of niobium nitride.

Quantum capacitance values obtained are compared with that of graphene. Results of our calculation indicate that the limitation of low quantum capacitance graphene electrodes can be overcome by using Nb_2N and Nb_4N_3-based electrodes. More significantly, our

calculations indicate that the pristine or doped niobium nitrides exhibit very high values for QC at both the positive and negative electrodes. The dependence of quantum capacitance on number of molecular layers, spin and temperature is also investigated. The method of calculation and results are discussed in the following sections.

2. Materials and Methods

The DFT calculations for density of states were performed using the Atomistix Toolkit (ATK) package from QuantumWise (now known as Synopsys). The generalized gradient approximation (GGA) with the PBE functional was used to describe the exchange correlation energy [58]. The norm-conserving pseudopotential generated with the Fritz-Haber Institute FHI code was selected along with double zeta polarized basis set. The plane-wave energy cut off was kept at 540 eV, with Monkhorst-pack k-point grid meshes sampled at $12 \times 12 \times 1$. The crystal structures of Nb_2N and Nb_4N_3 were built using the crystal builder, as shown in Figure 1. The crystal parameters used for the computation are given in Table 1.

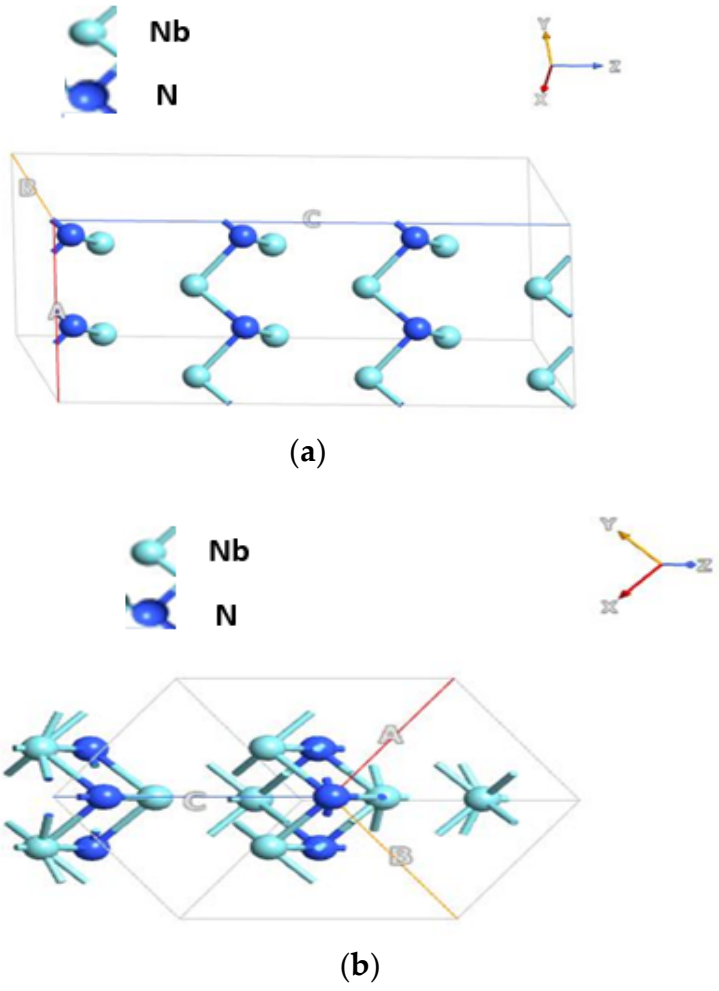


Figure 1. Chemical structures of pristine niobium nitride: (**a**) Nb_2N; (**b**) Nb_4N_3.

Table 1. Crystal parameters used for calculations.

Material	Crystal Structure	Space Group	Angles
Nb_2N	Hexagonal	6, Pm	$\alpha = \beta = 90°, \gamma = 120°$
Nb_4N_3	Body-centered tetragonal	8, Cm	$\alpha = \beta = \gamma = 90°$

Both structures of niobium nitride were doped (added) with 2 atoms of cobalt to investigate the doping effect on quantum capacitance, as shown in Figure 2. Geometry optimization for doped structures was done using the QuasiNewton optimizer method of the ATK package, with maximum force and stress 0.05 eV/Å and 0.05 eV/Å^3, respectively. The density of states was computed for the geometry optimized structures of doped Nb_2N and Nb_4N_3.

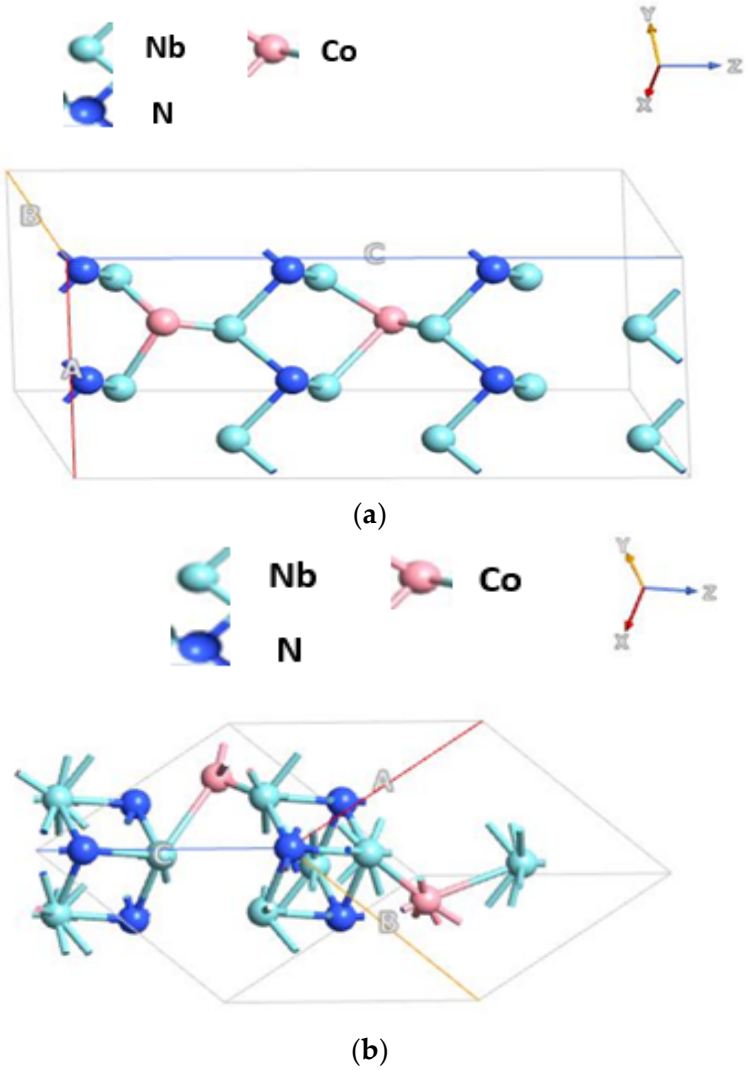


Figure 2. Chemical structures of doped niobium nitride: (**a**) Nb_2N-2Co; (**b**) Nb_4N_3-2Co.

Quantum capacitance of electrodes was calculated using the computed density of states (DOSs). If ϕ is the operating voltage and Q is the surface charge on niobium nitride, then, from density of state DOS (E), we can find quantum capacitance using Equations (2)–(4) [59,60]:

$$Q = e\int_{-\infty}^{+\infty} DOS(E)[f(E) - f(E - e\phi)]\, dE \tag{2}$$

$$f(E) = \frac{1}{1 + \exp\left(\frac{E}{kT}\right)}, \tag{3}$$

where e is the electronic charge, $f(E)$ is the Fermi-Dirac distribution function and E is the energy w.r.t the Fermi energy.

By definition, one can obtain quantum capacitance by differentiating Q w.r.t ϕ, that is,

$$QC = \frac{dQ}{d\phi} = e^2 \int_{-\infty}^{+\infty} DOS(E) \times \frac{sech^2\left(\frac{E-e\phi}{2kT}\right)}{4kT} dE. \quad (4)$$

Doping impacts the electronic structure of materials, thus changing the density of states. Due to these changes, the quantum capacitance gets modified [61]. The variation in the electronic DOS and corresponding change in the value of quantum capacitance were studied for different operating voltages for pristine and doped structures.

The dependence of quantum capacitance on spin, number of layers and temperature was also investigated.

3. Results and Discussion

3.1. Unpolarised Pristine Structures

Density of states are determined to calculate the quantum capacitance of pristine Nb_2N and Nb_4N_3 using the DFT method without spin. The calculated density of states are shown in Figure 3a,b, respectively.

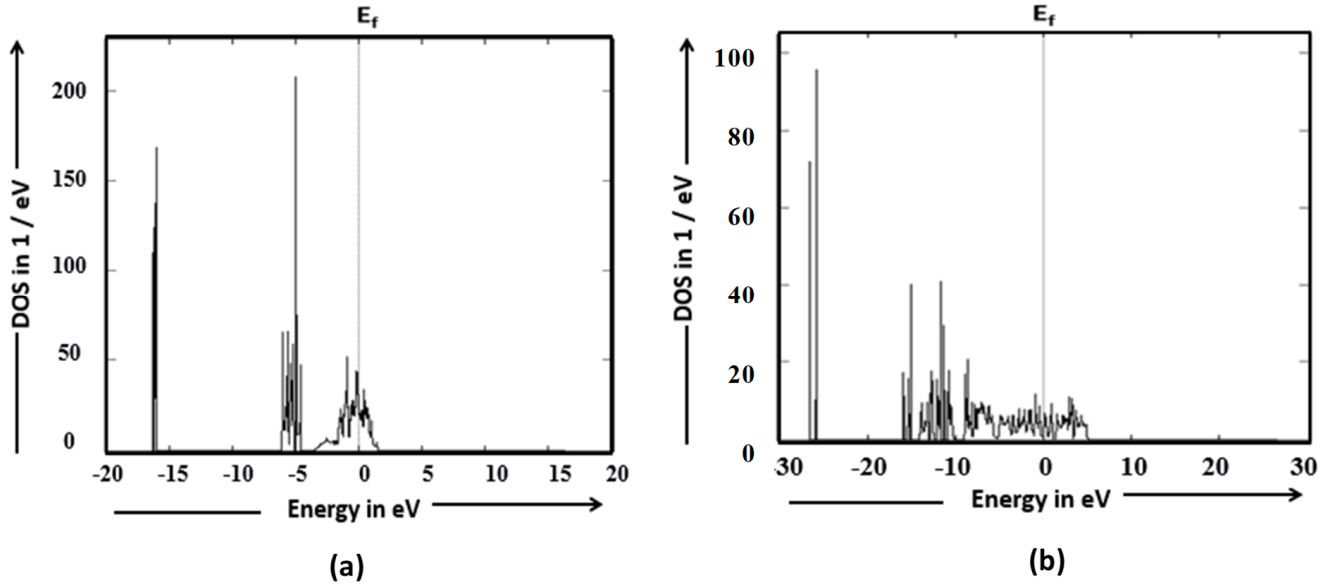


Figure 3. The density of states (DOSs) for (**a**) Nb_2N and (**b**) Nb_4N_3.

In Figure 3a, pronounced peaks in DOS are observed for Nb_2N at and near Fermi level (in the range of interest). The peaks of the density of states close to the Fermi level are expected to make a major contribution to the QC as per Equation (4). For Nb_2N, the calculations show very high values of quantum capacitance at different bias voltages, the highest being 1196.28 μF cm^{-2} at −1 V, as shown in Figure 4. However, for Nb_4N_3, the peaks are not that pronounced (Figure 3b) but are high enough to give a quantum capacitance value of 174.86 μF cm^{-2}, near Fermi level. These values obtained for Nb_4N_3 at different bias voltages around Fermi level are lower than that of Nb_2N but are higher than that of graphene, the most widely used electrode material for supercapacitor. It is well known that the quantum capacitance of pristine graphene electrode is very low due to its low density of state (DOS) near the Fermi level. The QC of pristine graphene has been investigated experimentally and theoretically [6,11,12,62], and it was found that the presence of Dirac point in DOS at Fermi level in the case of graphene results in extremely low values of quantum capacitance (in the range of 4~6 μF cm^{-2}).

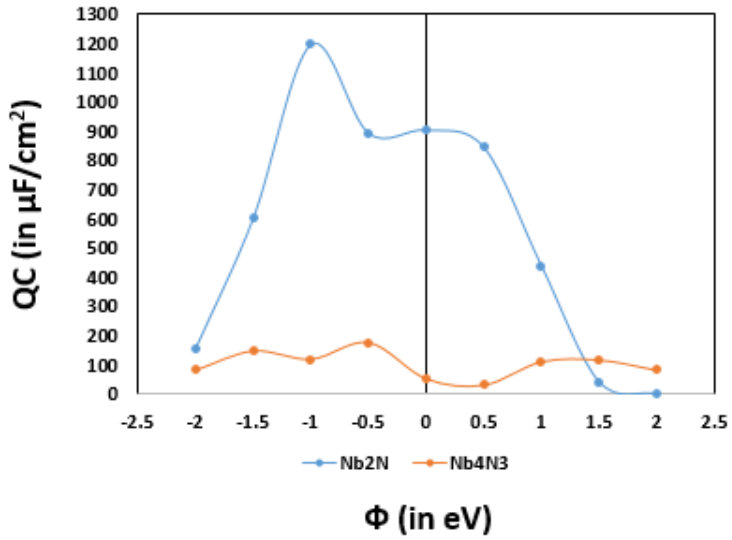


Figure 4. Variation in quantum capacitance (QC) for pristine unpolarized niobium nitride structures under bias voltage.

The QC values obtained for both structures at different bias voltages are compared in Figure 4. It is found that quantum capacitance of Nb_2N remains higher than Nb_4N_3 for most of the bias voltage range. Although QC values for Nb_4N_3 are lower than Nb_2N, they are still high enough (Figure 4) for use as electrode material for supercapacitors.

3.2. Effect of Number of Layers

In order to investigate the impact of increasing molecular layers in the crystal structure, these calculations were repeated for up to three layers. The values of quantum capacitance are found to increase with increase in number of layers for both Nb_2N and Nb_4N_3, as shown in Figure 5a,b, respectively.

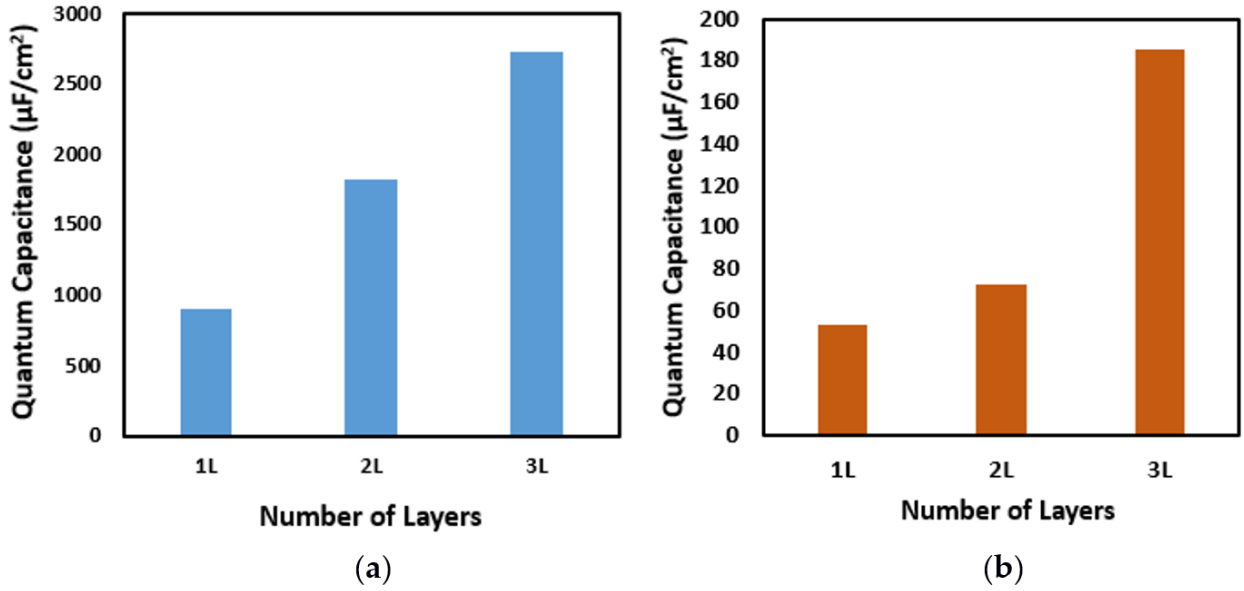
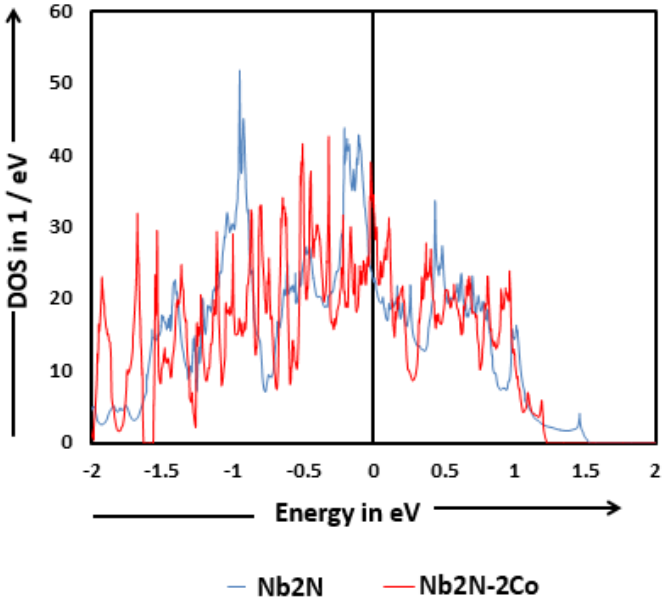


Figure 5. Variation of quantum capacitance QC with number of layers for (**a**) Nb_2N and (**b**) Nb_4N_3.

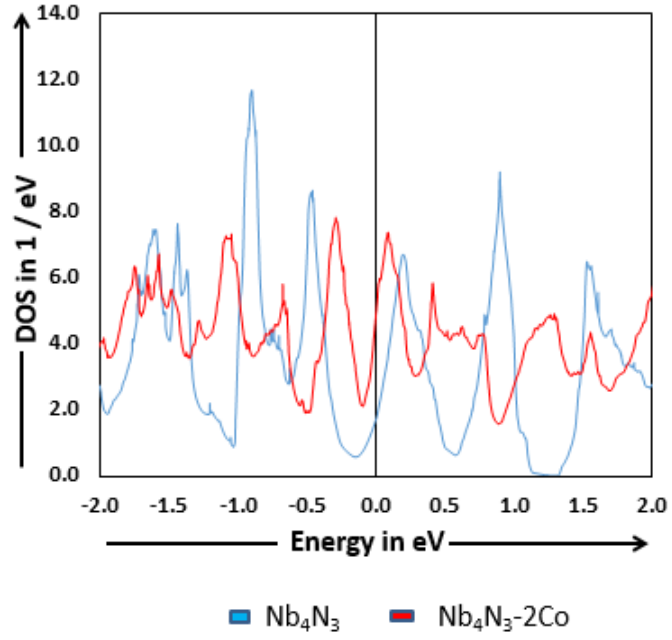
A similar trend of increase in QC with increase in layers is also reported in the case of graphene [59].

3.3. Effect of Cobalt Doping

The impact of cobalt doping on density of states and, subsequently, on quantum capacitance of both structures of niobium nitride was investigated. Comparison of density of states of pristine and doped structures of Nb_2N and Nb_4N_3 are shown in Figure 6. The density of states for pristine Nb_2N and Nb_4N_3 are increased at Fermi level when they are doped with two atoms of cobalt, as shown in Figure 6a,b. This rise in DOS at Fermi level is mainly due to the contribution in DOS from the 3d electrons of cobalt dopant. Little contribution to the rise in DOS also comes from the electrons of the 4s subshell of cobalt. This increase in the density of states contributes to the increase in QC.



(**a**)



(**b**)

Figure 6. Comparison of the density of states at and near Fermi Level of (**a**) Nb_2N and Nb_2N-2Co; (**b**) Nb_4N_3 and Nb_4N_3-2Co.

The calculated quantum capacitance values for unpolarized Nb_4N_3-2Co and Nb_2N-2Co depicts a rise in QC in comparison to their pristine counterparts at Fermi level, as shown in Figure 7. At Fermi level, rise in QC by factors of 2.5 and 1.2 is observed in doped Nb_4N_3 and Nb_2N, respectively. The increase is in agreement to the increase in the total density of states of Nb_4N_3 and Nb_2N after doping at Fermi level, which is clearly visible in Figure 6. For cobalt-doped Nb_4N_3, the QC is in the range of 65.85 to 135.2 μF cm^{-2} in the area of interest, as shown in Figure 7a. It is found that the low values of quantum capacitance at Fermi level obtained in the case of pristine Nb_4N_3 can be increased when doping with cobalt.

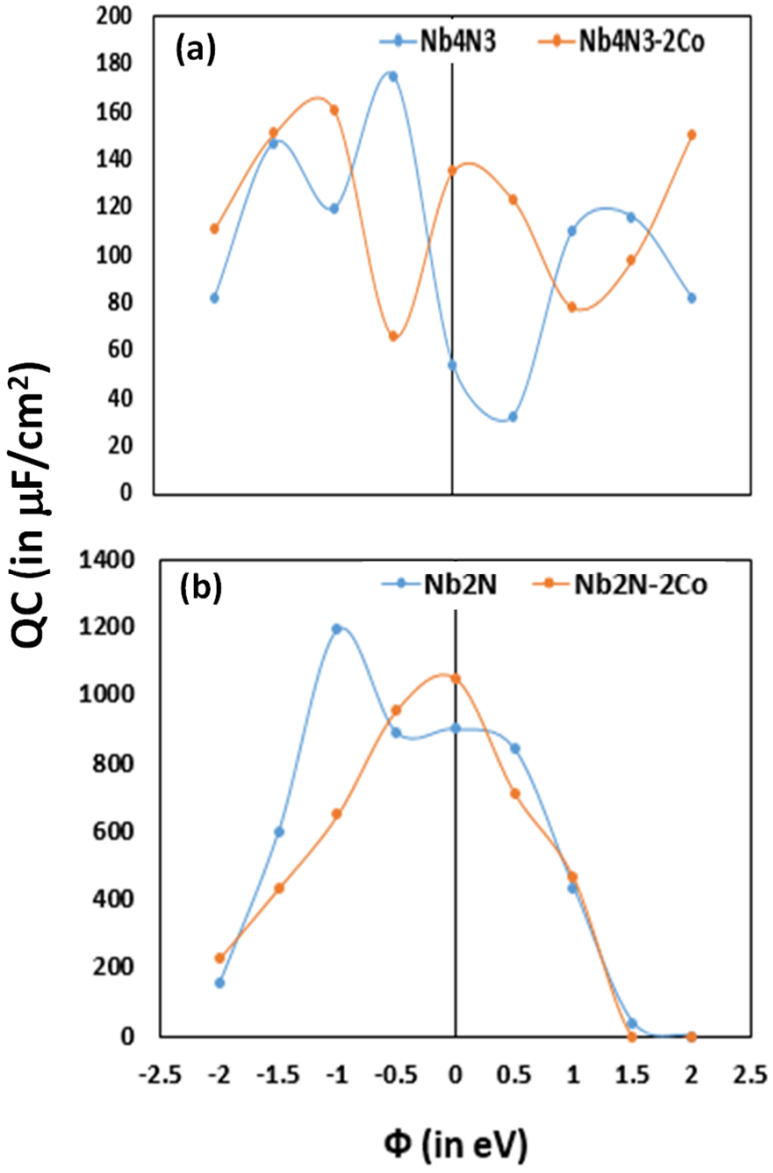


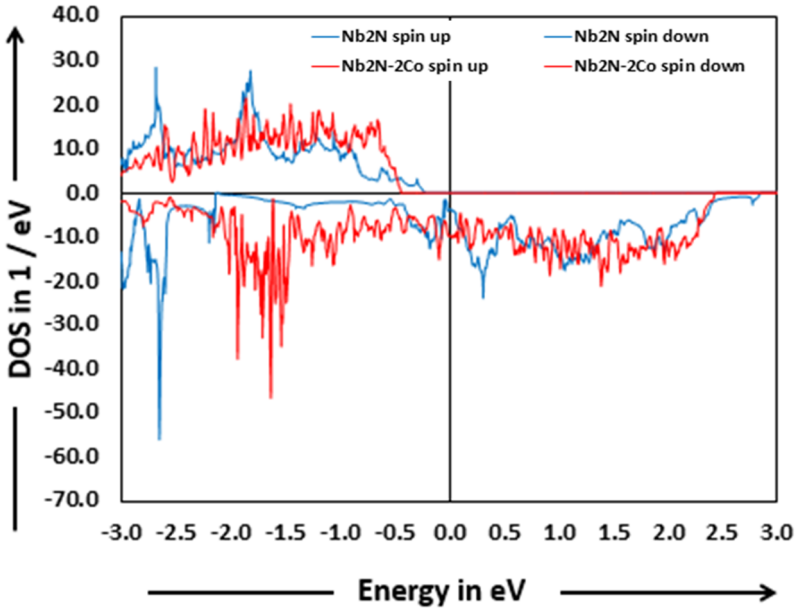
Figure 7. Comparison of calculated QC at different bias voltages for pristine and doped unpolarized structures. (**a**) Nb_4N_3 and Nb_4N_3-2Co; (**b**) Nb_2N and Nb_2N-2Co.

However, doping with cobalt shows only a slight increase in the QC at Fermi level in the case of Nb_2N, reaching to value 1052.2 μF cm^{-2} (Figure 7b). At all other bias voltages, pristine Nb_2N shows similar or slightly higher values for QC than doped Nb_2N. The variation in QC of pristine Nb_2N after doping with cobalt can be completely understood by comparing the DOS of pristine and doped structures of Nb_2N. As shown in Figure 6a, the DOS for doped Nb_2N is slightly higher than that of its pristine counterpart, resulting in

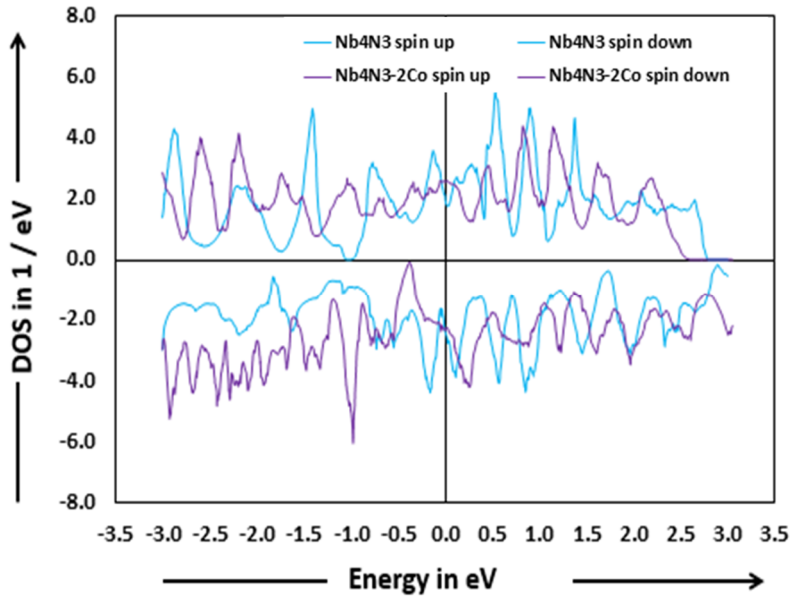
a slight increase in QC at Fermi level. For positive energies, the DOSs are almost similar for both pristine and doped structures, hence showing similar values of QC for positive bias voltages. The fall in QC in doped Nb_2N at −1 V is attributed to a fall in its DOS near −1 eV as shown in Figure 6a.

3.4. Effect of Spin on Pristine and Doped Structures

The spin polarized calculations were also done on pristine and doped Nb_2N and Nb_4N_3 structures. The comparison of density of states near Fermi level and QC value obtained at Fermi level of pure and doped structures are plotted and given in Figures 8 and 9.



(**a**)



(**b**)

Figure 8. Comparison of the density of states of spin polarized (**a**) Nb_2N and Nb_2N-2Co and (**b**)Nb_4N_3 and Nb_4N_3-2Co.

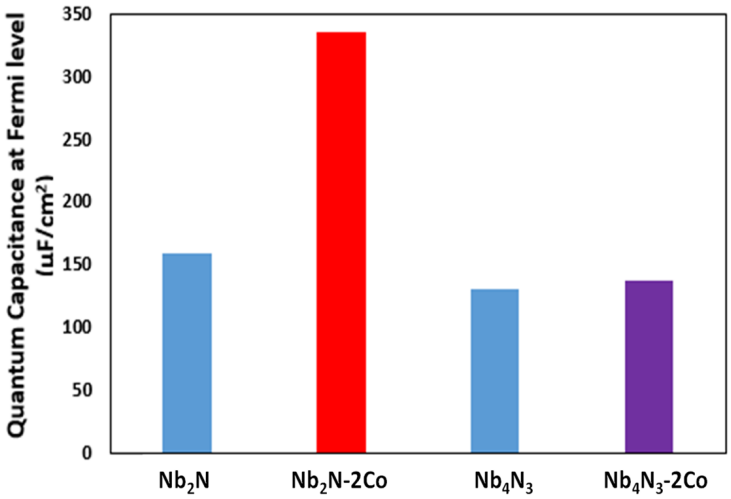


Figure 9. Comparison of calculated QC for pristine and doped polarized structures at Fermi level.

In case of Nb_2N, there is an increase in DOS at and near Fermi level after cobalt doping, as shown in Figure 8a. The increase is due to the contribution of 4d and 5s electrons of cobalt. This increase doubles the QC value at Fermi level for doped Nb_2N as compared to its pristine counterpart, as shown in Figure 9 (Histo). Whereas, in the case of Nb_4N_3, not much increase is seen in DOS (Figure 8b) at Fermi level after doping, resulting in a very small increase in QC at Fermi Level, as shown in Figure 9.

3.5. Effect of Temperature on Quantum Capacitance

Calculations for quantum capacitance were done at three different temperatures (i.e., 233, 300 and 353 K). No significant change was noted in the DOSs profile. For pristine unpolarized Nb_2N and Nb_4N_3, a change in temperature from 233 to 353 K increases the QC at Fermi level slightly from 878.3 to 921 μF cm^{-2} and 51.72 to 54.34 μF cm^{-2}, respectively. In case of cobalt-doped structures of Nb_2N and Nb_4N_3, the change observed is 5% and 8%, respectively. The slight change in the QC values is mainly due to the Fermi Dirac distribution function present in the equations used for calculating quantum capacitance. Similar studies done for graphene at different temperature ranges have also shown negligible impact of temperature on QC of graphene [63].

4. Conclusions

DFT calculations are performed to investigate the quantum capacitance of niobium nitrides Nb_2N and Nb_4N_3 for their possible use as supercapacitor electrode materials. Out of the two pristine structures investigated, Nb_2N is the most promising candidate for fabrication of supercapacitor electrodes, with theoretical QC reaching up to 1196.28 μF cm^{-2} at −1 V for unpolarized Nb_2N. Even for positive bias voltage range, quantum capacitance values for Nb_2N exceeds the QC values of Nb_4N_3, reaching a value of 844.8 μF cm^{-2} at 0.5 V. Impact of increase in layers on QC is also investigated and it is found that the quantum capacitance increases with increase in layers for both pristine niobium nitrides.

A viable method is proposed to enhance the quantum capacitance of niobium nitride using suitable dopant. The results show that the value of QC of pristine structures at Fermi level can be further increased by doping with cobalt. The maximum value of quantum capacitance in doped structures is obtained for unpolarized doped Nb_2N (1052.2 μF cm^{-2}) at Fermi level. The impact of polarization is also studied on both pure and doped structures and a substantial increase is seen in QC at Fermi level for Nb_2N after doping with cobalt. The calculations done for pristine and cobalt-doped Nb_2N and Nb_4N_3 structures show no significant temperature dependence of DOS and a slight change in quantum capacitance with temperature.

Author Contributions: B. and S.S.—Modelling, simulation, computations and analysis of results, preparation of manuscript and figures; Y.K. and G.A.—Conceptualization, analysis, and overall supervision; P.B.—Critical analysis and presentation of results. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Acknowledgments: Authors acknowledge the help from University Science and Instrumentation Centre, USIC, JNU, Delhi for providing the computing resources.

Conflicts of Interest: The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

1. Hughes, Z.E.; Walsh, T.R. Computational chemistry for graphene-based energy applications: Progress and challenges. *Nanoscale* **2015**, *7*, 6883. [CrossRef] [PubMed]
2. Ponnamma, D.; Vijayan, P.; Al-Maadeed, M.A.A. 3D architectures of titania nanotubes and graphene with efficient nanosynergy for supercapacitors. *Mater. Des.* **2017**, *117*, 203. [CrossRef]
3. Wang, G.; Zhang, L.; Zhang, J. A review of electrode materials for electrochemical supercapacitors. *Chem. Soc. Rev.* **2012**, *41*, 797. [CrossRef]
4. Paek, E.; Pak, A.J.; Kweon, K.E.; Hwang, G.S. On the origin of the enhanced supercapacitor performance of nitrogen-doped graphene. *J. Phys. Chem. C* **2013**, *117*, 5610. [CrossRef]
5. Pak, A.J.; Paek, E.; Hwang, G.S. Relative contributions of quantum and double layer capacitance to the supercapacitor performance of carbon nanotubes in an ionic liquid. *Phys. Chem. Chem. Phys.* **2013**, *15*, 19741. [CrossRef] [PubMed]
6. Stoller, M.D.; Magnuson, C.W.; Zhu, Y.; Murali, S.; Suk, J.W.; Piner, R.; Ruoff, R.S. Interfacial capacitance of single layer graphene. *Energy Environ. Sci.* **2011**, *4*, 4685. [CrossRef]
7. Xia, J.; Chen, F.; Li, J.; Tao, N. Measurement of the quantum capacitance of graphene. *Nat. Nanotechnol.* **2009**, *4*, 505. [CrossRef]
8. Zhao, X.; Sanchez, B.M.; Dobson, P.J.; Grant, P.S. High-performance symmetric electrochemical capacitor based on graphene foam and nanostructured manganese oxide. *Nanoscale* **2011**, *3*, 839. [CrossRef]
9. Simon, P.; Gogotsi, Y. Materials for electrochemical capacitors. *Nat. Mater.* **2008**, *7*, 845. [CrossRef] [PubMed]
10. Zhang, L.L.; Zhao, X. Carbon-based materials as supercapacitor electrodes. *Chem. Soc. Rev.* **2009**, *38*, 2520. [CrossRef]
11. John, D.L.; Castro, L.C.; Pulfrey, D.L. Quantum capacitance in nanoscale device modeling. *J. Appl. Phys.* **2004**, *96*, 5180. [CrossRef]
12. Paek, E.; Pak, A.J.; Hwang, G.S. A computational study of the interfacial structure and capacitance of graphene in [BMIM][PF_6] ionic liquid. *J. Electrochem. Soc.* **2013**, *160*. [CrossRef]
13. Dong, S.; Chen, X.; Zhang, X.; Cui, G. Nanostructured transition metal nitrides for energy storage and fuel cells. *Coord. Chem. Rev.* **2013**, *257*, 1946. [CrossRef]
14. Balogun, M.S.; Qiu, W.; Wang, W.; Fang, P.; Lu, X.; Tong, Y. Recent advances in metal nitrides as high-performance electrode materials for energy storage devices. *J. Mater. Chem. A* **2015**, *3*, 1364. [CrossRef]
15. Choi, D.; Blomgren, G.E.; Kumta, P.N. Fast and reversible surface redox reaction in nanocrystalline vanadium nitride supercapacitors. *Adv. Mater.* **2006**, *18*, 1178. [CrossRef]
16. Choi, D.; Kumta, P.N. Nanocrystalline TiN derived by a two-step halide approach for electrochemical capacitors. *J. Electrochem. Soc.* **2006**, *153*, A2298. [CrossRef]
17. Choi, D.; Kumta, P.N. Synthesis, structure, and electrochemical characterization of nanocrystalline tantalum and tungsten nitrides. *J. Am. Ceram. Soc.* **2007**, *90*, 3113. [CrossRef]
18. Choi, D.; Kumta, P.N. Synthesis and characterization of nanostructured niobium and molybdenum nitrides by a two-step transition metal halide approach. *J. Am. Ceram. Soc.* **2011**, *94*, 2371. [CrossRef]
19. Lu, X.; Wang, G.; Zhai, T.; Yu, M.; Xie, S.; Ling, Y.; Liang, C.; Tong, Y.; Li, Y. Stabilized TiN nanowire arrays for high-performance and flexible supercapacitors. *Nano Lett.* **2012**, *12*, 5376. [CrossRef]
20. Lu, X.; Yu, M.; Zhai, T.; Wang, G.; Xie, S.; Liu, T.; Liang, C.; Tong, Y.; Li, Y. High energy density asymmetric quasi-solid-state supercapacitor based on porous vanadium nitride nanowire anode. *Nano Lett.* **2013**, *13*, 2628. [CrossRef]
21. Xie, Y.; Wang, Y.; Du, H. Electrochemical capacitance performance of titanium nitride nanoarray. *Mater. Sci. Eng. B* **2013**, *178*, 1443. [CrossRef]
22. Dong, S.; Chen, X.; Gu, L.; Zhou, X.; Xu, H.; Wang, H.; Liu, Z.; Han, P.; Yao, J.; Wang, L. Facile preparation of mesoporous titanium nitride microspheres for electrochemical energy storage. *ACS Appl. Mater. Interfaces* **2011**, *3*, 93. [CrossRef] [PubMed]
23. Lu, X.; Liu, T.; Zhai, T.; Wang, G.; Yu, M.; Xie, S.; Ling, Y.; Liang, C.; Tong, Y.; Li, Y. Improving the cycling stability of metal-nitride supercapacitor electrodes with a thin carbon shell. *Adv. Energy Mater.* **2014**, *4*, 1300994. [CrossRef]
24. Zou, Y.; Qi, X.; Zhang, C.; Ma, S.; Zhang, W.; Li, Y.; Chen, T.; Wang, X.; Chen, Z.; Welch, D.; et al. Discovery of superconductivity in hard hexagonal ε-NbN. *Sci. Rep.* **2016**, *6*, 22330. [CrossRef] [PubMed]
25. Oya, G.-i.; Onodera, Y. Transition temperatures and crystal structures of single-crystal and polycrystalline NbN_X films. *J. Appl. Phys.* **1974**, *45*, 1389. [CrossRef]

26. Patel, U.; Avci, S.; Xiaoa, Z.L.; Hua, J.; Yu, S.H.; Ito, Y. Synthesis and superconducting properties of niobium nitride nanowires and nanoribbons. *Appl. Phys. Lett.* **2007**, *91*, 162508. [CrossRef]
27. Wang, P.; Wang, R.; Lang, J.; Zhang, X.; Chena, Z.; Yan, X. Porous niobium nitride as a capacitive anode material for advanced Li-ion hybrid capacitors with superior cycling stability. *J. Mater. Chem. A* **2016**, *4*, 9760. [CrossRef]
28. Wei, B.; Ming, F.; Liang, H.; Wenshen, H.; Wanga, Z. All nitride asymmetric supercapacitors of niobium titanium nitride-vanadium nitride. *J. Power Sour.* **2021**, *481*, 228842. [CrossRef]
29. Cui, H.; Zhu, G.; Liu, X.; Liu, F.; Xie, Y.; Yang, C.; Lin, T.-q.; Gu, H.; Huang, F. Niobium nitride Nb_4N_5 as a new high-performance electrode material for supercapacitors. *Adv. Sci.* **2015**, *2*, 1500126. [CrossRef]
30. Ng, V.M.H.; Huang, H.; Zhou, K.; Lee, P.S.; Que, W.; Xu, J.Z.; Kong, L.B. Recent progress in layered transition metal carbides and/or nitrides (MXenes) and their composites: Synthesis and applications. *J. Mater. Chem. A* **2017**, *5*, 3039. [CrossRef]
31. Barsoum, M.W. The $M_{N+1}AX_N$ phases: A new class of solids: Thermodynamically stable nanolaminates. *Prog. Solid State Chem.* **2000**, *28*, 201. [CrossRef]
32. Naguib, M.; Mashtalir, O.; Carle, J.; Presser, V.; Lu, J.; Hultman, L.; Gogotsi, Y.; Barsoum, M.W. Two-dimensional transition metal carbides. *ACS Nano* **2012**, *6*, 1322. [CrossRef]
33. Naguib, M.; Kurtoglu, M.; Presser, V.; Lu, J.; Niu, J.; Heon, M.; Hultman, L.; Gogotsi, Y.; Barsoum, M.W. Two-dimensional nanocrystals produced by exfoliation of Ti_3AlC_2. *Adv. Mater.* **2011**, *23*, 4248. [CrossRef]
34. Pang, J.; Mendes, R.G.; Bachmatiuk, A.; Zhao, L.; Ta, H.Q.; Liu, T.G.H.; Liu, Z.; Rummeli, M.H. Applications of 2D MXenes in energy conversion and storage systems. *Chem. Soc. Rev.* **2019**, *48*, 72. [CrossRef] [PubMed]
35. Gogotsi, Y.; Anasori, B. The rise of MXenes. *ACS Nano* **2019**, *13*, 8491. [CrossRef] [PubMed]
36. Khazaei, M.; Mishra, A.; Venkataramanan, N.S.; Singh, A.K.; Yunoki, S. Recent advances in MXenes: From fundamentals to applications. *Curr. Opin. Solid State Mater. Sci.* **2019**, *23*, 164. [CrossRef]
37. Khazaei, M.; Arai, M.; Sasaki, T.; Chung, C.Y.; Venkataramanan, N.S.; Estili, M.; Sakka, Y.; Kawazoe, Y. Novel electronic and magnetic properties of two-dimensional transition metal carbides and nitrides. *Adv. Funct. Mater.* **2013**, *23*, 2185. [CrossRef]
38. Ling, Z.; Ren, C.E.; Zhao, M.Q.; Yang, J.; Giammarco, J.M.; Qiu, J.; Barsoum, M.W.; Gogotsi, Y. Flexible and conductive MXene films and nanocomposites with high capacitance. *Proc. Nat. Acad. Sci. USA* **2014**, *111*, 16676. [CrossRef]
39. Guo, Z.L.; Zhou, J.; Si, C.; Sun, Z.M. Flexible two-dimensional Tin+1Cn (n = 1, 2 and 3) and their functionalized MXenes predicted by density functional theories. *Phys. Chem. Chem. Phys.* **2015**, *17*, 15348. [CrossRef]
40. Naguib, M.; Mochalin, V.N.; Barsoum, M.W.; Gogotsi, Y. 25th anniversary article: MXenes: A new family of two-dimensional materials. *Adv. Mater.* **2014**, *26*, 992. [CrossRef]
41. Li, Z.; Wang, L.; Sun, D.; Zhang, Y.; Liu, B.; Hu, Q.; Zhou, A. Synthesis and thermal stability of two-dimensional carbide MXene Ti_3C_2. *Mater. Sci. Eng. B* **2015**, *191*, 33. [CrossRef]
42. Khazaei, M.; Ranjbar, A.; Arai, M.; Sasaki, T.; Yunoki, S. Electronic properties and applications of MXenes: A theoretical review. *J. Mater. Chem. C* **2017**, *5*, 2488. [CrossRef]
43. Chen, C.; Ji, X.; Xu, K.; Zhang, B.; Miao, L.; Jiang, J. Prediction of T- and H-phase two dimensional transition-metal carbides/nitrides and their semiconducting-metallic phase transition. *Chem. Phys. Chem.* **2017**, *18*, 1897. [CrossRef]
44. Liu, H.; Duan, C.; Yang, C.; Shen, W.; Wang, F.; Zhu, Z. A novel nitrite biosensor based on the direct electrochemistry of hemoglobin immobilized on MXene-Ti_3C_2. *Sensor. Actuators B Chem.* **2015**, *218*, 60. [CrossRef]
45. Anasori, B.; Lukatskaya, M.R.; Gogotsi, Y. 2D metal carbides and nitrides (MXenes) for energy storage. *Nat. Rev. Mater.* **2017**, *2*, 16098. [CrossRef]
46. Zhou, Y.; Luo, K.; Zha, X.; Liu, Z.; Bai, X.; Huang, Q.; Guo, Z.; Lin, C.; Du, S. Electronic and transport properties of Ti_2Co_2 MXene nanoribbons. *J. Phys. Chem. C* **2016**, *120*, 17143. [CrossRef]
47. Mortazavi, B.; Shahrokhi, M.; Makaremi, M.; Rabczuk, T. Anisotropic mechanical and optical response and negative Poisson's ratio in Mo_2C nanomembranes revealed by first-principles simulations. *Nanotechnology* **2017**, *28*, 115705. [CrossRef]
48. Lipatov, A.; Alhabeb, M.; Lukatskaya, M.R.; Boson, A.; Gogotsi, Y.; Sinitskii, A. Efect of synthesis on quality, electronic properties and environmental stability of individual monolayer Ti_3C_2 MXene fakes. *Adv. Electron. Mater.* **2016**, *2*, 1600255. [CrossRef]
49. Mortazavi, B.; Shahrokhi, M.; Makaremi, M.; Rabczuk, T. Theoretical realization of Mo_2P; a novel stable 2D material with superionic conductivity and attractive optical properties. *Appl. Mater. Today* **2017**, *9*, 292. [CrossRef]
50. Zhao, P.; Jin, H.; Lv, X.; Huang, B.; Ma, Y.; Dai, Y. Modifed MXene: Promising electrode materials for constructing ohmic contacts with MoS_2 for electronic device applications. *Phys. Chem. Chem. Phys.* **2018**, *20*, 16551. [CrossRef]
51. Eames, C.; Islam, M.S. Ion intercalation into two-dimensional transition-metal car-bides: Global screening for new high-capacity battery materials. *J. Am. Chem. Soc.* **2014**, *136*, 16270. [CrossRef]
52. Naguib, M.; Come, J.; Dyatkin, B.; Presser, V.; Taberna, P.L.; Simon, P.; Barsoum, M.W.; Gogotsi, Y. MXene: A promising transition metal carbide anode for lithium-ion batteries. *Electrochem. Commun.* **2012**, *16*, 61. [CrossRef]
53. Yu, Y.X. Prediction of mobility, enhanced storage capacity, and volume change during sodiation on interlayer-expanded functionalized Ti_3C_2 MXene anode materials for sodium-ion batteries. *J. Phys. Chem. C* **2016**, *120*, 5288. [CrossRef]
54. Liang, X.; Garsuch, A.; Nazar, L.F. Sulfur cathodes based on conductive MXene nanosheets for high performance lithium-sulfur batteries. *Angew. Chem. Int. Ed.* **2015**, *54*, 3907. [CrossRef] [PubMed]

55. Lukatskaya, M.R.; Mashtalir, O.; Ren, C.E.; Dall'Agnese, Y.; Rozier, P.; Taberna, P.L.; Naguib, M.; Simon, P.; Barsoum, M.W.; Gogotsi, Y. Cation intercalation and high volumetric capacitance of two-dimensional titanium carbide. *Science* **2013**, *341*, 1502. [CrossRef]
56. Hu, M.; Li, Z.J.; Hu, T.; Zhang, C.; Wu, Z.; Wang, X.H. Self-assembled $Ti_3C_2T_X$ MXene film with high gravimetric capacitance. *Chem. Commun.* **2015**, *51*, 13531. [CrossRef]
57. Ge, W.; Wang, L.; Li, C.; Wang, C.; Wang, D.; Qian, Y.; Xu, L. Conductive cobalt doped niobium nitride porous spheres as efficient polysulfide convertor for advanced lithium-sulfur batteries. *J. Mater. Chem. A* **2020**, *8*, 6276. [CrossRef]
58. Perdew, J.P.; Burke, K.; Ernzerhof, M. Generalized gradient approximation made simple. *Phys. Rev. Lett.* **1996**, *77*, 3865. [CrossRef]
59. Zhan, C.; Neal, J.; Wu, J.; Jiang, D.E. Quantum effects on the capacitance of graphene-based electrodes. *J. Phys. Chem. C* **2015**, *119*, 22297. [CrossRef]
60. Yang, G.M.; Zhang, H.Z.; Fan, X.F.; Zheng, W.T. Density functional theory calculations for the quantum capacitance performance of graphene-based electrode material. *J. Phys. Chem. C* **2015**, *119*, 6464. [CrossRef]
61. Elias, D.C.; Gorbachev, R.V.; Mayorov, A.S.; Morozov, S.V.; Zhukov, A.A.; Blake, P.; Ponomarenko, L.A.; Grigorieva, I.V.; Novoselov, K.S.; Guinea, F.; et al. Dirac cones reshaped by interaction effects in suspended graphene. *Nat. Phys.* **2011**, *7*, 701. [CrossRef]
62. Frackowiak, E. Carbon materials for supercapacitor application. *Phys. Chem. Chem. Phys.* **2007**, *9*, 1774. [CrossRef] [PubMed]
63. Vatamanu, J.; Ni, X.; Liu, F.; Bedrov, D. Tailoring graphene-based electrodes from semiconducting to metallic to increase the energy density in supercapacitors. *Nanotechnology* **2015**, *26*, 46. [CrossRef] [PubMed]

EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 8
349-354
Year: 2020

DEXAMETHASONE: COVID-19`S LAST RESORT A COMPLETE REVIEW

Maheipeube Ndang*, Gaurav Kumar Sharma and Dr. Kaushal K. Chandrul

Department of Pharmacy, Mewar University, Chittorgarh (312901), Rajasthan, India.

***Corresponding Author: Maheipeube Ndang**
Department of Pharmacy, Mewar University, Chittorgarh (312901), Rajasthan, India.

Article Received on 15/06/2020 **Article Revised on 05/07/2020** **Article Accepted on 26/07/2020**

ABSTRACT
Dexamethasone is a corticosteriod commonly used as anti-inflammatory and immunosupressant. It is cheap and globally available. Dexamethasone may modulate inflammation-mediated lung injury and thereby reduce progression to respiratory failure and death. A study found out that in Covid-19 patients dexamethasone reduced deaths by 1/3rd in ventilated patients and 1/5th in other patients receiving oxygen only.

KEYWORDS:

INTRODUCTION

Dexamethasone is a glucocorticoid that stops the discharge of drugs within the body that cause inflammation.It was initial synthesized by Duke of Edinburgh Showalter Hench in 1957.It had been introduced for medical use in 1958. It has been listed on the WHO Model List of Essential Medicines since 1977 in multiple formulations, and is currently off-patent and affordably available in most countries.

Dexamethasone is employed to treat many alternative inflammatory conditions resembling allergic disorders and skin conditions.

It is additionally accustomed treat inflammatory bowel disease, arthritis, lupus, psoriasis, and respiratory disorders.

It might also be used for functions ex-directory during this medication guide. It can be taken by using mouth, as a pill or elixir, as an injection into a muscle, intravenously, or through an eye fixed drop.It bind to the glucocorticoid receptor, inhibiting pro-inflammatory signals, and promoting anti-inflammatory signals.

Dexamethasone's duration of action varies depending on the route. Corticosteroids have a wide therapeutic window as patients may require doses that are multiples of what the body naturally produces. Patients taking corticosteroids should be counselled regarding the risk of hypothalamic-pituitary- adrenal axis suppression and increased susceptibility to infections.

Randomization,trial procedures and analysis.

A baseline statistics of sufferers inclined for the trial have been accumulated which covered demographic statistics, the extent of breathing help, essential coexisting illnesses, the suitability of the trial for a selected patient, and remedy availability at trial site. Routine fitness care and registry statistics which include statistics on essential status, discharge from the health facility, and breathing and renal help remedy have been obtained.

Selected sufferers have been assigned in a 2:1 ratio to acquire the standard wellknown of care by myself or the standard wellknown care of care plus oral or intravenous dexamethasone at a dose of 6 mg as soon as every day for 10 days.

If 28-day mortality turned into 20%, then the enrollment of as a minimum 2,000 sufferers withinside the dexamethasone group and 4,000 withinside the l usual care group could offer a power of as a minimum 90% at a facet P-price of 0.01% to stumble on a clinically applicable proportional reduction of 20% between the groups.

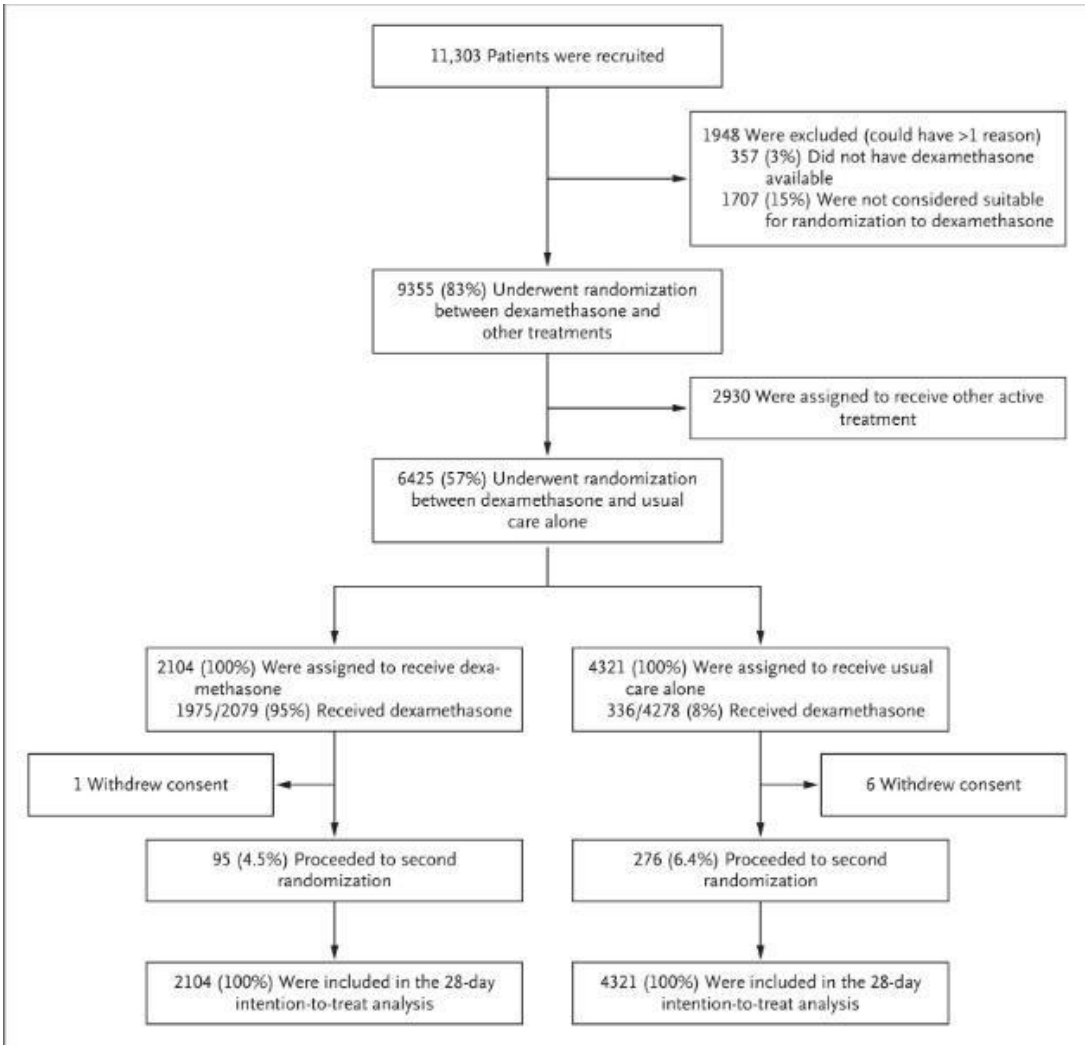
The number one final results turned into measured primarily based totally at the mortality inside 28 days after randomization. Whereas, the secondary final results turned into measured primarily based totally at the time till discharge from the health facility and amongst sufferers now no longer receiving invasive mechanical air flow or death. Other prespecified scientific consequences covered cause-particular mortality, receipt of renal hemodialysis or hemofiltration essential cardiac arrhythmia and receipt, and length of air flow. The risk ratio from Cox regression turned into carried out for the number one final results of 28-day mortality. Kaplan

Meier survival curves have been built to expose cumulative mortality over the 28-day period. Cox regression turned into extensively utilized to decide the secondary final results of health facility discharge inside 28 days with censoring of statistics on the next day for sufferers who had died at some point of hospitalization. The log- binomial regression version turned into carried out to calculate the chance ratio amongst sufferers now no longer receiving invasive mechanical air flow at randomization. Since the mean age turned into 1.1 years older amongst sufferers in dexamethasone, to stability the rate ratio have been adjusted for the baseline age into <70 years, 70-79 years and >80 years.

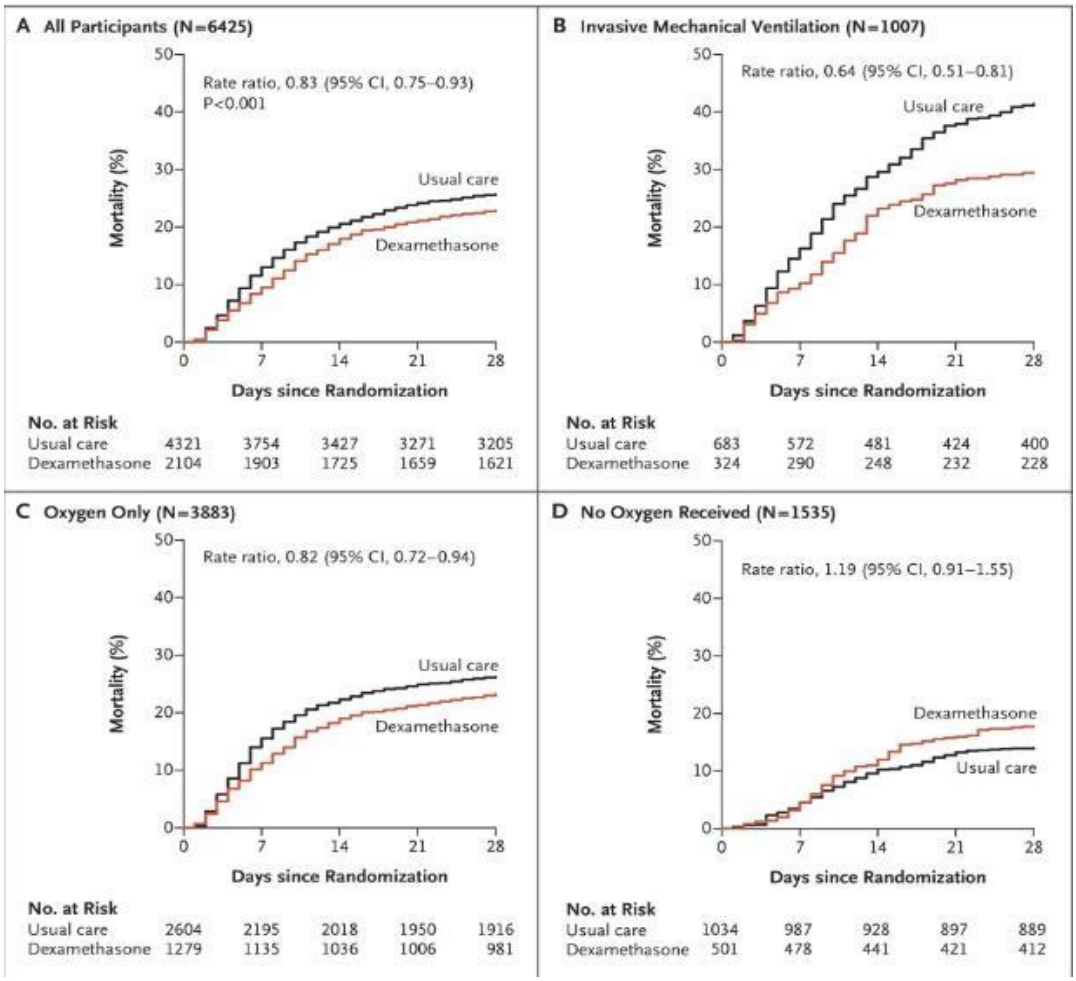
Table 1. Characteristics of the Patients at Baseline, According to Treatment Assignment and Level of Respiratory Support.*

Characteristic	Treatment Assignment		Respiratory Support Received at Randomization		
	Dexamethasone (N=2104)	Usual Care (N=4321)	No Receipt of Oxygen (N=1535)	Oxygen Only (N=3883)	Invasive Mechanical Ventilation (N=1007)
Age†					
Mean — yr	66.9±15.4	65.8±15.8	69.4±17.5	66.7±15.3	59.1±11.4
Distribution — no. (%)					
<70 yr	1141 (54)	2504 (58)	659 (43)	2148 (55)	838 (83)
70 to 79 yr	469 (22)	859 (20)	338 (22)	837 (22)	153 (15)
≥80 yr	494 (23)	958 (22)	538 (35)	898 (23)	16 (2)
Sex — no. (%)					
Male	1338 (64)	2749 (64)	891 (58)	2462 (63)	734 (73)
Female‡	766 (36)	1572 (36)	644 (42)	1421 (37)	273 (27)
Median no. of days since symptom onset (IQR)§	8 (5–13)	9 (5–13)	6 (3–10)	9 (5–12)	13 (8–18)
Median no. of days since hospitalization (IQR)	2 (1–5)	2 (1–5)	2 (1–6)	2 (1–4)	5 (3–9)
Respiratory support received — no. (%)					
No oxygen	501 (24)	1034 (24)	1535 (100)	NA	NA
Oxygen only	1279 (61)	2604 (60)	NA	3883 (100)	NA
Invasive mechanical ventilation	324 (15)	683 (16)	NA	NA	1007 (100)
Previous coexisting disease					
Any	1174 (56)	2417 (56)	911 (59)	2175 (56)	505 (50)
Diabetes	521 (25)	1025 (24)	342 (22)	950 (24)	254 (25)
Heart disease	586 (28)	1171 (27)	519 (34)	1074 (28)	164 (16)
Chronic lung disease	415 (20)	931 (22)	351 (23)	883 (23)	112 (11)
Tuberculosis	6 (<1)	19 (<1)	8 (1)	11 (<1)	6 (1)
HIV infection	12 (1)	20 (<1)	5 (<1)	21 (1)	6 (1)
Severe liver disease¶	37 (2)	82 (2)	32 (2)	72 (2)	15 (1)
Severe kidney impairment‖	166 (8)	358 (8)	119 (8)	253 (7)	152 (15)
SARS-CoV-2 test result					
Positive	1850 (88)	3848 (89)	1333 (87)	3416 (88)	949 (94)
Negative	247 (12)	453 (10)	193 (13)	452 (12)	55 (5)
Test result not yet known	7 (<1)	20 (<1)	9 (1)	15 (<1)	3 (<1)

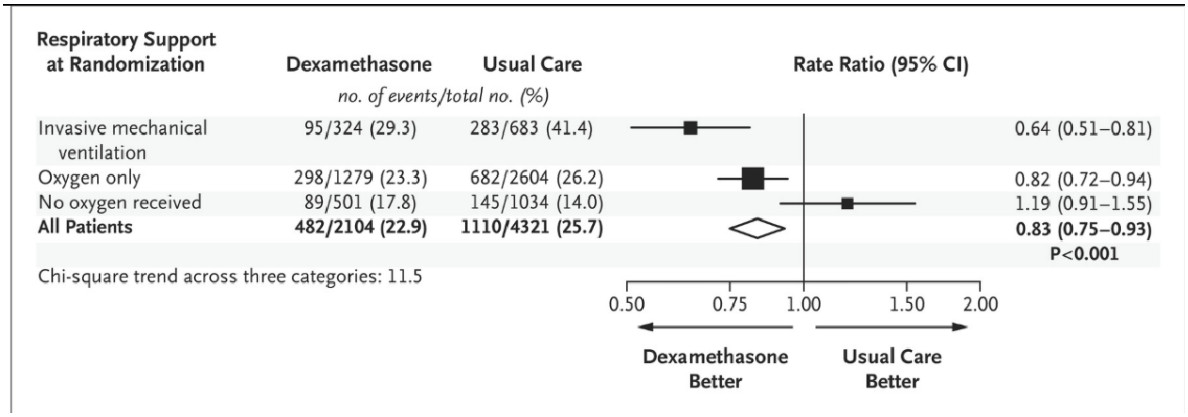
* Plus–minus values are means ±SD. HIV denotes human immunodeficiency virus, IQR interquartile range, NA not applicable, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.
† There was a significant (P=0.01) difference in the mean age between patients in the dexamethasone group and those in the usual care group, but there were no significant differences between the groups in any other baseline characteristic.
‡ Included in this category were 6 pregnant women.
§ Data regarding the number of days since symptom onset were missing for 4 patients in the dexamethasone group and 13 patients in the usual care group; these patients were excluded from estimates of the median number of days since onset.
¶ Severe liver disease was defined as requiring ongoing specialist care.
‖ Severe kidney impairment was defined as an estimated glomerular filtration rate of less than 30 ml per minute per 1.73 m^2.



Dexamethasone was being examined on sufferers as a part of the randomized assessment of the Covid-19 remedy trial, primarily based totally at Oxford University. During the trial, a complete of 2,104 sufferers are assigned to acquire dexamethasone 6mg in step with day, both through mouth or through intravenous injection, for 20 days and had been in comparison with a manipulate organization of 4,321 sufferers randomized to regular care alone. Among the sufferers withinside the manipulate organization, mortality after 28 days changed into observed to be maximum in people who required ventilation (41%), intermediate in the ones sufferers who required oxygen only (25%), and lowest amongst people who did now no longer require any breathing intervention (13%). The consequences cautioned that dexamethasone decreased deaths through 35% in ventilated sufferers and through 20% in every other sufferers receiving oxygen only. There had been no blessings amongst the ones sufferers who did now no longer require breathing support. Based on those consequences, demise might be avoided through the remedy of round ei ght ventilated sufferers or round 25 sufferers requiring oxygen alone.



Mortality at 28 days in all patients and according to Respiratory support randomization.



Effect of Dexamethasone on 28-day mortality based on randomization.

The primary outcome of the trial shows that death rate was lower in the dexamethasone group than the usual care group, with 482 deaths out of 2104 and in 1110 of 4321 patients. Whereas the secondary outcome reveals that sufferers in the dexamethasone group had a shorter duration of hospitalization than those in the usual care group and a greater probability of discharge alive within 28 days.

Table 2. Primary and Secondary Outcomes.

Outcome	Dexamethasone (N=2104)	Usual Care (N=4321)	Rate or Risk Ratio (95% CI)*
	no./total no. of patients (%)		
Primary outcome			
Mortality at 28 days	482/2104 (22.9)	1110/4321 (25.7)	0.83 (0.75–0.93)
Secondary outcomes			
Discharged from hospital within 28 days	1413/2104 (67.2)	2745/4321 (63.5)	1.10 (1.03–1.17)
Invasive mechanical ventilation or death†	456/1780 (25.6)	994/3638 (27.3)	0.92 (0.84–1.01)
Invasive mechanical ventilation	102/1780 (5.7)	285/3638 (7.8)	0.77 (0.62–0.95)
Death	387/1780 (21.7)	827/3638 (22.7)	0.93 (0.84–1.03)

* Rate ratios have been adjusted for age with respect to the outcomes of 28-day mortality and hospital discharge. Risk ratios have been adjusted for age with respect to the outcome of receipt of invasive mechanical ventilation or death and its subcomponents.
† Excluded from this category are patients who were receiving invasive mechanical ventilation at randomization.

Dexamethasone is commonly safe. It affords a good advantage-danger profile, mainly in sufferers with excessive types of pneumonia, whilst the advantage is much less distinguished in sufferers with non-excessive pneumonia. As the remedy is brief, even at excessive doses, corticosteroids aren't related to severe aspect effects. Potentially better blood glucose levels (hyperglycemia) are temporary.

Prolonged use (I.E., used for greater than weeks) can be related to unfavorable activities together with glaucoma, cataract, fluid retention, hypertension, mental effects (e.G., temper swings, reminiscence issues, confusion or irritation), weight gain, or elevated danger of infections and osteoporosis.

To reiterate: All those unfavorable activities aren't related to brief-time period use (aside from hyperglycemia that may get worse diabetes).

REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med, 2020; 382: 727-733.
2. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis, 2020; 20: 669-677.
3. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet, 2020; 395: 1054-1062.
4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet, 2020; 395: 507-513.
5. Cao J, Tu W-J, Cheng W, et al. Clinical features and short-term outcomes of 102 patients with corona virus disease 2019 in Wuhan, China. Clin Infect Dis 2020 April 2 (Epub ahead of print).
6. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med, 2020; 46: 846-848.
7. Docherty AB, Harrison EM, Green CA, et al. Features of 20,133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ, 2020; 369: m1985-m1985.
8. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 — preliminary report. N Engl J Med. DOI: 10.1056/NEJMoa2007764.
9. Carsana L, Sonzogni A, Nasr A, et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study. Lancet Infect Dis 2020 June 8 (Epub ahead of print).
10. de Jong MD, Simmons CP, Thanh TT, et al. Fatal outcome of human influenza A (H5N1) is associated with high viral load and hypercytokinemia. Nat Med, 2006; 12: 1203-1207.
11. Wong CK, Lam CWK, Wu AKL, et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin Exp Immunol, 2004; 136: 95-103.
12. Baillie JK, Digard P. Influenza — time to target the host? N Engl J Med, 2013; 369: 191-193.
13. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet, 2020; 395: 497-506.
14. Moore JB, June CH. Cytokine release syndrome in severe COVID-19. Science, 2020; 368: 473-474.
15. Shang L, Zhao J, Hu Y, Du R, Cao B. On the use of corticosteroids for 2019-nCoV pneumonia. Lancet, 2020; 395: 683-684.
16. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet, 2020; 395: 473-475.

17. Corral L, Bahamonde A, Arnaiz de las Revillas F, et al. GLUCOCOVID: a controlled trial of methylprednisolone in adults hospitalized with COVID-19 pneumonia. June 18, 2020 (https://www.medrxiv.org/content/10.1101/2020.06.17.20133579v1. opens in new tab). preprint.
18. Dagens A, Sigfrid L, Cai E, et al. Scope, quality, and inclusivity of clinical guidelines produced early in the covid-19 pandemic: rapid review. BMJ, 2020; 369: m1936-m1936.
19. Zhao JP, Hu Y, Du RH, et al. Expert consensus on the use of corticosteroid in patients with 2019-nCoV pneumonia. Zhonghua Jie He He Hu Xi Za Zhi, 2020; 43: 183-184. (In Chinese.).
20. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA, 2020; 323: 1061-1069.
21. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ, 2020; 368: m606-m606.
22. Villar J, Ferrando C, Martínez D, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med, 2020; 8: 267-276.
23. Yusuf S, Collins R, Peto R. Why do we need some large, simple randomized trials? Stat Med, 1984; 3: 409-422.
24. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. Lancet, 1988; 2: 349-360.
25. Collins R, Bowman L, Landray M, Peto R. The magic of randomization versus the myth of real-world evidence. N Engl J Med, 2020; 382: 674-678.
26. Rojek AM, Horby PW. Modernising epidemic science: enabling patient-centred research during epidemics. BMC Med, 2016; 14: 212-212.
27. Whitty C. Dexamethasone in the treatment of COVID-19: Implementation and management of supply for treatment in hospitals. London: Medicines and Healthcare Products Regulatory Agency, June
28. 16, 2020 (https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?A lertID=103054. opens in new tab).
29. Stockman LJ, Bellamy R, Garner P. SARS: systematic review of treatment effects. PLoS Med, 2006; 3(9): e343-e343.
30. Arabi YM, Mandourah Y, Al-Hameed F, et al. Corticosteroid therapy for critically ill patients with Middle East respiratory syndrome. Am J Respir Crit Care Med, 2018; 197: 757-767.
31. Lansbury LE, Rodrigo C, Leonardi-Bee J, Nguyen-Van-Tam J, Shen Lim W. Corticosteroids as adjunctive therapy in the treatment of influenza: an updated Cochrane systematic review and meta-analysis. Crit Care Med 2020;48(2):e98-e106.
32. Siemieniuk RA, Meade MO, Alonso-Coello P, et al. Corticosteroid therapy for patients hospitalized with community-acquired pneumonia: a systematic review and meta- analysis. Ann Intern Med, 2015; 163: 519-528.
33. Lee N, Allen Chan KC, Hui DS, et al. Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients. J Clin Virol, 2004; 31: 304-309.
34. Lee N, Chan PKS, Hui DSC, et al. Viral loads and duration of viral shedding in adult patients hospitalized with influenza. J Infect Dis, 2009; 200: 492-500.
35. Cheng PKC, Wong DA, Tong LKL, et al. Viral shedding patterns of coronavirus in patients with probable severe acute respiratory syndrome. Lancet, 2004; 363: 1699- 1700.
36. To KK-W, Tsang OT-T, Leung W-S, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis, 2020; 20: 565-574.
37. Zhou R, Li F, Chen F, et al. Viral dynamics in asymptomatic patients with COVID-19. Int J Infect Dis, 2020; 96: 288-290.
38. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med, 2020; 26: 672-675.
39. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature, 2020; 581: 465-469.
40. COVID-19 treatment guidelines. Bethesda, MD: National Institutes of
41. Health, 2020 (https://www.covid19treatmentguidelines.nih.gov/dexamethasone/. opens in new tab).

Ceramics International xxx (xxxx) xxx

Contents lists available at ScienceDirect

Ceramics International

journal homepage: www.elsevier.com/locate/ceramint

DFT computation of quantum capacitance of pure and doped niobium nitrides for supercapacitor applications

Bharti [a,b], Gulzar Ahmed [a], Yogesh Kumar [c,*], Shatendra Sharma [d]

[a] Department of Physics, Mewar University, Gangrar, Chittorgarh, 312901, Rajasthan, India
[b] Department of Physics, Shivaji College, University of Delhi, New Delhi, 110027, India
[c] Department of Physics, ARSD College, University of Delhi, New Delhi, 110021, India
[d] School of Engineering and USIC, Jawaharlal Nehru University, New Delhi, 110067, India

ARTICLE INFO

Keywords:
Density of states
Quantum capacitance
Niobium nitrides

ABSTRACT

The density of states and quantum capacitance of pure and doped niobium nitrides are investigated using density functional theory calculations. Out of pristine structures investigated, NbN is the most promising candidate for fabrication of supercapacitor electrodes with quantum capacitance values reaching up to 834.5 and 1683.7 Fg^{-1} at negative and positive electrodes respectively. These calculations are also performed for cobalt doped niobium nitrides. The results suggest that doping of niobium nitrides with cobalt can further increase the quantum capacitance significantly. Quantum capacitance of both pristine and doped niobium nitrides is found to be much higher than that of graphene near fermi level, thus suggesting that these structures can be preferred over graphene for supercapacitor electrodes. The temperature dependence of quantum capacitance is also investigated.

1. Introduction

An increased demand of electronic devices and electric vehicles have given rise to the demand for electrical energy sources [1]. Day by day environment deterioration has led to the search of environment friendly energy sources like supercapacitor SC. Supercapacitors are not only environment friendly but also have high energy and power densities and good discharging/charging performance [2,3]. Studies [4–6] have shown that the total capacitance C of an electrode in a supercapacitor is a resultant of series combination of two capacitances namely EDLC capacitance C_{EDL} and quantum capacitance QC as given in equation (1).

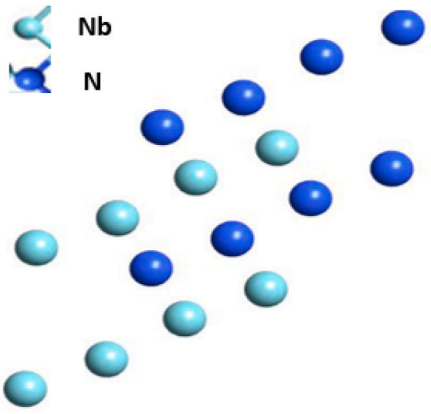
$$\frac{1}{C} = \frac{1}{QC} + \frac{1}{C_{EDL}} \quad (1)$$

From equation (1), it is clear that materials with low quantum capacitance value will exhibit low overall capacitance. Therefore, it becomes necessary to investigate the quantum capacitance values of supercapacitor electrode materials.

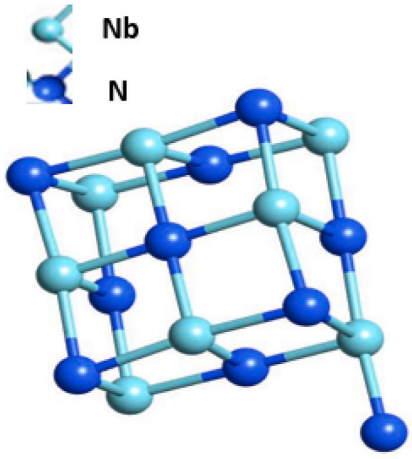
Carbon, Metal oxides and conducting polymers are the most common material used for supercapacitor electrodes [7–9]. Although a lot of experimentation has been done on various materials for supercapacitor electrodes but still no electrode material is found to be perfect. Carbon electrodes have low capacitance values. Conducting polymer or metal oxide electrodes exhibit poor electrochemical stability and electrical conductivity. For better electrode materials, researchers have started exploring the potential of transition metal nitrides for fabrication of supercapacitor electrodes. Transition metal nitrides are cost effective and exhibit good chemical stability, excellent electrochemical property and fair conductivity. All these features make them promising candidate for supercapacitor electrodes [10,11]. Transition metal nitrides like vanadium nitride, titanium nitride, tungsten nitride etc., have already been investigated [12–21] as electrode materials. Among them, vanadium nitride is reported to have quite high value (1340 Fg^{-1}) of capacitance [12]. Different nanostructures of titanium nitride are prepared [21–24] to see their effectiveness as high energy supercapacitor electrodes. Capacitance reported for WN is 30 Fg^{-1} [14] and for Mo_2N is 172 Fg^{-1} [25]. Nb_4N_5 nanochannels have been prepared exhibiting an aerial capacitance of 225.8 $mFcm^{-2}$ [26]. Thin films of NbN prepared by reactive magnetron sputtering are also been studied to investigate their electrochemical performance [27]. The NbN electrodes exhibited excellent cycling stability and volumetric capacitance of value 707.1 F cm^{-3} [27]. The results show that NbN thin films may prove to be good materials for supercapacitors electrode fabrication. An asymmetric supercapacitor assembled using nanostructured TiNbN films [28] has also shown a high specific capacitance of 59.3 $mFcm^{-2}$. But apart from these studies not much work has been reported on niobium nitrides for

* Corresponding author.
E-mail address: ykumar@arsd.du.ac.in (Y. Kumar).

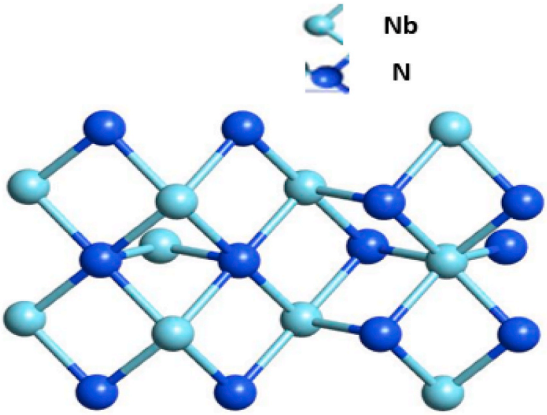
https://doi.org/10.1016/j.ceramint.2021.03.237
Received 23 January 2021; Received in revised form 21 March 2021; Accepted 21 March 2021
Available online 24 March 2021



(a)

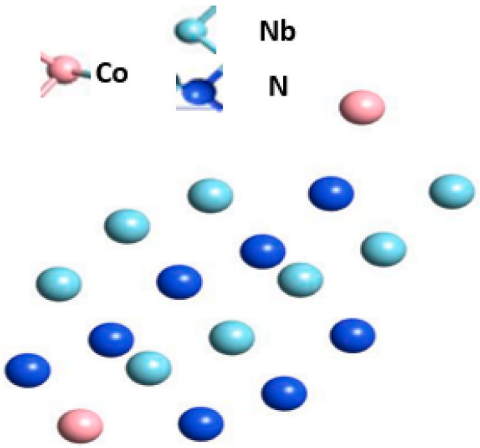


(b)

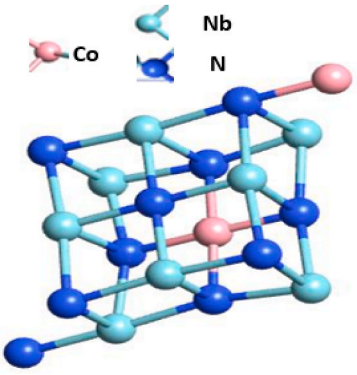


(c)

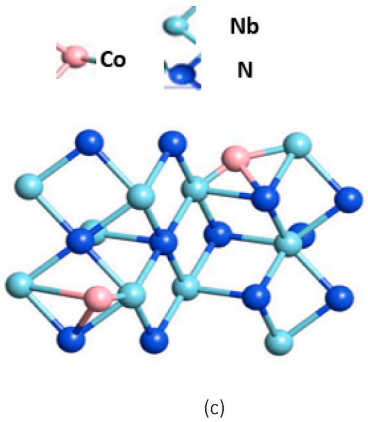
Fig. 1. The structures used for pristine Niobium Nitride (a) NbN (b) Nb_4N_5 (c) Nb_5N_6.



(a)



(b)



(c)

Fig. 2. The structures used for Cobalt doped Niobium nitride (a) NbN–
2Co (b) Nb_4N_5–2Co (c) Nb_5N_6–2Co.

Table 1
Details of crystal structures.

Material	Crystal structure	Space group	Angles
NbN	Face centred cubic	225,Fm-3m	$\alpha = \beta = \gamma = 90^\circ$
Nb_4N_5	Simple tetragonal	6,Pm	$\alpha = \beta = \gamma = 90^\circ$
Nb_5N_6	Hexagonal	193,$P6_3$/mcm	$\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$

supercapacitor applications. A thorough theoretical investigation on their QC is required to assess their potential as supercapacitor electrode material.

Density functional theory (DFT) is a powerful and effective tool that can be used for predicting the density of state (DOS) of a material. Density functional theory is widely used to predict and calculate the electronic properties of crystal structure with good accuracy. The assumption of DFT that energy of a system can be calculated using the functional of the electronic density rather than solving the complex many body Schrodinger equations reduces the computational difficulty and time significantly. In the present work, DFT calculations are used to calculate the band structure, DOS and QC of a series of niobium nitride structures. Effect of doping on quantum capacitance of these structures is also studied. In case of niobium nitrides, the major contribution in the bands formed near Fermi level comes from the d-states of the transition metal Nb. The partial density of states of d electrons of Nb contribute the most to the total density of states of niobium nitrides. Doping these structures with another transition metal like cobalt may enrich the d electrons of Nb thus increasing the total density of states of niobium nitrides resulting in increase in quantum capacitance. Among transition metals, cobalt is used because of a recent experimental study [29] which has already explored the great potential of cobalt doped NbN for lithium-sulfur batteries. The study has shown a huge rise in capacity of niobium nitride after cobalt doping. Results of our calculation show very high values of QC for both pure and doped niobium nitride structures at both the positive and negative electrodes and thus indicate that the quantum capacitance limitation of graphene electrodes can be overcome by niobium nitride based electrodes. These calculations are performed at different temperatures to investigate the temperature dependence of quantum capacitance.

2. Methodology and simulation details

Calculations for band structure, density of states and quantum capacitance are performed using the spin unpolarised method based on density functional theory technique utilizing Atomistix Toolkit (ATK) package from Synopsys. Generalized gradient approximation is used with exchange correlation energy described by PBE functional [30]. The plane-wave energy cut off was kept at 540 eV sampled at 12 × 12 × 1 Monk horst-pack k-point grid meshes. The crystal structures of niobium nitrides NbN, Nb_4N_5 and Nb_5N_6 as shown in Fig. 1(a)-1(c) are built using

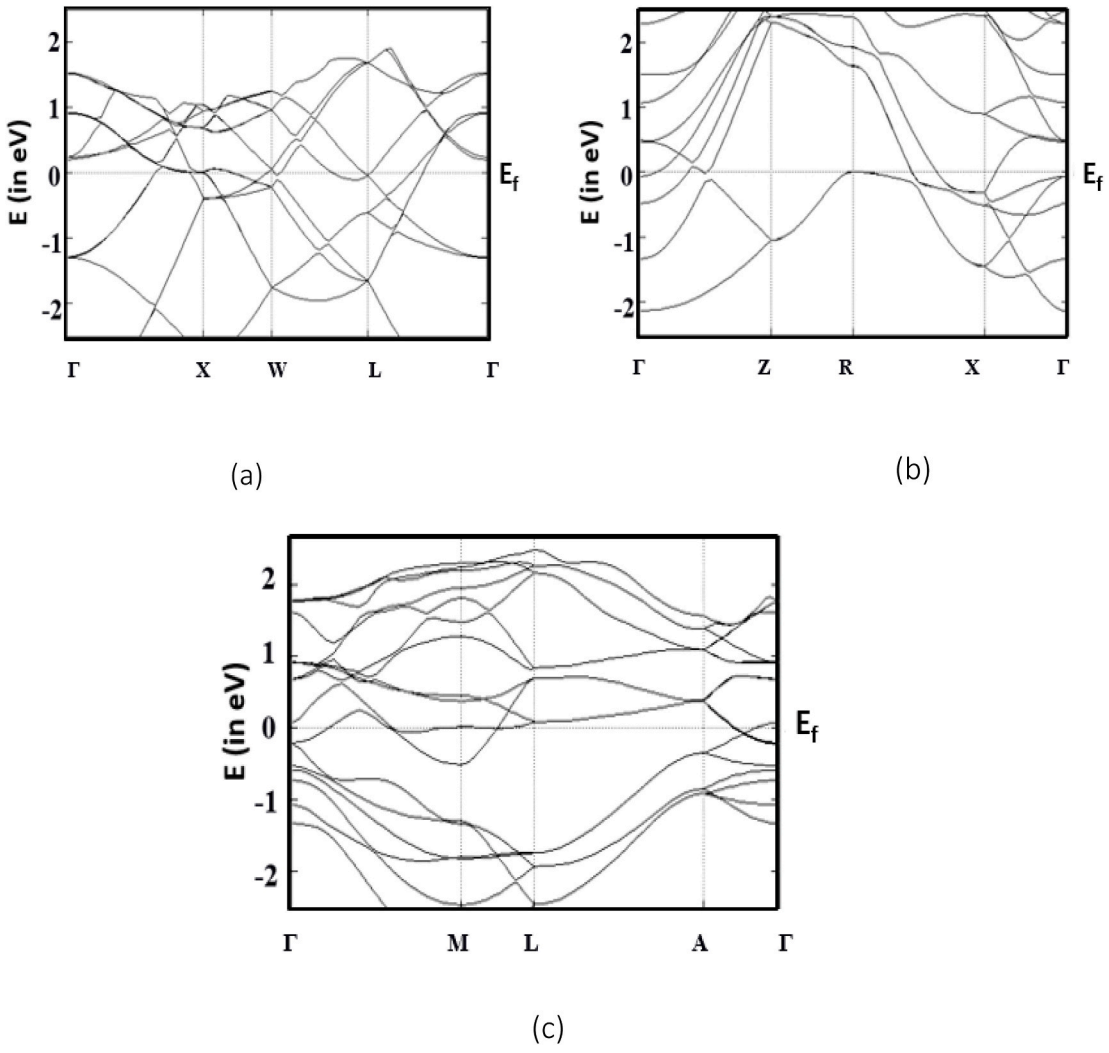
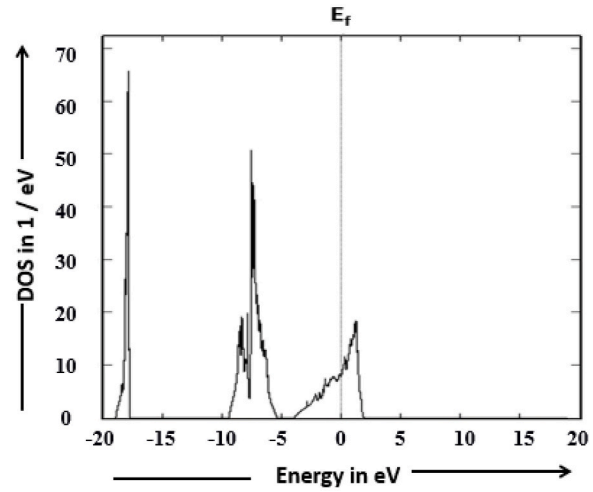
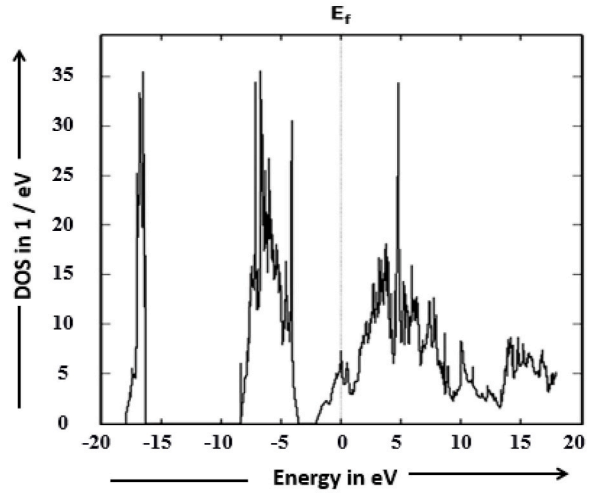


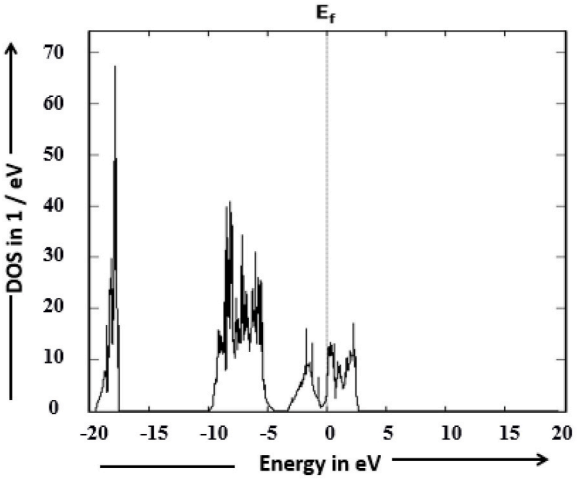
Fig. 3. The Band structure for (a) NbN (b) Nb_4N_5 (c) Nb_5N_6.



(a)



(b)



(c)

Fig. 4. The density of states for (a) NbN (b) Nb_4N_5 (c) Nb_5N_6.

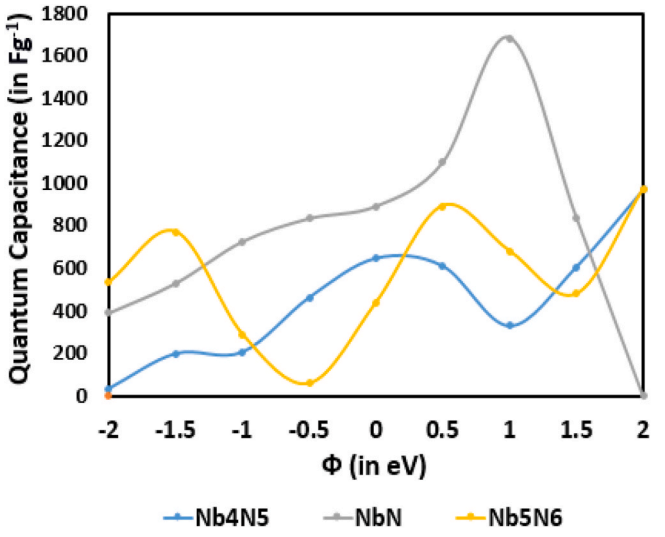


Fig. 5. Variation in QC for pristine niobium nitride structures with bias voltage.

the crystal builder of the software.

The details of the crystal structure used are given in Table 1.

Doped structures as shown in Fig. 2(a)-2(c) are built by adding two cobalt atoms in pristine niobium nitrides. Doped structures are optimized for geometry using quasi newton optimizer and then the electronic DOS and band structures are computed. Quantum capacitance of electrodes is calculated using the computed DOS. If φ is the operating voltage and Q is the surface charge on niobium nitride then from density of state DOS (E), we can find quantum capacitance using equations (2)–(4) [31,32]:

$$Q = e \int_{-\infty}^{+\infty} DOS(E)[f(E) - f(E - e\varphi)]\, dE \tag{2}$$

$$f(E) = \frac{1}{1 + \exp\left(E/kT\right)} \tag{3}$$

Where, e is the electronic charge.

$f(E)$ is the Fermi-Dirac distribution function and E is the energy w. r.t the Fermi energy.

By definition, one can obtain quantum capacitance by differentiating Q w. r.t φ i.e.

$$QC = \frac{dQ}{d\varphi} = e^2 \int_{-\infty}^{+\infty} DOS(E) \times \frac{sech^2\left(\frac{E-e\varphi}{2kT}\right)}{4kT}\, dE \tag{4}$$

The variation in the value of quantum capacitance are studied for different operating voltages for pristine and doped niobium nitrides. It is expected that such results obtained theoretically for pristine and cobalt doped niobium nitrides may help in designing high quantum capacitance electrodes for supercapacitor.

3. Results and discussion

DFT calculations are performed to explore the quantum capacitance of a series of pristine and doped niobium nitrides in Fg^{-1} (also known as gravimetric capacitance). The band structure and DOS of pristine niobium nitrides are given in Figs. 3 and 4 respectively.

The band structures in Fig. 3 of pristine niobium nitrides indicate that they are metallic in nature. The peaks of the density of states close to the Fermi level make important contribution to the QC. Pronounced peaks in DOS as shown in Fig. 4 are observed for pristine niobium

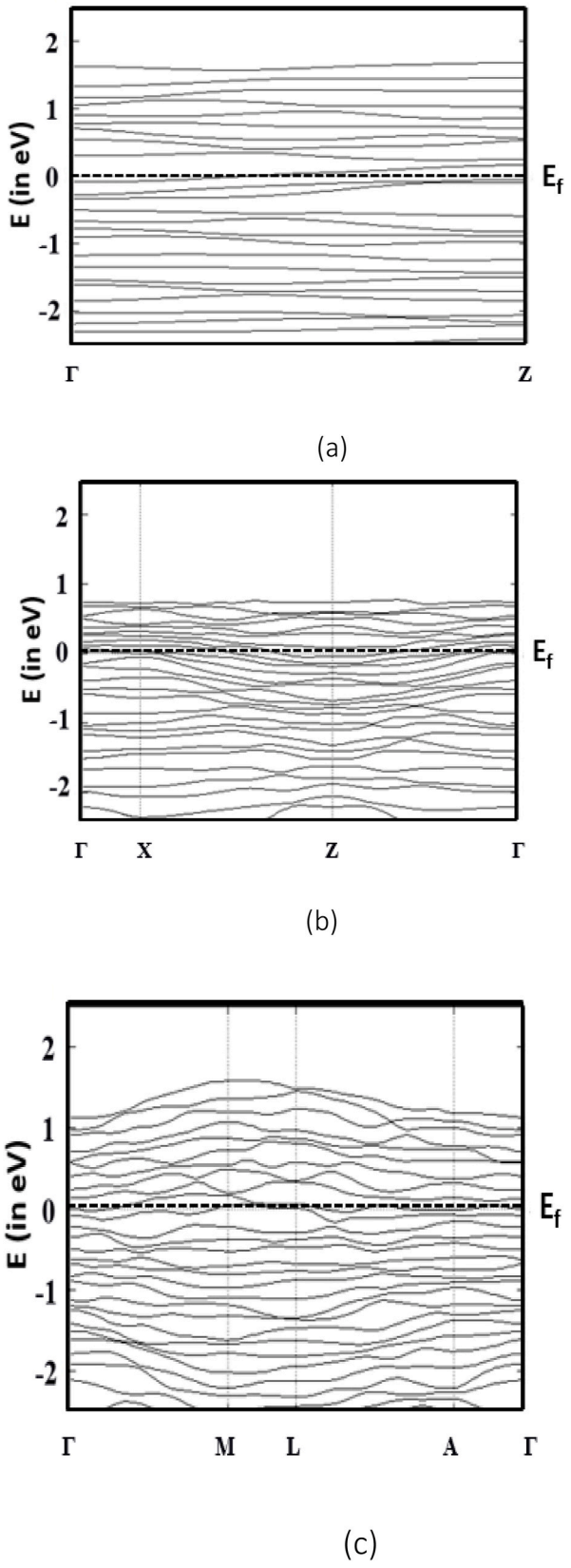


Fig. 6. The Band structure for cobalt doped niobium nitrides (a) NbN–2Co (b) Nb_4N_5–2Co (c) Nb_5N_6–2Co.

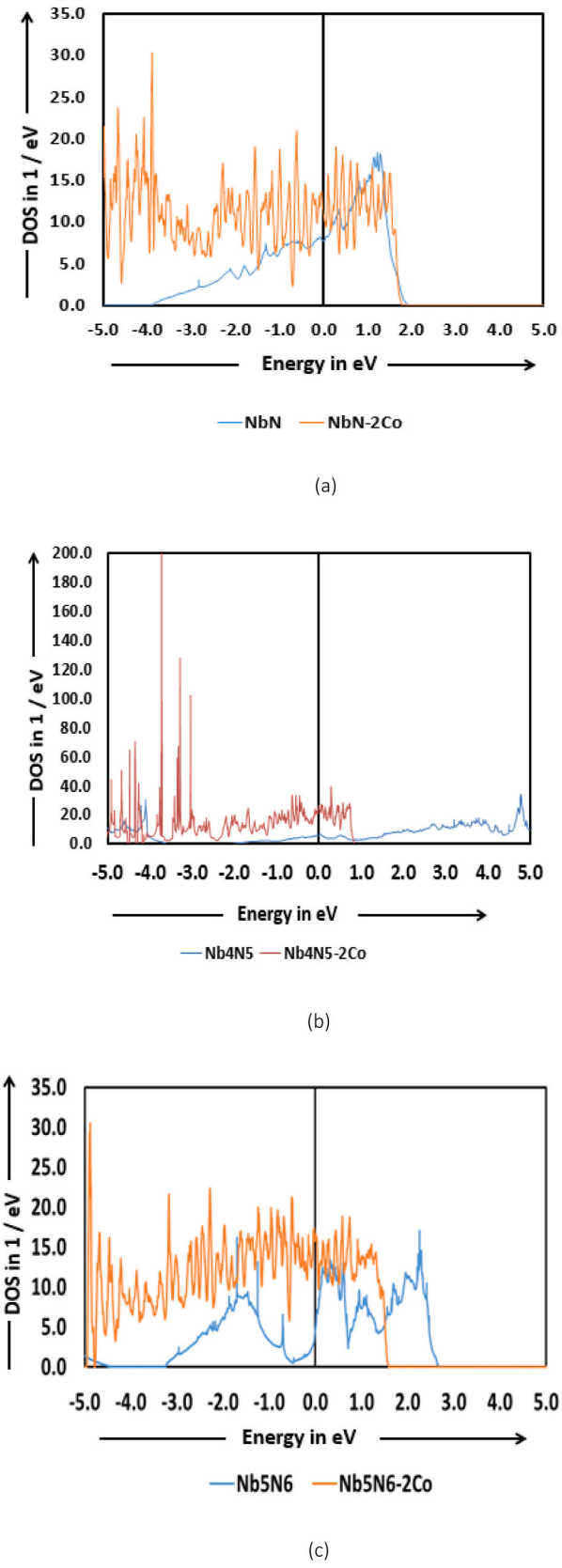
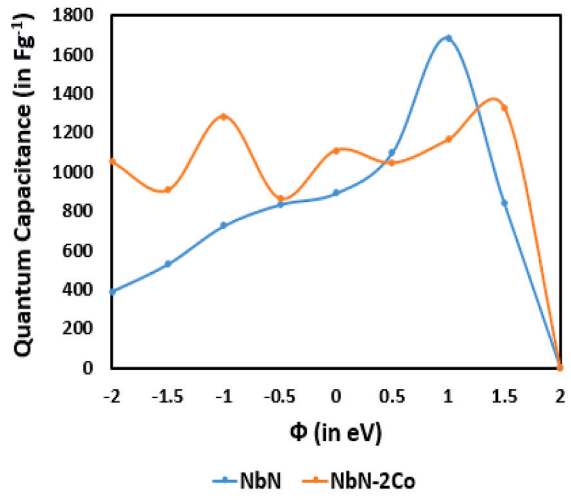
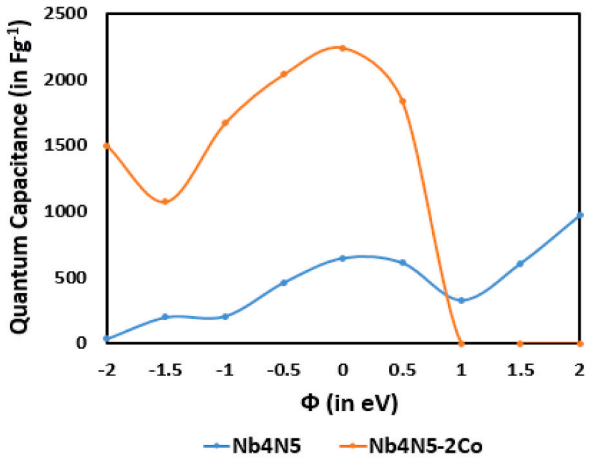


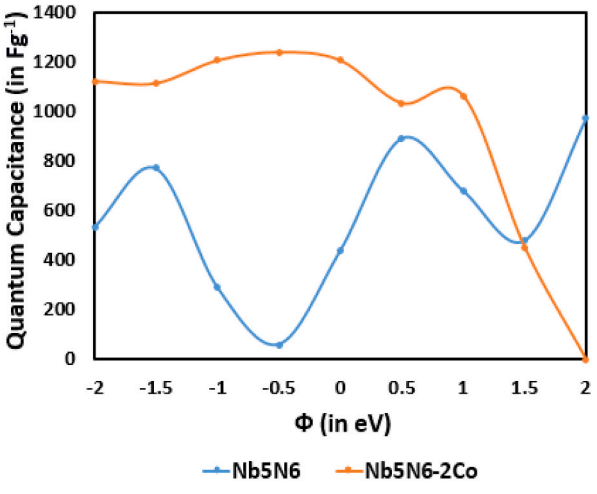
Fig. 7. The density of states for cobalt doped niobium nitrides (a) NbN–2Co (b) Nb_4N_5–2Co (c) Nb_5N_6–2Co.



(a)



(b)



(c)

Fig. 8. Comparison of calculated QC at different bias voltages for pristine and doped structures.

nitrides at and near fermi level (in the range of interest). The partial density of states of the d electron states of niobium are majorly responsible for these pronounced peaks. As per equations (2)–(4), these peaks contribute towards the huge values of quantum capacitance obtained for pristine niobium nitrides. QC as a function of electrode potential (φ) for pristine Niobium Nitrides is shown in Fig. 5. Our theoretical calculations show remarkable values of quantum capacitance for all combinations of pristine niobium nitride as shown in Fig. 5.

Highest QC of remarkable value 1684 Fg^{-1} is obtained for NbN at 1 V potential. It is found that quantum capacitance of NbN remains higher than all other niobium nitrides for values of bias voltage ranging from −1.0 to +2.0 V. Nb_5N_6 shows graphene like dip in quantum capacitance value near fermi level at bias voltage −0.5 V.

Experimental studies have already suggested Nb_4N_5 [26] and NbN [27] as potential candidate for supercapacitor electrode. In our work, high quantum capacitance values in the range of interest are obtained for both NbN and Nb_4N_5 indicating their usefulness as electrode material for supercapacitors and are thus in agreement to the conclusions made in the experimental studies done for Nb_4N_5 [26] and NbN [27].

The results are compared with graphene, the widely investigated electrode material for supercapacitor [32–36]. The large specific surface area and interesting electronic properties make graphene [37,38] most sought after material for fabrication of supercapacitor electrodes. However, the monolayer of graphene has relatively low value for quantum capacitance [36]. Fig. 5 shows that NbN, Nb_4N_5 and Nb_5N_6 perform much better than graphene, with maximum values for QC reaching 1684 Fg^{-1} in case of NbN at positive electrode. For negative electrode, performance of NbN and Nb_4N_5 are much better than that of graphene with maximum value 834.5 Fg^{-1} for NbN. These values imply that NbN and Nb_4N_5 are preferable materials for both positive and negative electrodes of supercapacitors.

The impact of doping is studied on electronic structure and subsequently on quantum capacitance of the series of niobium nitrides. The band structure and DOS of doped niobium nitrides are given in Figs. 6 and 7 respectively. An obvious difference in density of states of pristine and doped niobium nitrides is observed in Fig. 7. The density of states at and near Fermi level becomes more pronounced when pristine niobium nitrides are doped with 2 atoms of cobalt. Doping impacts the electronic structure of materials thus changing the density of states. The major contribution in this rise in total density of states comes from the partial density of states PDOS of the 3 d electrons followed by the PDOS of 4s electrons of the cobalt dopant. This increase in the density of states increases the quantum capacitance [33].

Thus, doping niobium nitrides with cobalt can increase the quantum

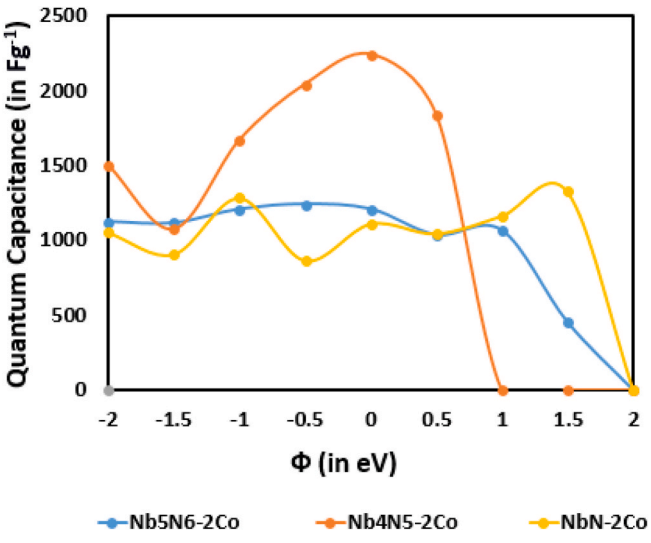


Fig. 9. Variation in QC for doped Niobium Nitride structures with bias voltage.

capacitance significantly as shown in Fig. 8(a)-8(c).

At Fermi level, remarkable rise in QC by factors of 3.46, and 2.741 is observed in doped Nb_4N_5 and Nb_5N_6 respectively (Fig. 8(b) and (c)). The increase is due to the corresponding change in the total density of states in the area of interest (near fermi level) which is clearly visible in Fig. 7 (b) and (c). The increase in QC is seen throughout the negative electrode potential as well in the positive electrode potential up to 1 V. In case of Nb_4N_5, doping with cobalt has increased the quantum capacitance remarkably to a huge value of 2241.2 Fg^{-1} at Fermi level (Fig. 8(b)). Doping with cobalt also increase the QC in case of NbN for negative bias voltage with maximum value achieved is 1284 Fg^{-1} (Fig. 8(a)) but the increase in values of QC is small w.r.t. other doped niobium nitrides. The QC in doped NbN shows fluctuations in the whole potential region unlike the cases of other doped niobium nitrides where there is almost a constant increase in QC throughout the negative electrode potential region. QC at the positive electrode for doped structures is in the range of 1045–1776.6 Fg^{-1} in the area of interest as shown in Fig. 9.

These calculations are done at three different temperatures i.e. 233, 300 and 353 K. These temperature are chosen as they corresponds to range −40 to 80 °C, which is the working range for most of the supercapacitors. No significant change with temperature was noted in the DOS profile for both pristine and doped structures. For pristine NbN, Nb_4N_5 and Nb_5N_6, a change in temperature from 233 K to 353 K increases the QC at Fermi level slightly from 886.6 to 895.7 Fg^{-1}, 647.4 to 648.1 Fg^{-1} and 434.0 to 442.5 Fg^{-1} respectively. In case of cobalt doped structures of NbN, Nb_4N_5 and Nb_5N_6 the change observed is 2.5%, 2.1% and 4.1% respectively. Since there is no significant change in DOS, the slight change in QC values in temperature range 233–353 K is mainly due to Fermi-Dirac distribution present in the equation for calculating quantum capacitance. Similar studies done for graphene for different temperature range has also shown weak dependence of QC on temperature [34].

4. Conclusions

DFT calculations are performed to investigate the quantum capacitance of a series of niobium nitride NbN, Nb_4N_5 and Nb_5N_6 for their use as supercapacitor electrode materials. A viable method is proposed to enhance the quantum capacitance of Niobium Nitrides using suitable dopant. The cobalt as a dopant changes the density of states and electronic structure of niobium nitrides remarkably. Out of pristine structures investigated, NbN is the most promising candidate for fabrication of supercapacitor electrodes with theoretical QC reaching up to 1683.7 Fg^{-1} at positive electrode. Even for negative bias voltage range zero to -1V, quantum capacitance values for NbN exceeds the QC values of all other niobium nitrides reaching a value of 834.5 Fg^{-1}.

The computations show that NbN, Nb_4N_5 and Nb_5N_6 have quite high values for QC which can be further increased by adding cobalt as dopant with maximum value for Quantum capacitance reaching 2241.2 Fg^{-1} for cobalt doped Nb_4N_5. The results indicate that niobium nitrides can overcome the low quantum capacitance barrier of graphene electrodes.

The present DFT calculations of pristine and cobalt doped NbN, Nb_4N_5 and Nb_5N_6 structures show no significant temperature dependence of band structure and DOS. However, a slight change in QC is observed with change in temperature.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The authors would like to acknowledge University Science and Instrumentation Centre, USIC, JNU, Delhi for providing the computing resources. YK acknowledges the financial support received from the SERB Department of Science and Technology (Government of India) file no. ECR/2016/001871.

References

[1] Z.E. Hughes, T.R. Walsh, Computational chemistry for graphene-based energy applications: progress and challenges, Nanoscale 7 (2015) 6883–6908, https://doi.org/10.1039/C5NR00690B.
[2] D. Ponnammaa, P. Vijayan P, M. Al Ali Al-Maadeed, 3D architectures of titania nanotubes and graphene with efficient nanosynergy for supercapacitors, Mater. Des. 117 (2017) 203–212, https://doi.org/10.1016/j.matdes.2016.12.090.
[3] G. Wang, L. Zhang, J. Zhang, A review of electrode materials for electrochemical supercapacitors, Chem. Soc. Rev. 41 (2012) 797–828, https://doi.org/10.1039/C1CS15060J.
[4] A.J. Pak, E. Paek, G.S. Hwang, Relative contributions of quantum and double layer capacitance to the supercapacitor performance of carbon nanotubes in an ionic liquid, Phys. Chem. Chem. Phys. 15 (2013) 19741–19747, https://doi.org/10.1039/C3CP52590B.
[5] M.D. Stoller, C.W. Magnuson, Y. Zhu, S. Murali, J.W. Suk, R. Piner, R.S. Ruoff, Interfacial capacitance of single layer graphene, Energy Environ. Sci. 4 (2011) 4685–4689, https://doi.org/10.1039/C1EE02322E.
[6] J. Xia, F. Chen, J. Li, N. Tao, Measurement of the quantum capacitance of graphene, Nat. Nanotechnol. 4 (2009) 505–509, https://doi.org/10.1038/nnano.2009.177.
[7] A. Bello, O.O. Fashedemi, J.N. Lekitima, M. Fabiane, D. Dodoo-Arhin, K. I. Ozoemena, Y. Gogotsi, A.T. Charlie Johnson, N. Manyala, High-performance symmetric electrochemical capacitor based on graphene foam and nanostructured manganese oxide, AIP Adv. 3 (2013), 082118, https://doi.org/10.1063/1.4819270.
[8] P. Simon, Y. Gogotsi, Materials for electrochemical capacitors, Nat. Mater. 7 (2008) 845–854, https://doi.org/10.1038/nmat2297.
[9] L.L. Zhang, X. Zhao, Carbon-based materials as supercapacitor electrodes, Chem. Soc. Rev. 38 (2009) 2520–2531, https://doi.org/10.1039/B813846J.
[10] S. Dong, X. Chen, X. Zhang, G. Cui, Nanostructured transition metal nitrides for energy storage and fuel cells, Coord. Chem. Rev. 257 (2013) 1946–1956, https://doi.org/10.1016/j.ccr.2012.12.012.
[11] M.-S. Balogun, W. Qiu, W. Wang, P. Fang, X. Lu, Y. Tong, Recent advances in metal nitrides as high-performance electrode materials for energy storage devices, J. Mater. Chem. A. 3 (2015) 1364–1387, https://doi.org/10.1039/C4TA05565A.
[12] D. Choi, G.E. Blomgren, P.N. Kumta, Fast and reversible surface redox reaction in nanocrystalline vanadium nitride supercapacitors, Adv. Mater. 18 (2006) 1178–1182, https://doi.org/10.1002/adma.200502471.
[13] D. Choi, P.N. Kumta, Nanocrystalline TiN derived by a two-step halide approach for electrochemical capacitors, J. Electrochem. Soc. 153 (2006) A2298–A2303, https://doi.org/10.1149/1.2359692.
[14] D. Choi, P.N. Kumta, Synthesis, structure, and electrochemical characterization of nanocrystalline tantalum and tungsten nitrides, J. Am. Ceram. Soc. 90 (2007) 3113–3120, https://doi.org/10.1111/j.1551-2916.2007.01873.x.
[15] D. Choi, P.N. Kumta, Synthesis and characterization of nanostructured niobium and molybdenum nitrides by a two-step transition metal halide approach, J. Am. Ceram. Soc. 94 (2011) 2371–2378, https://doi.org/10.1111/j.1551-2916.2011.04412.x.
[16] X. Lu, M. Yu, T. Zhai, G. Wang, S. Xie, T. Liu, C. Liang, Y. Tong, Y. Li, High energy density asymmetric quasi-solid-state supercapacitor based on porous vanadium nitride nanowire anode, Nano Lett. 13 (2013) 2628–2633, https://doi.org/10.1021/nl400760a.
[17] Y. Liu, Q. Wu, L. Liu, P. Manasa, L. Kanga, F. Ran, Vanadium nitride for aqueous supercapacitors: a topic review, J. Mater. Chem. A. 8 (2020) 8218–8233, https://doi.org/10.1039/D0TA01490G.
[18] T. He, W. Zhang, P. Manasa, F. Ran, Quantum dots of molybdenum nitride embedded in continuously distributed polyaniline as novel electrode material for supercapacitor, J. Alloys Compd. 812 (2020) 152138, https://doi.org/10.1016/j.jallcom.2019.152138.
[19] Y. Wu, F. Ran, Vanadium nitride quantum dot/nitrogen-doped microporous carbon nanofibers electrode for high-performance supercapacitors, J. Power Sources 344 (2017) 1–10, https://doi.org/10.1016/j.jpowsour.2017.01.095.
[20] Y. Yang, L. Zhao, K. Shen, Y. Liu, X. Zhao, Y. Wu, Y. Wang, F. Ran, Ultra-small vanadium nitride quantum dots embedded in porous carbon as high performance electrode materials for capacitive energy storage, J. Power Sources 333 (2016) 61–71, https://doi.org/10.1016/j.jpowsour.2016.09.151.
[21] X. Lu, G. Wang, T. Zhai, M. Yu, S. Xie, Y. Ling, C. Liang, Y. Tong, Y. Li, Stabilized TiN nanowire arrays for high-performance and flexible supercapacitors, Nano Lett. 12 (2012) 5376–5381, https://doi.org/10.1021/nl302761z.
[22] Y. Xie, Y. Wang, H. Du, Electrochemical capacitance performance of titanium nitride nanoarray, Mater. Sci. Eng. B 178 (2013) 1443–1451, https://doi.org/10.1016/j.mseb.2013.09.005.
[23] S. Dong, X. Chen, L. Gu, X. Zhou, H. Xu, H. Wang, Z. Liu, P. Han, J. Yao, L. Wang, Facile preparation of mesoporous titanium nitride microspheres for electrochemical energy storage, ACS Appl. Mater. Interfaces 3 (2011) 93–98, https://doi.org/10.1021/am100951h.
[24] X. Lu, T. Liu, T. Zhai, G. Wang, M. Yu, S. Xie, Y. Ling, C. Liang, Y. Tong, Y. Li, Improving the cycling stability of metal–nitride supercapacitor electrodes with a

thin carbon shell, Adv. Energy Mater. 4 (2014) 1300994, https://doi.org/10.1002/aenm.201300994.

[25] X.-L. Li, X. Yan, W. Hua, H.-L. Wang, W.-D. Wang, X.-Y. Chen, Synthesis and characterization of uniform nanoparticles of γ-Mo_2N for supercapacitors, Trans. Nonferrous Met. Soc. 19 (2009) 620–625, https://doi.org/10.1016/S1003-6326(08)60323-4.

[26] H. Cui, G. Zhu, X. Liu, F. Liu, Y. Xie, C. Yang, T. Lin, H. Gu, F. Huang, Niobium nitride Nb_4N_5 as a new high-performance electrode material for supercapacitors, Adv. Sci. 2 (2015) 1500126, https://doi.org/10.1002/advs.201500126.

[27] H. Shen, B. Wei, D. Zhang, Z. Qi, Z. Wang, Magnetron Sputtered NbN Thin Film Electrodes for Supercapacitors Materials Letters, vol. 229, 2018, pp. 17–20, https://doi.org/10.1016/j.matlet.2018.06.052.

[28] B. Wei, F. Ming, H. Liang, Z. Qi, W. Hu, Z. Wang, All nitride asymmetric supercapacitors of niobium titanium nitride-vanadium nitride, J. Power Sources 481 (2021) 228842, https://doi.org/10.1016/j.jpowsour.2020.228842.

[29] W. Ge, L. Wang, C. Li, C. Wang, D. Wang, Y. Qian, L. Xu, Conductive cobalt doped niobium nitride porous spheres as efficient polysulfide convertor for advanced lithium-sulfur batteries, J. Mater. Chem. A. 8 (2020) 6276–6282, https://doi.org/10.1039/D0TA00800A.

[30] J.P. Perdew, K. Burke, M. Ernzerhof, Generalized gradient approximation made simple, Phys. Rev. Lett. 77 (1996) 3865–3868, https://doi.org/10.1103/PhysRevLett.77.3865.

[31] C. Zhan, J. Neal, J. Wu, D.E. Jiang, Quantum effects on the capacitance of graphene-based electrodes, J. Phys. Chem. C 119 (2015) 22297–22303, https://doi.org/10.1021/acs.jpcc.5b05930.

[32] G.M. Yang, H.Z. Zhang, X.F. Fan, W.T. Zheng, Density functional theory calculations for the quantum capacitance performance of graphene-based electrode material, J. Phys. Chem. C 119 (2015) 6464–6470, https://doi.org/10.1021/jp512176r.

[33] D.C. Elias, R.V. Gorbachev, A.S. Mayorov, S.V. Morozov, A.A. Zhukov, P. Blake, L. A. Ponomarenko, I.V. Grigorieva, K.S. Novoselov, F. Guinea, A.K. Geim, Dirac cones reshaped by interaction effects in suspended graphene, Nat. Phys. 7 (2011) 701–704, https://doi.org/10.1038/nphys2049.

[34] J. Vatamanu, X. Ni, F. Liu, D. Bedrov, Tailoring graphene-based electrodes from semiconducting to metallic to increase the energy density in supercapacitors, Nanotechnology 26 (2015) 46, https://doi.org/10.1088/0957-4484/26/46/464001.

[35] A. Karayel Bharti, M. Gupta, G. Ahmad, Y. Kumar, S. Sharma, Physical properties of heteroatom doped graphene monolayers in relation to supercapacitive performance, IJPAP 58 (2020) 885–891. http://nopr.niscair.res.in/handle/123456789/55703.

[36] S.M. Mousavi-Khoshdel, E. Targholi, Exploring the effect of functionalization of graphene on the quantum capacitance by first principle study, Carbon 89 (2015) 148–160, https://doi.org/10.1016/j.carbon.2015.03.013.

[37] Y.- Xin Yu, Grphenylene: a promising anode material for lithium-ion batteries with high mobility and storage, J. Mater. Chem. A. 1 (2013) 13559–13566, https://doi.org/10.1039/C3TA12639K.

[38] H.M. Jeong, J.W. Lee, W.H. Shin, Y.J. Choi, H.J. Shin, J.K. Kang, J.W. Choi, Nitrogen-doped graphene for high-performance ultra capacitors and the importance of nitrogen-doped sites at basal planes, Nano Lett. 11 (2011) 2472–2477, https://doi.org/10.1021/nl2009058.

WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Diabetes Mellitus : A Review of Current Trends

Md Fazlur Rahman[1], Dr.Gaurav Kr Sharma[2], Dr. Gaurav Kr Sharma[3]., Dr Kaushal Kishore Chandrul[4]

[1]Student Of B.Pharmacy 4th Year,[2]professor,[3]h.O.D,4princple.
Department Of Pharmacy, Mewar University Chittorgarh Rajasthan (India)

Introduction

Diabetes mellitus is a chronic disorder of carbohydrates, fats and protein metabolism. A defective or deficient insulin secretary response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, as is the resulting hyperglycemias

[1] Diabetes mellitus (DM) is commonly referred to as a "sugar" and it is the most common endocrine disorder and usually occurs when there is deficiency or absence of insulin or rarely, impairment of insulin activity (insulin resistance) [2]. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 [3].

Insulin and glucagon hormones both are secreted by the pancreas. Insulin is secreted by the beta (ß) cells and glucagon is secreted by the alpha (α) cells both are located in the islets of Langerhan's. Insulin decreases the blood glucose level by the disorders, and malignancy in future life of fetus after delivery [6]. Type II diabetes mellitus comprises 80% to 90% of all cases of diabetes mellitus. Geographical variation can contribute in the magnitude of the problems and to overall morbidity and mortality [7, 8]. Moreover, people with diabetes who undertake moderate amounts of physical activity are at inappreciably lower risk of death than inactive persons [24] It is now well established that a specific genetic constitution is required for such an event to cause [9] The growing burden of diabetes and other non- communicable diseases is one of the major health challenges to economic developments bedeviling WHO African Region states [10]. See figure (1 and 2).In diabetes, there is an aberration either in the synthesis or secretion of insulin as seen in Type 1 diabetes mellitus (T1DM) and stenosis in the pancreatic duct, or the development of resistance to insulin or its subnormal production as in the case of Type 2 diabetes (T2DM) andcertain secondary diabetes.

Classification of Diabetes Mellitus

The first mostly accepted classification of diabetes mellitus was published by WHO in the year 1980 [11] and, it is modified in the year 1985 [12]. The most common and important form of Primary or idiopathic diabetes mellitus, which is focus of our discussion. It must be different from secondary diabetes mellitus which includes forms of hyperglycemia associated with glycogenesis and transport glucose into the muscles, liver and adipose tissue. Neural tissue and erythrocytes do not required insulin for glucose utilization whereas alpha (α) cells plays an important role in controlling blood glucose by producing the glucagon and it increases the blood glucose level by accelerating the glycogenolysis [4, 5].

In addition to increased risk of obesity, metabolic and cardiovascular identifiable causes in which destruction of pancreatic islets is induced by inflammatory Pancreatic diseases, surgery, tumors, certain drugs, iron overloaded (Hemochromatosis) and certain acquired or genetic endocrinopathies [1].The classification encompasses both clinical stages and aetiological types of diabetes mellitus and other categories of hyperglycemia [13].Assigning a type of diabetes to an individual often depends on the circumstances present at the time of diagnosis, and many diabetic individuals do not easily fit into a single class [14] Primary diabetes mellitus probably represents a heterogeneousgroup of disorders that have hyperglycemia as a commonfeature [1].

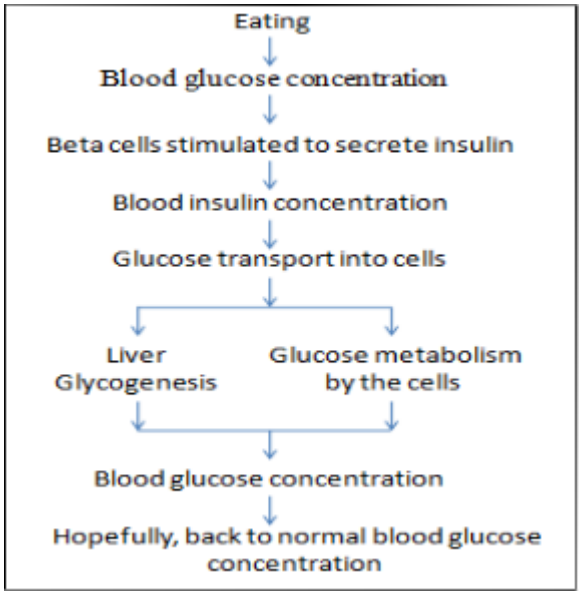


Fig 1: Glucose Metabolism

The new classification of diabetes mellitus contains stages which reflect the various degrees of hyperglycemia in individual subjects with any of the disease processes which may lead to diabetes mellitus [15, 16]

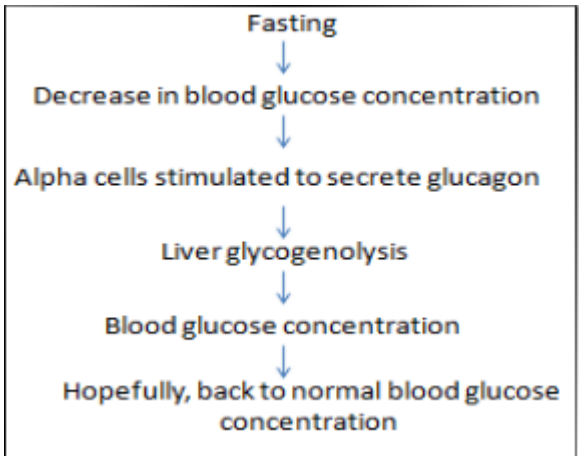


Fig 2: Normal response to fasting [10, 11]

The old and new terms of insulin-dependent(IDDM) or non- insulin-dependent (NIDDM) which were proposed by WHO in1980 and 1985 have disappeared and the terms of new classification system identifies four types of diabetes mellitus: type 1(IDDM), type 2(NIDDM),"other specific types" and
gestational diabetes (WHO Expert Committee 1999). These were reflected in the subsequent International Nomenclature of Diseases (IND) in1991and the tenth revision of the International Classification of Diseases (ICD-10) in 1992 [13]. Hence, classification of diabetes mellitus is described as below:

1. Insulin Dependent Diabetes Mellitus (Type1 IDDM) This type of diabetes mellitus is also called autoimmune diabetes and previously known as juvenile-onset or ketosis- prone diabetes. The individual may also seek with other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, and Addison's disease [17]. Type I diabetes mellitus is also known as insulin- dependent diabetes mellitus (IDDM), this occurs mainly in children and young adults; the onset is usually sudden and can be life threatenin [4]. Type 1 is usually characterized by the presence of anti–glutamic acid decarboxylase, islet cell or insulin antibodies which identify the autoimmune processes which leads to beta-cell destruction [34]. Type 1 diabetes (due to the destruction of b-cell which is usually leading to absolute insulin deficiency) (American Diabetes Association, 2014). The rate of destruction of beta- cell is quite variable; it can be occur rapidly in some individuals and slow in others [18]. There is a severe deficiency or absence of insulin secretion due to destruction of ß-islets cells of the pancreas. Treatment with injections of insulin is required [4]. Markers of immune destruction, including islet cell auto-antibodies, and/or auto antibodies to insulin, and auto antibodies to glutamic acid decarboxylase (GAD) are present in 85-90 % of individuals with Type 1 diabetes mellitus when fasting diabetic hyperglycemia is initially detected [19]. The exact cause of diabetes mellitus is remain unknown, although, in most people, there is evidence of an autoimmune mechanism involving auto-antibodies that destroy the beta-

islet cells [4].

2. Non-Insulin Dependent Diabetes Mellitus(Type2 Niddm) Type 2 diabetes mellitus is also known as adult-onset diabetes. The progressive insulin secretary defect on the background of insulin resistance (American Diabetes Association, 2014) [20]. People with this type of diabetes frequently are resistant to the action of insulin [21]. The long-term complications in blood vessels, kidneys, eyes and nerves occur in both types and are the major causes of morbidity and death from diabetes [1]. The causes are multifunctional and predisposing factor includes: Obesity, Sedentary lifestyle, increasing age (affecting middle- aged and older people), Genetic factor (Ross and Wilson 2010), such patients are at increased risk of developing macrovascular and micro vascular complications [22, 23].

3. Gestational Diabetes Mellitus

The glucose intolerance occurring for the first time or diagnosed during pregnancy is referred to as gestational diabetes mellitus (GDM) [2]. Women who develop Type1 diabetes mellitus during pregnancy and women with undiagnosed asymptomatic Type 2 diabetes mellitus that is discovered during pregnancy are classified with Gestational Diabetes Mellitus (GDM) [16]. Gestational diabetes mellitus (GDM) (diabetes diagnosed during pregnancy that is not clearly over diabetes) [17]. The gestational diabetes mellitus may develops during pregnancy and may disappear after delivery; In the longer term, children born to mothers with GDM are at greater risk of obesity and type 2 diabetes in later life, a phenomenon attributed to the effects of intrauterine exposure to hyperglycaemia.

4. Other Specific Type (Monogenic Types)

The most common form of monogenic types of diabetes is developed with mutations on chromosome 12 in a hepatic transcription factor referred to as hepatocyte nuclear factor (HNF)-1a.They also referred to as genetic defects of beta cells. These forms of diabetes are frequently characterized by onset of hyperglycemia at an early age (generally before age of 25 years). They are also referred to as maturity onset diabetes of the young (MODY)[12] or maturity-onset diabetes in youth or with defects of insulin action; persons with diseases of the exocrine pancreas, such as pancreatitis or cystic fibrosis; persons with dysfunction associated with other endocrinopathies (e.g. acromegaly); and persons with pancreatic dysfunction caused by drugs, chemicals or infections[16]. Some drugs also used in the combination with the treatment of HIV/ AIDS or after organ transplantation. Genetic abnormalities that result in the inability to convert proinsulin to insulin have been identified in a few families, and such traits are inherited in an autosomal dominant pattern. They comprise less than 10% of DM cases [11].

Some Common Sign and Symptoms

In diabetes mellitus, cells fails to metabolized glucose in the normal manner, effectively become starved [2]. The long term effect of diabetes mellitus which includes progressive development of the specific complications of retinopathy with potential blindness, nephropathy that may lead to renal failure, and neuropathy with risk of foot ulcer, Charcot joint and features of autonomic dysfunctions and sexual dysfunction [24] People with diabetes are at increases risk of diseases. See table(1).

Other, various symptoms are observed due to-

i. Gluconeogenesis from amino acids and body protein, causing muscle wasting, tissue breakdown and furtherincreases the blood glucose level.
ii. Catabolism of body fat, releasing some of its energy and excess production of ketone bodies [2]

Etiology of Diabetes Mellitus

The word etiology is derived from Greek word "aetiologia". Hence, etiology is defined as the science of finding causes and origins in which a disease is arise, It includes –

1. It is currently believed that the juvenile-onset (insulindependent) form has an auto immune etiology.
2. Viruses may also play a role in the etiology of diabetes like coxsackieB.
3. Mumps and rubella viruses all have been shown to produce morphologic changes in the islet-cell structure.
4. The genetic role in the etiology of diabetes is controversial. Possibly a genetic trait makes an = individual's pancreas more susceptible to one of the aboveviruses [45].

Causes of Diabetes Milliteus

Disturbances or abnormality in gluco-receptor of ß cell so that they respond to higher glucose concentration or relative ß cell deficiency. In either way, insulin secretion is impaired; may progress to ß cell failure [25]. The theory of principal in micro vascular disease leading to neural hypoxia, and the directeffects of hyperglycaemia on neuronal metabolism [26].

1. Reduced sensitivity of peripheral tissues to insulin: reduction in number of insulin receptors, 'down regulation' of insulin receptors. Many hypersensitive

and hyperinsulinaemic, but normal glycaemic; and have

associated dyslipideaemic, hyperuriaemiac, abdominal obesity. Thus there is relative insulin resistance, particularly at the level of liver, muscle and fat. Hyperinsulinaemic has been implicated in causing angiopathy [24].

2. Excess of hyperglycaemia hormone (glucagon) etc.
/obesity; causes relative insulin deficiency –the ß cells lag behind. Two theories have demonstrated abnormalities in nitric oxide metabolism, resulting in altered perineural blood flow and nerve damage [25].
3. Other rare forms of diabetes mellitus are those due to specific genetic defects (type 3) like "maturity onset diabetes of young" (MODY) other endocrine disorders, pancreatectomy and gestational diabetes mellitus (GDM).
[24].
4. Due to imbalance of specific receptor can cause diabetes mellitus. Some specific receptors are Glucagon-like peptide-1(GLP-1) receptor, peroxisomes proliferator- activated (γ) receptor (PPARγ), beta3 (ß3) ardent-receptor some enzymes like α glycosidase, dipeptidyl peptidase IV enzyme etc [24].
5. Current research on diabetic neuropathy is focused on oxidative stress, advanced glycation-end products, protein kinase C and the polyol pathway [26].

Diagnosis of Diabetes Mellitus

The diagnosis of diabetes in an asymptomatic subject should neverbe made on the basis of a single abnormal blood glucose value. If a diagnosis of diabetes is made, the clinician must feel confident that the diagnosis is fully established since the consequences for the individual are considerable and lifelong [27]. The diagnosis of diabetes mllitus include, urine sugar, blood sugar, glucose tolerance test, renal threshold of glucose, diminished glucose tolerance, increased glucose tolerance, renal glycosuria, extended glucose tolerance curve, cortisone stressed glucose tolerance test, intravenous glucose tolerance test, oral glucose tolerance test.

Treatment of Diabetes Mellitus

The treatment is to overcome the precipitating cause and to give high doses of regular insulin. The insulin requirement comes back to normal once the condition has been controlled
[65] the aims of management of diabetes mellitus can be achieved by:

1. To restore the disturbed metabolism of the diabetic asnearly to normal as is consistent with comfort and safety.
2. To prevent or delay progression of the short and long termhazards of the disease.
3. To provide the patient with knowledge, motivation andmeans to undertake this own enlightened care.

A. Types of Therapy Involved In Diabetes Mellitus

1. Stem cell therapy

Researchers have shown that monocytes/ macrophages may be main players which contribute to these chronic inflammations and insulin resistance in T2DM patients [28]. Stem cell educator therapy, a novel technology, is designed to control or reverse immune dysfunctions [29]. The procedure includes: collection of patients' blood circulating through a closed-loop system, purification of lymphocytes from the whole blood, co-culture of them with adherent cord blood-derived multi-potent stem cells (CB-SCs) *in vitro* and administration of the educated lymphocytes (but not the CB-SCs) to the patient's circulation

1 Antioxidant therapy

A variety of antioxidants, such as vitamins, supplements, plant-derived active substances and drugs with antioxidant effects, have been used for oxidative stress treatment in T2DM patients. Vitamin C, vitamin E and β carotene are ideal supplements against oxidative stress and its complications. [30]Antioxidant which play an important role in lowering the risk of developing diabetes and its complications.

Anti-inflammatory treatment

The changes indicate that inflammation plays a pivotal role in the pathogenesis of T2DM and its complications [31, 32]. In T2DM, especially in adipose tissue, pancreatic islets, the liver, the vasculature and circulating leukocytes, [33] which include altered levels of specific cytokines and chemokines, the number and activation state of different leukocyte populations,increased apoptosis and tissue fibrosis. [33, 34] Immunomodulatorydrugs are provided.

B. Dietary Management

Adequate caloric value Dietary management should be takenproperly by the both diabetic and non-diabetic patient such as:

1. Balanced in regard to protein, carbohydrate and fats, in allcases it is necessary to restrict carbohydrate intake.
2. Should conform as closely as possible to normal
3. Food intake should be divided into regularly spaced mealsof similar size
4. Reduce total calorie intake by decreasing both fat andcarbohydrate
5. Patient must be advised to be constant in his dietary habitsfrom day to day.

C. Newer Insulin Delivery Devices

A number of innovations have been made to improve ease and accuracy of insulin administration as well as to achieve tight glycaemia control. These are insulin syringes, pen devices, inhaled insulin, insulin pumps, implantable pumps, other routes of insulin delivery.

D Oral Hypoglycaemic or Antidiabetic Agents

Clinically useful biguanide phenformin was produced parallel to sulfonylurea's in 1957. Newer approaches have constantly been explored and have lately yielded thiazolidinediones, meglitinide analogues, α-glucosidase inhibitors, and the latest are dipeptidyl peptidase-4(DPP-4) inhibitors [24].

Important Features of Oral Hypoglycaemic Agents

Diabetes mellitus can be considered a disease of the modern world with a great impact of morbidity, morality and the quality of type of the affected individual. Diabetes mellitus is a frequent complication of cushing syndrome which is caused by chronic exposure to Glucocorticoids by several clinical symptoms such as central obesity, proximal muscles weakness, hirsutism and neurophysiological disturbance, macro-vascular complication autonomic neuropathy, digestiveproblems, dental problems etc. [24].

Conclusion

Diabetes mellitus is a serious complication in today life. The lifestyle and day today circumstances are play major role in occurring this type of serious complications. In this review weget some idea regarding diabetes mellitus.

REFERENCES

1. Tripathi KD. Essentials Medicals Pharmacology, Jaypee Brothers Medical Publisher (P) LTD, 7th edition, 2013, Page no 258-281
2. Ross and Wilson. Anatomy and Pathophysiology in Health and Illness, Churchill Livingstone Elsevier, 11th edition, 2010, 227-229.
3. American Diabetes Association, Diagnosis and classification of diabetes mellitus, Diabetes Care, 2014, 1.
4. DeFronzo RA, Bonadonna RC, Ferrannini E, Zimmet P. Pathogenesis of NIDDM, International Textbook of Diabetes Mellitus. 1997, 635-712.
5. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E et al., Insulin resistance and insulin secretory dysfunction as precursors of non–insulin–dependent diabetes, N Engl J Med. 1993;329:1988-92.
6. Mooy JM, Grootenhuis PA, de Vries H, Valkenburg HA, Bouter LM, Kostense PJ et al., Prevalence and determinants of glucose intolerance in a Dutch population, Diabetes Care. 1995; 18:1270-73.
7. Alberti KGMM, Zimmet PZ. The WHO Consultation. Definition, diagnosis and classification of diabetes
8. WHO. Study Group Diabetes Mellitus, Technical report series no.727, World Health Organisation, Geneva, 1985

9. Leonardo Jacob S, Pharmacology. The national medical series from Williams and Wilkins Bartiarco, Hong Kong, London, 3rd edition, 1987, 221-225.
10. Blood A, Hayes TM, Gamble DR. Register of newly diagnosed diabetic children, BMJ. 1975; 3:580-583.
11. .
12. Dyck PJ, Kratz KM, Karnes JL. The prevalence staged of various types of diabetic neuropathy retinopathy and nephropathy in a population-basedcohort: the Rochester Diabetic Neuropathy Study, Neurology, 1993; 43:817-24.

13. COLOR ATLAS OF PHARMACOLOGY, THIME FLEXIBOOK, 2nd EDITION REVISED AND EXPANDED HEINZ LULLMANN,KLAUS MOHR , ALBRECHT ZIEGLER , DETLEF BIEGER, 2000.PAGE NO 256-265

14. BASIC AND CLINICAL PHARMACOLOGY ,12th edition PUBLISHER MC GRAW HILL LANGE, BETRAM G.SUSAN B.MASTERS, ANTHONY J. TREVOR 2009 PAGE NO-743-758

15. REVIEW OF PHARMACOLOGY, PUBLISHER JAYPEE BROTHERS MEDICALTHE HEALTH SCIENCE PUBLISHER,GARG AND GUPTA EDITION 9th ,2015 page no -

16. Gupta OP, Joshi MH, Daves SK. Prevalence of Diabetes in India, Adv Metab Disord. 1978; 9:147-65.

17. Alemu S, Dessie A, Seid E. Insulin-requiring diabetes in rural Ethiopia: should we reopen the case for malnutrition- related diabetes, Diabetologia. 2009; 52:1842-1845.

18. Wild S, Roglic G, Green A, Sicree R, King. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030, Diabetes Care. 2004; 27:1047-53.

19. Mohan V, Pradeepa R. Epidemiology of diabetes in different regions of India. 2009; 22:1-18.

20. Kadiki OA, Reddy MR, Marzouk AA. Incidence of insulin-dependent diabetes(IDDM) and non-insulin- dependent diabetes (NIDDM) (0-34 years at onset) in Benghazi, Libya, Diabetes Res Clin Pract. 1996; 32:165- 173.

21. Shaw J, Zimmet P, de Courten M, Dowse G, Chitson P, Gareeboo Het al., Impaired fasting glucose or impaired glucose tolerance, Diabetes Care. 1999; 22:399-402

22. Ramachandran A, Snehalatha C, Latha E, Vijay V, Viswanathan M. Rising prevalence of NIDDM in an urban population in India Diabetologia1997; 40:232-237.

23. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance, Diabetes Atlas International Diabetes Federation, 2006, 15-103.

24. Sridhar GR, Rao PV, Ahuja MMS. Epidemiology of diabetes and its complications In: RSSDI textbook of diabetesmellitus, 2002, 95-

EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 5
388-393
Year: 2018

DIABETES MELLITUS: AN OVERVIEW

Mohd Shabaz Khan*, Shubam Sehgal, Tanvay Jaithliya, Mohd Zubir, Manooj Kumar and Atul Tiwari[1]

Department of Pharmaceutical Sciences, Mewar University, Chittorgarh, 312901, India.
[1]Assistant Professor, Department of Pharmaceutical Sciences, Mewar University, Chittorgarh.

***Corresponding Author: Shubam Sehgal**
Department of Pharmaceutical Sciences, Mewar University, Chittorgarh, 312901, India.

Article Received on 11/03/2018 **Article Revised on 01/04/2018** **Article Accepted on 22/04/2018**

ABSTRACT
Diabetes mellitus is an endocrinological and/or metabolic disorder marked by elevated levels of sugar in the blood. It is a silent killer disease and affects millions of peoples in the world. It is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by ineffectiveness of the insulin produced. High blood glucose levels are symptomatic of diabetes mellitus as a consequence of inadequate pancreatic insulin secretion or poor insulin-directed mobilization of glucose by target cells. It is the second leading cause of blindness and renal disease worldwide. Impaired insulin secretion and increased insulin resistance, the main pathophysiological features of type 2 diabetes. The goal of diabetes treatment is to secure a quality of life (QOL) and lifespan comparable to those of healthy people, and a prerequisite for this is the prevention of onset and progression of vascular complications. This article focuses on the causes, types, factors affecting DM, incidences, preventive measures, treatment and future perspectives of the acute and chronic complications of diabetes directly associated with hypoglycemia and severe metabolic disturbances.

KEYWORDS: Diabetes mellitus, endocrinology, insulin, hypoglycemia, metabolism.

INTRODUCTION
Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects of insulin secretion and increased cellular resistance to insulin. Chronic hyperglycemia and other metabolic disturbances of DM lead to long-term tissue and organ damage as well as dysfunction involving the eyes, kidneys and nervous and vascular system.[1,2,3]

CLASSIFICATION OF DIABETES MELLITUS
1. β- cell destruction (Type 1 diabetes - IDDM)
- Immune mediated
- Idiopathy
2. Insulin resistance (Type 2 diabetes - NIDDM)
3. Genetic defects of β- cell function
- Glucokinase
- Hepatocyte nuclear transcription factor – 4 α
- Insulin promoter factor
- Mitochondrial DNA
- Proinsulin or insulin conversion
4. Genetic defects in insulin processing or insulin actions defects in
- Proinsulin conversion.
- Insulin gene mutation
- Insulin receptor mutation
5. Exocrine pancreatic defects
6. Endocrinopathy
- Acromegaly
- Cushing syndrome
- Hyperthyroidism
- Pheochrmocytoma
- Glucocanonama
7. Infections
- Cytomegalovirus
- Coxhacivirus
8. Drugs
- Glucocorticoid
- Thyroid hormone
- Thiazides
- Phenytoins
9. Genetic syndrome associated with diabetes
- Down‘s syndrome
- Kleinfelter‘s syndrome
- Turner‘s syndrome
10. Gestational diabetes mellitus[36,37]

Signs and Symptoms of diabetes?
The classic symptoms of untreated diabetes are weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger).[7] Symptoms may develop rapidly (weeks or months) in type 1 DM, while they usually develop much more slowly and may be subtle or absent in type 2 DM.

Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurry vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes.[8]

CAUSES

Diabetes mellitus is classified into four broad categories: type 1, type 2, gestational diabetes, and "other specific types".[5] The "other specific types" are a collection of a few dozen individual causes.[5] Diabetes is a more variable disease than once thought and people may have combinations of forms.[9] The term "diabetes", without qualification, usually refers to diabetes mellitus.

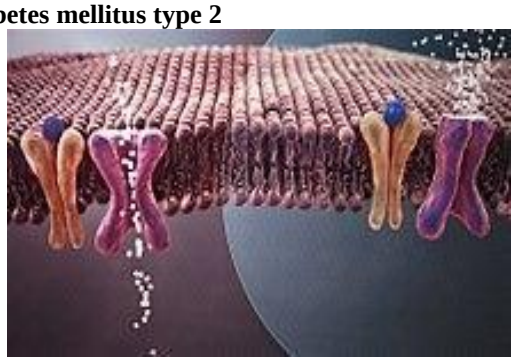
Diabetes mellitus type 1

- Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the pancreatic islets, leading to insulin deficiency. This type can be further classified as immune- mediated or idiopathic. The majority of type 1 diabetes is of the immune-mediated nature, in which a T cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin.[10] It causes approximately 10% of diabetes mellitus cases in North America and Europe. Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages. Type 1 diabetes can affect children or adults, but was traditionally termed "juvenile diabetes" because a majority of these diabetes cases were in children.
- "Brittle" diabetes, also known as unstable diabetes or labile diabetes, is a term that was traditionally used to describe the dramatic and recurrent swings in glucose levels, often occurring for no apparent reason in insulin-dependent diabetes. This term, however, has no biologic basis and should not be used.[11] Still, type 1 diabetes can be accompanied by irregular and unpredictable high blood sugar levels, frequently with ketosis, and sometimes with serious low blood sugar levels. Other complications include an impaired counter regulatory response to low blood sugar, infection, gastroparesis (which leads to erratic absorption of dietary carbohydrates), and endocrinopathies (e.g., Addison's disease).[11] These phenomena are believed to occur no more frequently than in 1% to 2% of persons with type 1 diabetes.[12]

Autoimmune attack in type 1 diabetes

- Type 1 diabetes is partly inherited, with multiple genes, including certain HLA genotypes, known to influence the risk of diabetes. In genetically susceptible people, the onset of diabetes can be triggered by one or more environmental factors,[13] such as a viral infection or diet. Several viruses have been implicated, but to date there is no stringent evidence to support this hypothesis in humans.[13][14] Among dietary factors, data suggest that gliadin (a protein present in gluten) may play a role in the development of type 1 diabetes, but the mechanism is not fully understood.[15][16]

Diabetes mellitus type 2



Reduced insulin secretion and absorption leads to high glucose content in the blood

- Type 2 DM is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion.[5]The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 DM is the most common type of diabetes mellitus.[4]
- In the early stage of type 2, the predominant abnormality is reduced insulin sensitivity. At this stage, high blood sugar can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce the liver's glucose production.
- Type 2 DM is primarily due to lifestyle factors and genetics.[17] A number of lifestyle factors are known to be important to the development of type 2 DM, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet,

stress, and urbanization.[6] Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders.[5]Even those who are not obese often have a high waist–hip ratio.[5]

Dietary factor also influence the risk of developing type 2 DM. Consumption of sugar sweetend drinks in excess is associated with an increase risk.[18,19] the type of fat in the diet is also important, with saturated fats and trans fat increase risk and polyunsaturated and monounsaturated fat deceased the risk.[17] eating lots of white rice also may increase the risk of diabetes.[20] A lack of physical activity is believed to cause 7% of cases.[21]

DIAGNOSIS

WHO diabetes diagnostic criteria[29, 30]

Condition	2 hour glucose	Fasting glucose	HbA1c	
Unit	**mmol/L(mg/dl)**	**mmol/L(mg/dl)**	**mmol/mol**	**DCCT%**
Normal	<7.8(<140)	<6.1(<110)	<42	<6.0
Impaired Fasting glycaemia	<7.8(<140)	>6.1(>110) and <7.0(<126)	42-46	6.0-6.4
Impaired glucose tolerance	>7.8(>140)	<7.0(>126)	42-46	6.0-6.4
Diabetes mellitus	>11.1(>200)	>7.0(>126)	>48	>6.5

Diabetes mellitus is characterized by recurrent or persistent high blood sugar, and is diagnose d by demonstrating any one of the following.[22]

- Fasting plasma glucose level ≥ 7.0 mmol/l (126 mg/dl).
- Plasma glucose ≥ 11.1 mmol/l (200 mg/dl) two hours after a 75 g oral glucose load as in aglucose tolerance test.
- Symptoms of high blood sugar and casual plasma glucose ≥ 11.1 mmol/l (200 mg/dl)
- Glycated hemoglobin (HbA_{1C}) ≥ 48 mmol/mol (≥ 6.5 DCCT %).[23]

A positive result, in the absence of unequivocal high blood sugar, should be confirmed by a repeat of any of the above methods on a different day. It is preferable to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete and offers no prognostic advantage over the fasting test.[24] According to the current definition, two fasting glucose measurements above 126 mg/dl (7.0 mmol/l) is considered diagnostic for diabetes mellitus.

Per the World Health Organization people with fasting glucose levels from 6.1 to 6.9 mmol/l (110 to 125 mg/dl) are considered to have impaired fasting glucose.[25] people with plasma glucose at or above 7.8 mmol/l (140 mg/dl), but not over 11.1 mmol/l (200 mg/dl), two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two prediabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus, as well as cardiovascular disease.[26] The American Diabetes Association since 2003 uses a slightly different range for impaired fasting glucose of 5.6 to 6.9 mmol/l (100 to 125 mg/dl).[27]

Glycated hemoglobin is better than fasting glucose for determining risks of cardiovascular disease and death from any cause.[28]

TREATMENT OF DIABETES[31,32,33,34,35]

ALLOPATHIC DRUGS	HERBAL DRUGS
Diabetes Medications Many different types of medications are available to help lower blood sugar levels in people with type 2 diabetes. Each type works in a different way. It is very common to combine two or more types to get the best effect with fewest side effects. **Sulfonylurea** These drugs stimulate the pancreas to make more insulin. **Biguanides** These agents decrease the amount of glucose produced by the liver. **Alpha-glucosidase inhibitors** These agents slow absorption of the starches and glucose. **Thiazolidinediones** These agents increase sensitivity to insulin. **Meglitinides:** These agents stimulate the pancreas to make more insulin. **D-phenylalanine derivatives** These agents stimulate the pancreas to produce more insulin more quickly. **Amylin synthetic derivatives** Amylin is a naturally occurring hormone secreted by the pancreas along with insulin. An amylin derivative, such as pramlintide (Symlin), is indicated when blood sugar control is not achieved despite optimal insulin therapy. **Incretin mimetics** Exenatide (Byetta) was the first incretin mimetic agent approved in the United States. It is indicated for diabetes mellitus type 2 in addition to metformin or a sulfonylurea when these agents have not attained blood sugar level control alone. **Insulins** Synthetic human insulin is now the only type of insulin. It is less likely to cause allergic reactions than animal-derived varieties of insulin used in the past. Different types of insulin are available and categorized according to their times of action onset and duration. Examples of rapid-acting insulins – Regular insulin (Humulin R, Novolin R) Insulin lispro (Humalog) Insulin aspart (Novolog) Insulin glulisine (Apidra) Prompt insulin zinc (Semilente, slightly slower acting)	Herbs for diabetes treatment are not new. Since ancient times, plants and plant extracts were used to combat diabetes. Here are some herbs that have been confirmed by scientific investigation, which appear to be most effective, relatively non-toxic and have substantial documentation of efficiency. **Cinnamon** Cinnamon is the inner bark and has insulin-like properties, which able to decrease blood glucose levels as well as triglycerides and cholesterol, all of which are important especially for type 2 diabetes patients. ***Pterocarpus marsupium*** It demonstrates to reduce the glucose absorption from the gastrointestinal tract, and improve insulin and pro-insulin levels. It also effective in β cellregeneration. **Bitter melon (*Momordica charantia*)** It lower blood glucose concentrations and acts on both the pancreas and in nonpancreatic cells, such as muscle cells. These include charantin and an insulin-like protein referred to as polypeptide-P, or plant insulin. ***Gynema Sylvestre*** It improves the ability of insulin to lower blood sugar in both type I and type II diabetes. This herb is showing up in more and more over the counter weight loss products and blood sugar balancing formulas. **Onion** It consists of an active ingredient called APDS (allyl propyl disulphide) and it block the breakdown of insulin by the liver and possibly to stimulate insulin production by the pancreas, thus increasing the amount of insulin and reducing sugar levels in the blood. **Fenugreek (*Trigonella foenum-graecum*)** The fiber-rich fraction of fenugreek seeds can lower blood sugar levels in people with diabetes, and to a lesser extent, for lowering blood cholesterol,weight control. **Blueberry (*Vaccinium myrtillus*)** Blueberry is a natural method of controlling or lowering blood sugar levels in the blood. It is a good astringent and helps relieve inflammation of the kidney, bladder and prostate. **Asian Ginseng** It has been shown to enhance the release of insulin from the pancreas and to increase the number of insulin receptors. It also has a direct blood sugar-lowering effect and improves psycho-physiological performance. **Ginkgo Biloba** The extract may prove useful for prevention and treatment of early-stage diabetic neuropathy. It has also been shown to prevent diabetic retinopathy.

REFERENCES

1. American Diabetes Association. Screening for diabetes. *Diabetes Care*, 1998; 21(suppl 1): s20-s22.
2. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care, 2009; 32(suppl 1): s62-s67.
3. American Diabetes Association. All about Diabetes. http://www.diabetes.org/aboutdiabetes. jsp (accessed 10 Feb 2009).
4. "Diabetes Fact sheet N°312".WHO. October 2013. Archived from the original on 26 August 2013. Retrieved 25 March 2014.
5. Shoback DG, Gardner D, eds. (2011). "Chapter 17". Greenspan's basic & clinical endocrinology (9th ed.). New York: McGraw-Hill Medical. ISBN 0-07-162243-8.
6. Williams textbook of endocrinology (12th ed.). Elsevier/Saunders. pp. 1371–1435. *ISBN 978- 1-4377-0324-5.*
7. Cooke DW, Plotnick L (November 2008). "Type 1 diabetes mellitus in pediatrics". Pediatrics in Review, 29(11): 374–84; quiz 385.doi:10.1542/pir.29-11-374. PMID 18977856.
8. Rockefeller, J. D. (2015-06-18). Diabetes: Symptoms, Causes, Treatment and Prevention. ISBN 9781514603055. Archived from the original on 2017-09-06.
9. Tuomi T, Santoro N, Caprio S, Cai M, Weng J, Groop L (March 2014). "The many faces of diabetes: a disease with increasing heterogeneity". Lancet, 383(9922): 1084 94. doi:10.1016/S0140-6736(13)62219-9.PMID 24315621.
10. Rother KI (April 2007). "Diabetes treatment--bridging the divide". The New England Journal of Medicine, 356(15): 1499–501. doi:10.1056/NEJMp078030. PMC 4152979 . PMID 17429082.
11. "Diabetes Mellitus (DM): Diabetes Mellitus and Disorders of Carbohydrate Metabolism: Merck Manual Professional". Merck Publishing. April 2010. Archived from the original on 2010-07-28. Retrieved, 2010-07-30.
12. Dorner M, Pinget M, Brogard JM (May 1977). "[Essential labile diabetes (author's transl)]". MMW, Munchener Medizinische Wochenschrift (in German), 119(19): 671– 4. PMID 406527.
13. Petzold A, Solimena M, Knoch KP (October 2015). "Mechanisms of Beta Cell Dysfunction Associated With Viral Infection". Current Diabetes Reports (Review), 15(10): 73. doi:10.1007/s11892-015-0654-x.PMC 4539350 . PMID 26280364. So far, none of the hypotheses accounting for virus-induced beta cell autoimmunity has been supported by stringent evidence in humans, and the involvement of several mechanisms rather than just one is also plausible.
14. Butalia S, Kaplan GG, Khokhar B, Rabi DM (December 2016). "Environmental Risk Factors and Type 1 Diabetes: Past, Present, and Future". Canadian Journal of Diabetes (Review), 40(6): 586–593.doi:10.1016/j.jcjd.2016.05.002. PMID 27545597.
15. Serena G, Camhi S, Sturgeon C, Yan S, Fasano A (August 2015). "The Role of Gluten in Celiac Disease and Type 1 Diabetes". Nutrients. 7 (9): 7143-62. doi:10.3390/nu7095329. PMC 4586524 . PMID 26343710.
16. Visser J, Rozing J, Sapone A, Lammers K, Fasano A (May 2009). "Tight junctions, intestinal permeability, and autoimmunity: celiac disease and type 1 diabetes paradigms". Annals of the New York Academy of Sciences, 1165: 195205. Bibcode: 2009NYASA1165..195V. doi:10.1111/j.17496632.2009.04037 x. PMC 2886850. PMID 19538307.
17. Risérus U, Willett WC, Hu FB (January 2009). "Dietary fats and prevention of type 2 diabetes". Progress in Lipid Research, 48(1): 4451. doi:10.1016/j.plipres.2008.10.002. PMC 2654180. PMID 19032965.
18. Malik VS, Popkin BM, Bray GA, Després JP, Hu FB (March 2010)."Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk". Circulation, 121(11): 135664. doi:10.1161/CIRCULATIONAHA.109.876185. PMC 28624 65. PMID 20308626.
19. Malik VS, Popkin BM, Bray GA, Després JP, Willett WC, Hu FB (November 2010). "Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta- analysis". Diabetes Care, 33(11): 2477-83. doi:10.2337/dc10-1079. PMC 2963518. PMID 20693348.
20. Hu EA, Pan A, Malik V, Sun Q (March 2012). "White rice consumption and risk of type 2 diabetes: metaanalysis and systematic review". BMJ.344:e1454. doi:10.1136/bmj.e1454. PMC 3307808 . PMID 22422870.
21. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT (July 2012). "Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy". Lancet, 380(9838): 219–doi:10.1016/S0140-6736(12)61031- 9. PMC 3645500. PMID 22818936.
22. "Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications" *(*PDF). World Health Organisation. 1999. Archived (PDF)from the original on 2003-03-08.
23. ""Diabetes Care" January 2010". American Diabetes Association.Archived from the original on 13 January 2010. Retrieved 29 January 2010.
24. Saydah SH, Miret M, Sung J, Varas C, Gause D, Brancati FL (August 2001). "P ostchallenge hyperglycemia and mortality in a national sample of U.S. adults". Diabetes Care, 24(8): 1397–402. doi:10.2337/diacare.24.8.1397. PMID 11473076.
25. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF

consultation (PDF). World Health Organization, 2006; 21. ISBN 978-92-4-159493-6. Archived (PDF) from the original on 11 May 2012.
26. Santaguida PL, Balion C, Hunt D, Morrison K, Gerstein H, Raina P, Booker L, Yazdi H. "Diagnosis, Prognosis, and Treatment of Impaired Glucose Tolerance and Impaired Fasting Glucose". Summary of Evidence Report/Technology Assessment, No. 128. Agency for Healthcare Research and Quality. Archived from the original on 16 September 2008. Retrieved20 July 2008.
27. Bartoli E, Fra GP, Carnevale Schianca GP (February 2011). "The oral glucose tolerance test (OGTT) revisited". European Journal of Internal Medicine. 22(1): 8–doi:10.1016/j.ejim.2010.07.008.PMID 21238885.
28. Selvin E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J, Coresh J, Brancati FL (March 2010). "Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults". The New England Journal of Medicine, 362(9): 80011. DOI:1056/NEJMoa0908359. PMID2872990. pmid20200384.
29. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation (PDF). Geneva*:* World Health Organization, 2006; 21. ISBN 978-92- 4-159493-6.
30. Vijan, S (March 2010). "Type 2 diabetes". Annals of Internal Medicine, 152(5): ITC31-15. doi:10.7326/0003-4819-152-5-201003020-01003. PMID 20194231.
31. A.D.A.M Medical Encyclopedia. America. Pubmed; 2012 Jun 27. Available from www.ncbi.nlm.nih.gov/pubmedhealth.
32. Nathan DM, Cleary PA, Backlund JY, et al: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *The New England Journal of Medicine*, 2005; 353(25): 2643–53.
33. Text Book Of Pharmacognosy, C. K.Kokate, A.P. Purohit, S.B. Gokhale, P: 223.
34. Jing Tian Xie, Sangeeta Mehendale and Chun-Su Yuan- Ginseng and Diabetes.
35. Ng T.B., Yeung H.W. – Hypoglycemic constituents of Panax ginseng.
36. Alarcon AFJ, Roman RR, Perez GS, Aguilar CA, Contreras WCC and Flores SJL: Study of the anti-hyperglycemic effect of plants used as Antidiabetics. J Ethno Pharm, 1998; 61: 101-10.
37. M. Ayyanar, K. Sankarasivaraman and S. Ignacimuthu Traditional Herbal Medicines Used for the Treatment of Diabetes among Two Major Tribal Groups in South Tamil Nadu, Ethnobotanical Leaflets, 2008; 12: 276-280.

DRUG PRICE CONTROL ORDERS (DPCO)

Article · May 2018

CITATIONS
0

READS
12,169

6 authors, including:

Tanvay Jaithliya
Mewar University
9 PUBLICATIONS **4** CITATIONS
SEE PROFILE

Jayesh Gadhiya
Mewar University
7 PUBLICATIONS **18** CITATIONS
SEE PROFILE

Gaurav Kumar Sharma
Mewar University
89 PUBLICATIONS **65** CITATIONS
SEE PROFILE

EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 5
953-956
Year: 2018

DRUG PRICE CONTROL ORDERS (DPCO)

Abdul Hamid*, Shubam Sehgal, Tanvay Jaithliya, Jayesh Gadhiya, Zakarya Noorani and Gaurav Kumar Sharma[1]

*Faculty of Pharmaceutical Sciences, Mewar University, Chittorgarh, 312901, India.
[1]Head of Department, Faculty of Pharmaceutical Sciences, Mewar University, Chittorgarh.

***Corresponding Author: Abdul Hamid**
Faculty of Pharmaceutical Sciences, Mewar University, Chittorgarh, 312901, India.

Article Received on 19/03/2018 **Article Revised on 09/04/2018** **Article Accepted on 30/04/2018**

ABSTRACT
Price controls are applicable to what is generally known as "Scheduled drugs" or "Scheduled formulations". Since 2013, scheduled formulations consist of the "Essential Medicines" declared so by the Government through its National List of Essential Medicines (NLEM). It does not mean that all drugs brought under price control are essential medicines. As per Para 19 of the DPCO-2013, the Government may, in case of extra-ordinary circumstances and in public interest, fix the ceiling price or retail price of any drug, whether scheduled or non-scheduled or a new drug for such period, as it may deem fit. Exchanging prices among competitors can also violate the antitrust laws.

KEYWORDS: Price controls are applicable can also violate the antitrust laws.

Drug Price Control Orders (DPCO)

Price controls are applicable to what is generally known as "Scheduled drugs" or "Scheduled formulations" that is, those medicines which are listed out in the Schedule I of Drug Price Control Order (DPCO), issued by the Government of India from time to time.[1] (It may be noted that the use of the word "Scheduled drugs" is a legacy of the DPCO-1995.[2] The latest DPCO 2013 only uses the word "Scheduled formulation" to refer to medicines in its first schedule since some of the bulk drugs when used as a single ingredient also act as a formulation. Hence, generally these medicines are referred even now as "scheduled drugs" from the perspective of price regulation). Since 2013, scheduled formulations consist of the "Essential Medicines" declared so by the Government through its National List of Essential Medicines (NLEM).[3] In fact, Schedule I of DPCO-2013 is the NLEM-2011 list. Thus, NLEM forms the basis of deciding which medicines should come under price control via DPCO. Any formulation based on combination of any one of these drugs appearing under NLEM can be subject to price fixation. In the earlier DPCOs (those prior to DPCO-2013), NLEM was not taken into consideration for price fixation or price monitoring.[4] Further, in the earlier DPCOs, only the bulk drugs were mentioned in Schedule-[5] and prices were fixed by the Government for both bulk drug as well as formulations based on any of these bulk drugs. Since 2013, all essential medicines (as defined under NLEM) are treated as scheduled formulations (under DPCO-2013). However, it does not mean that all drugs brought under price control are essential medicines. As per Para 19 of the DPCO-2013, the Government may, in case of extra-ordinary circumstances and in public interest, fix the ceiling price or retail price of any drug, whether scheduled or non-scheduled or a new drug for such period, as it may deem fit. It also has powers to revise (either increase or decrease) the ceiling price or retail price of the drug which is already fixed and notified, irrespective of annual wholesale price index for that year (based on which companies are automatically permitted under DPCO to revise the prices annually).[6] Price controls are applicable irrespective of whether it is generic or branded.[7] National Pharmaceutical Pricing Policy (NPPP) is the policy governing price control and DPCO is the order by which price control is enforced. The Drug Price Control Orders are issued by Ministry of Chemicals and Fertilisers, which is the main nodal administrative ministry for pharmaceutical companies.[8] Under the latest DPCO 2013, the prices of 348 drugs appearing in the National List of Essential Medicines-2011 covering around 628 formulations have been brought under the purview of price control[9]

Drug Price Control Orders

The NPPA regularly publishes lists of medicines and their maximum ceiling prices. The latest DPCO was released in 2013 which has a list of 384 drugs.[10,11,12,13,14,15]

Functions

- To implement and enforce the provisions of the Drugs (Prices Control) Order in accordance with the powers delegated to it.
- To deal with all legal matters arising out of the decisions of the Authority.
- To monitor the availability of drugs, identify shortages, if any, and to take remedial steps.
- To collect/ maintain data on production, exports and imports, market share of individual companies, profitability of companies etc, for bulk drugs and formulations.
- To undertake and/ or sponsor relevant studies in respect of pricing of drugs/ pharmaceuticals.
- To recruit/ appoint the officers and other staff members of the Authority, as per rules and procedures laid down by the Government.
- To render advice to the Central Government on changes/ revisions in the drug policy.[16]
- To render assistance to the Central Government in the parliamentary matters relating to the drug pricing.[17]

Price fixing is an agreement between participants on the same side in a market to buy or sell a product, service, or commodity only at a fixed price, or maintain the market conditions such that the price is maintained at a given level by controlling supply and demand. The intent of price fixing may be to push the price of a product as high as possible, generally leading to profits for all sellers but may also have the goal to fix, peg, discount, or stabilize prices. The defining characteristic of price fixing is any agreement regarding price, whether expressed or implied. International price fixing by private entities can be prosecuted under the antitrust laws of many countries. Examples of prosecuted international cartels are those that controlled the prices and output of lysine, citric acid, graphite electrodes, and bulk vitamins.[18] In the United States, price fixing can be prosecuted as a criminal federal offense under Section 1 of the Sherman Antitrust Act.[19] Private individuals or organizations may file lawsuits for triple damages for antitrust violations and, depending on the law, recover attorneys fees and costs expended on prosecution of a case.[20,21,22] Under American law, exchanging prices among competitors can also violate the antitrust laws. That includes exchanging prices with the intent to fix prices or the exchange affecting the prices individual competitors set. Proof that competitors have shared prices can be used as part of the evidence of an illegal price fixing agreement.[23] Experts generally advise that competitors avoid even the appearance of agreeing on price.[24] Since 1997, US courts have divided price fixing into two categories: vertical and horizontal maximum price fixing.[25] Vertical price fixing includes a manufacturer's attempt to control the price of its product at retail.[26]

Maximum retail price

A maximum retail price (MRP) is a manufacturer calculated price that is the highest price that can be charged for a product sold in India and Bangladesh.[27,28]

All retail products in India must be marked with MRP. Shops cannot charge customers over the MRP. Some shops may charge slightly below MRP to draw more customers to their stores. In some remote areas, tourist spots, and in situations where a product is difficult to obtain, consumers are often charged illegally over the MRP.[29]

In April 2015, it was reported that milk vendors in Mumbai were threatening a boycott after it was discovered they had been charging above MRP and the Maharashtra state government threatened to intervene.[30]

Price fixing is an agreement between participants on the same side in a market to buy or sell a product, service, or commodity only at a fixed price, or maintain the market conditions such that the price is maintained at a given level by controlling supply and demand. The intent of price fixing may be to push the price of a product as high as possible, generally leading to profits for all sellers but may also have the goal to fix, peg, discount, or stabilize prices. The defining characteristic of price fixing is any agreement regarding price, whether expressed or implied. International price fixing by private entities can be prosecuted under the antitrust laws of many countries. Examples of prosecuted international cartels are those that controlled the prices and output of lysine, citric acid, graphite electrodes, and bulk vitamins.[31] In the United States, price fixing can be prosecuted as a criminal federal offense under Section 1 of the Sherman Antitrust Act.[32] Private individuals or organizations may file lawsuits for triple damages for antitrust violations and, depending on the law, recover attorneys fees and costs expended on prosecution of a case.[33,34,35] Under American law, exchanging prices among competitors can also violate the antitrust laws. That includes exchanging prices with the intent to fix prices or the exchange affecting the prices individual competitors set. Proof that competitors have shared prices can be used as part of the evidence of an illegal price fixing agreement.[36] Experts generally advise that competitors avoid even the appearance of agreeing on price.[37] Since 1997, US courts have divided price fixing into two categories: vertical and horizontal maximum price fixing.[38] Vertical price fixing includes a manufacturer's attempt to control the price of its product at retail.[39]

Calculation of retail price of formulation

The retail price of a formulation shall be calculated by the Government in accordance with the following formula, namely: - R.P. = (M.C.+C.C.+P.M.+P.C.) X (1+MAPE/100) + ED Where “R.P.” means retail price: “M.C.” means material cost and includes the cost of drugs and other pharmaceutical aids used including overages, if any, plus process loss there on specified as a norm from time to time by notification in the Official Gazette in this behalf; “C.C.” means conversion cost worked out in accordance with established procedures of

costing and shall be fixed as a norm every year by notification in the Official Gazette in this behalf; "P.M." means cost of the packing material used in the packing of concerned formulation, including process loss, and shall be fixed as a norm every year by notification in the Official Gazette in this behalf; "P.C." means packing charges worked out in accordance with established procedures of costing and shall be fixed as a norm every year by notification in the Official Gazette in this behalf; "MAPE" (Maximum Allowable Post-manufacturing Expenses) means all costs incurred by a manufacturer from the stage of ex-factory cost to retailing and includes trade margin and margin for the manufacturer and it shall not exceed one hundred per cent for indigenously manufactured Scheduled formulations; "E.D." means excise duty: Provided that in the case of an imported formulation, the landed cost shall form the basis for fixing its price along with such margin to cover selling and distribution expenses including interest and importer's profit which shall not exceed fifty per cent of the landed cost. Explanation: For the purpose of this proviso, "landed cost" means the cost of import of formulation inclusive of customs duty and clearing charges.

CONCLUSION

A maximum retail price (MRP) is a manufacturer calculated price that is the highest price that can be charged for a product sold in India and Bangladesh. The NPPA regularly publishes lists of medicines and their maximum ceiling prices. NLEM forms the basis of deciding which medicines should come under price control via DPCO. price fixing can be prosecuted as a criminal federal offense under Section 1 of the Sherman Antitrust Act.

REFERENCE

1. Scheduled drugs does not mean the drugs appearing in the various schedules to Drugs & Cosmetic Act and Rules, 1945.
2. DPCO had only used the words "Scheduled Bulk drugs" and "Scheduled formulations". "Scheduled drugs" was the umbrella term commonly used to refer to both "Scheduled Bulk drugs" and "Scheduled formulations" which were brought under price control., 1995.
3. "National List of Essential Medicines" is defined in the Drug Price Control Order to mean National List of Essential Medicines, published by the Ministry of Health and Family Welfare as updated or revised from time to time and included in the first schedule of DPCO by the Government through a notification in the Official Gazette., 2011.
4. Out of the 348 medicines listed in the NLEM-2011, only 34 drugs were included amongst the 74 drugs listed in the First Schedule of "The Drugs (Prices Control) Order, 1995 DPCO 1995.
5. NLEM consists of items like insulin, ibuprofen, sulphamethoxazole, rifampicin, streptomycin, Ranitidine, etc which are bulk drugs and at the same time medicines or formulations as well when these are manufactured as single ingredient formulations. The NLEM contains the generic name or salts or chemical names.
6. An internal guideline issued under para 19 of DPCO on 29.05.2014 outlining the criteria and methodology for fixing / revising prices of non-scheduled formulations on the basis of inter-brand price differentials and for fixing the launch prices of new non-scheduled formulations was withdrawn on However, this withdrawal does not take away the powers of the Government as mentioned in Para 19 of DPCO-2013 to fix the prices of non-scheduled formulations. It was generally perceived that the guideline went beyond the scope of para, 22 September 2014; 19.
7. In India, we also have branded generic medicines.
8. The M/o Health and Family Welfare and Ministry of AYUSH also govern various aspects relating to pharmaceutical companies.
9. Total Number of NLEM Medicines comes to 680. However, 52 medicines appear in more than one therapeutic group. Hence, the net number of medicines subject to price fixation is 628 (as mentioned in Annual report of Department of Pharmaceuticals 2014-15.
10. V, NALINAKANTHI (2014-09-29). "All you wanted to know about: DPCO". The Hindu Business Line. Retrieved 2017-10-29.
11. "Notified prices of bulk drugs as specified in first schedule of dpco,". www.nppaindia.nic.in. retrieved 2017-10-29.
12. "Notified prices of bulk drugs as specified in first schedule of dpco,". www.nppaindia.nic.in. retrieved 2017-10-29.
13. "Notified prices of bulk drugs as specified in first schedule of dpco,". www.nppaindia.nic.in. retrieved 2017-10-29.
14. "National pharmaceutical pricing authority". www.nppaindia.nic.in. retrieved 2017- 10-29.
15. "Dpco/nppa | department of pharmaceuticals". pharmaceuticals.gov.in. retrieved 2017-10-29.
16. "Official national pharmaceutical pricing authority".
17. "National pharmaceutical pricing authority (nppa)". department of pharmaceuticals, ministry of chemicals and fertilizers. archived from the original on 28 july 2014. retrieved 20 july 2014.
18. Connor, john m. (april 2004). "extraterritoriality of the sherman act and deterrence of private international cartels". american agricultural economics association agm 2005. retrieved september 30, 2014.
19. "Us code: title 15,1. trusts, etc., in restraint of trade illegal; penalty". law.cornell.edu. retrieved 2012-03-25.
20. "www.ag.ny.gov - new york state attorney general". retrieved 15 june 2016.
21. Art Publishers Association, Bulletin: Be Careful About Antitrust Law (Feb. 2000) archived 2004-10-22 at the wayback machine.

22. "Archived copy". archived from the original on 2007-09-27. retrieved 2016-06-15.
23. "Antitrust law developments (2002); art publishers association, bulletin: be careful about antitrust law (february 2000)". archived from the original on 27 september 2007. retrieved 15 june 2016.
24. "Art publishers association, bulletin: be careful about antitrust law (february 2000)". archived from the original on 27 september 2007. retrieved 15 june 2016.
25. Tsui, tat chee, interstate comparison – use of contribution margin in determination of price fixing (2011). pace int'l law review online companion, vol. 1, april 2011. at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1839223
26. Sauer, raymond d. "vertical price fixing". archived from the original on 8 july 2013. retrieved 9 july 2013.
27. "Mrp: maximum retail price for packaged goods in india". fullstopindia. retrieved 23 april 2015.
28. {{cite web|url=http://print.thefinancialexpress-bd.com/2014/11/27/68117/print
29. Title=vat on commissions for drug sales raised |quote=the nbr policy guidelines say the drug administration will set the maximum retail price of drugs based on the trade price.
30. "New law in making to punish vendors charging over mrp". *the indian express*. retrieved 12 october 2016.
31. "Milk vendors charging more than mrp threaten boycott". *times of india*. retrieved 23 april 2015.
32. Connor, john m. (april 2004). *"extraterritoriality of the sherman act and deterrence of private international cartels". american agricultural economics association* agm 2005. *retrieved september 30, 2014*.
33. "Us code: title 15,1. trusts, etc., in restraint of trade illegal; penalty". law.cornell.edu. retrieved 2012-03-25.
34. "Www.Ag.Ny.Gov - New York State Attorney General". retrieved 15 june 2016.
35. Art Publishers Association, Bulletin: Be Careful About Antitrust Law (Feb. 2000) archived 2004-10-22 at the wayback machine.
36. "Archived copy". archived from the original on 2007-09-27. retrieved 2016-06-15.
37. "Antitrust law developments (2002); art publishers association, bulletin: be careful about antitrust law (february 2000)". archived from the original on 27 september 2007. retrieved 15 june 2016.
38. "Art publishers association, bulletin: be careful about antitrust law (february 2000)". archived from the original on 27 september 2007. retrieved 15 june 2016.
39. Tsui, tat chee, interstate comparison – use of contribution margin in determination of price fixing (2011). pace int'l law review online companion, vol. 1, april 2011. at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1839223
40. Sauer, raymond d. "vertical price fixing". archived from the original on 8 july 2013. retrieved 9 july 2013.

WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.632
Volume 10, Issue 9, 1324-1337 Review Article ISSN 2278 – 4357

DRUG SOLUBILITY

[1]*Amit Choubay, [2]Dr. Gaurav Kumar Sharma and [3]Dr. Kaushal Kishore Chandrul

[1]Student of B. Pharma 4th Yr, [2]H.O.D, [3]Principal

Department of Pharmacy, Mewar University, Chittorgarh, India.

Article Received on
01 July 2021,

Revised on 22 July 2021,
Accepted on 11 August 2021,

DOI: 10.20959/wjpps20219-19876

***Corresponding Author**
Amit Choubay
Student of B. Pharma 4th Yr,
Department of Pharmacy,
Mewar University,
Chittorgarh, India.

ABSTRACT

Solubility, the phenomenon of dissolution of solute in solvent to give a homogenous system, is one of the important parameters to achieve desired concentration of drug in systemic circulation for desired (anticipated) pharmacological response. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as for the generic development. More than 40% NCEs (new chemical entities) developed in pharmaceutical industry are practically insoluble in water. Solubility is a major challenge for formulation scientist. Any drug to be absorbed must be present in the form of solution at the site of absorption. Various techniques are used for the enhancement of the solubility of poorly soluble drugs which include physical and chemical modifications of drug and other methods like particle size reduction, crystal engineering, salt formation, solid dispersion, use of surfactant, complexation, and so forth. Selection of solubility improving method depends on drug property, site of absorption, and required dosage form characteristics.

KEYWORDS: Solubility, Homogenous, Absorption, Poorly Water Soluble drug; Dissolution.

INTRODUCTION

Solubility is the property of a solid, liquid, or gaseous chemical substance called solute to dissolve in a solid, liquid, or gaseous solvent to form a homogeneous solution of the solute in the solvent .The solubility of a substance fundamentally depends on the solvent used as well as on temperature and pressure. The extent of solubility of a substance in a specific solvent is measured as the saturation concentration where adding more solute does not increase its concentrationin the solution.[1]

The solvent is generally a liquid, which can be a pure substance or a mixture of two liquids. One may also speak of solid solution, but rarely of solution in a gas. The extent of solubility ranges widely, from infinitely soluble (fully miscible) such as ethanol in water, to poorly soluble, Such as silver chloride in water. The term insoluble is often applied to poorly or very poorly soluble compounds.[2]

Solubility occurs under dynamic equilibrium, which means that solubility results from the simultaneous and opposing processes of dissolution and phase joining (e.g., precipitation of solids). Solubility equilibrium occurs when the two processes proceed at a constant rate. Under certain conditions equilibrium solubility may be exceeded to give a socalled supersaturated solution, which is metastable.[3]

Solubility is not to be confused with the ability to dissolve or liquefy a substance, since these processes may occur not only because of dissolution but also because of a chemical reaction. For example, zinc is insoluble in hydrochloric acid, but does dissolve in it by chemically reacting into zinc chloride and hydrogen, where zinc chloride is soluble in hydrochloric acid. Solubility does not also depend on particle size or other kinetic factors; given enough time, even large Particles will eventually dissolve.[4]

IUPAC defines solubility as the analytical composition of a saturated solution expressed as a proportion of a designated solute in a designated solvent. Solubility may be stated in units of concentration, molality, mole fraction, mole ratio, and other units.[5]

Extensive use of solubility from different perspective has led to solubility being expressed in various manners. It is commonly expressed as a concentration, either by mass (g of solute per kg of solvent, g per dL (100 mL) of solvent), molarity, molality, mole fraction, or other similar Descriptions of concentration. The maximum equilibrium amount of solute that can dissolve per amount of solvent is.

Table 1: USP and BP solubility criteria.

Descriptive term Part of solvent required per part of solute

Very soluble Less than 1

Freely soluble From 1 to 10

Soluble From 10 to 30

Sparingly soluble From 30 to 100

Slightly soluble From 100 to 1000
Very slightly soluble From 1000 to 10,000

Practically insoluble 10,000 and over the solubility of that solute in that solvent under the specified conditions.[6]

The advantage of expressing solubility in this manner is its simplicity, while the disadvantage is that it can strongly depend on the presence of other species in the solvent (e.g., the common ion effect). The Flory-Huggins solution theory is a theoretical model describing the solubility of polymers. The Hansen Solubility Parameters and the Hildebrand solubility parameters are empirical methods for the prediction of solubility. It is also possible to predict solubility from other physical constants such as the enthalpy of fusion. The partition coefficient (Log P) is a measure of differential solubility of a compound in a hydrophobic solvent (octanol) and a hydrophilic solvent (water). The logarithm of these two values enables compounds to be ranked in terms of hydrophilicity (or hydrophobicity). USP and BP classify the solubility regardless of the solvent used, just only in terms of quantification and have defined the criteria as given in Table 1.[7, 8]

The Biopharmaceutics Classification System (BCS) is a guide for predicting the intestinal drug absorption provided by the U.S. Food and Drug Administration. This system restricts the prediction using the parameters solubility and intestinal permeability. Solubility is based on the highest-dose strength of an immediate release product.

A drug is considered highly soluble when the highest dose strength is soluble in 250mL or less of aqueous media over the pH range of 1 to 7.5. The volume estimate of 250mL is derived from typical bioequivalence study protocols that prescribe administration of a drug product to fasting human volunteers with a glass of water.[9]

The intestinal permeability classification is based on a comparison to the intravenous injection. All those factors are highly important, since 85% of the most sold drugs in the USA and Europe are orally administered. All drugs have been divided into four classes: class I—high soluble and high permeable, class II—low soluble and high permeable, class III—low soluble and high permeable and class IV—low soluble and low permeable.

2. Importance of Solubility

Oral ingestion is the most convenient and commonly employed route of drug delivery due to its ease of administration, high patient compliance, costeffectiveness, least sterility constraints, and flexibility in the design of dosage form. As a result, many of the generic drug companies are inclinedmore to produce bioequivalent oral drug products.[10]

However, the major challenge with the design of oral dosage forms lies with their poor bioavailability. The oral bioavailability depends on several factors including aqueous solubility, drug permeability, dissolution rate, first-pass metabolism, presystemic metabolism, and susceptibility to efflux mechanisms. The most frequent causes of low oral bioavailability are attributed to poor solubility and low permeability. Solubility also plays a major role for other dosage forms like parenteral formulations as well.[11] Solubility is one of the important parameters to achieve desired concentration of drug in systemic circulation for achieving required pharmacological response.[12] Poorly water soluble drugs often require high doses in order to reach therapeutic plasma concentrations after oral administration. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as generic development. Any drug to be absorbed must be present in the form of an aqueous solution at the site of absorption. Water is the solvent of choice for liquid pharmaceutical formulations. Most of the drugs are either weakly acidic or weakly basic having poor aqueous solubility. More than 40% NCEs (new chemical entities) developed in pharmaceutical industry are practically insoluble in water. These poorly water soluble drugs having slow drug absorption leads to inadequate and variable bioavailability and gastrointestinalmucosal toxicity. For orally administered drugs solubility is the most important one rate limiting parameter to achieve their desired concentration in systemic circulation for pharmacological response. Problem of solubility is a major challenge for formulation scientist.[13] The improvement of drug solubility thereby its oral bioavailability remains one of the most challenging aspects of drug development process especially for oral-drug delivery system. There are numerous approaches available and reported in literature to enhance the solubility of poorly water-soluble drugs. The techniques are chosen on the basis of certain aspects such as properties of drug under consideration, nature of excipients to be selected, and nature of intended dosage form. The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastrointestinal fluids often cause insufficient bioavailability. Especially for class II (low solubility and high permeability) substances according to the BCS, the bioavailabilitymay be enhanced by increasing the solubility and

dissolution rate of the drug in the gastrointestinal fluids. As for BCS class II drugs rate limiting step is drug release from the dosage form and solubility in the gastric fluid and not the absorption, so increasing the solubility in turn increases the bioavailability for BCS class II drugs.[10, 13, 14] The negative effect of compounds with low solubility include poor absorption and bioavailability, insufficient solubility for IV dosing, development challenges leading to increasing the development cost and time, burden shifted to patient (frequent high-dose administration).[11]

3. Techniques for Solubility

Enhancement Solubility improvement techniques can be categorized in to physical modification, chemical modifications of the drug substance, and other techniques.

Physical Modifications

Particle size reduction like micronization and nanosuspension, modification of the crystal habit like polymorphs, amorphous form and cocrystallization, drug dispersion in carriers like eutectic mixtures, solid dispersions, solid solutions and cryogenic techniques.

Chemical Modifications

Change of ph, use of buffer, derivatization, complexation, and salt formation.

Miscellaneous Methods

Supercritical fluid process, use of adjuvant like surfactant, solubilizers, cosolvency, hydrotrophy, and novel excipients.

4. Particle Size Reduction

The solubility of drug is often intrinsically related to drug particle size; as a particle becomes smaller, the surface area to volume ratio increases. The larger surface area allows greater interaction with the solvent which causes an increase in solubility.

Conventional methods of particle size reduction, such as comminution and spray drying, rely upon mechanical stress to disaggregate the active compound. Particle size reduction is thus permitting an efficient, reproducible, and economic means of solubility enhancement. However, the mechanical forces inherent to comminution, such as milling and grinding, often impart significant amounts of physical stress upon the drug product which may induce degradation. The thermal stress which may occur during comminution and spray drying is also a concern when processing thermosensitive or unstable active compounds. Useing

traditional approaches for nearly insoluble drugs may not be able to enhance the solubility up to desired level.

Micronization is another conventional technique for the particle size reduction. Micronization increases the dissolution rate of drugs through increased surface area, it does not increase equilibrium solubility. Decreasing the particle size of these drugs, which cause increase in surface area, improve their rate of dissolution. Micronization of drugs is done by milling techniques using jet mill, rotor stator colloid mills and so forth micronization is not suitable for drugs having a high dose number because it does not change the saturation solubility of the drug.[15]

These processes were applied to griseofulvin, progesterone, spironolactone diosmin, and fenofibrate. For each drug, micronization improved their digestive absorption and consequently their bioavailability and clinical efficacy. Micronized fenofibrate exhibited more than 10-fold (1.3% to 20%) increase in dissolution in at 30 minutes biorelevant media.[16, 17]

5. Solid Dispersions

The concept of solid dispersions was originally proposed by Sekiguchi and Obi, who investigated the generation and dissolution performance of eutectic melts of a sulfonamide drug and a water- soluble carrier in the early 1960s.[18]

Solid dispersions represent a useful pharmaceutical technique for increasing the dissolution, absorption, and therapeutic efficacy of drugs in dosage forms. The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The most commonly used hydrophilic carriers for solid dispersions include polyvinylpyrrolidone (Povidone, PVP), polyethylene glycols (PEGs), Plasdone- S630. Surfactants like Tween-80, docusate sodium, Myrj-52, Pluronic-F68, and sodium lauryl sulphate (SLS) also find a place in the formulation of solid dispersion. The solubility of celecoxib, halofantrine, and ritonavir can be improved by solid dispersion using suitable hydrophilic carriers like celecoxib with povidone (PVP) and ritonavir with gelucire. Various techniques to prepare the solid dispersion of hydrophobic drugs with an aim to improve their aqueous solubility are listed here.[19–21]

5.1. Hot-Melt Method (Fusion Method)

The main advantages of this direct melting method is its simplicity and economy. The melting or fusion method was first proposed by Sekiguchi and Obi to prepare fast release solid dispersion dosage forms. In this method, the physical mixture of a drug and a water-soluble carrier are heated directly until the two melts. The melted mixture is then cooled and solidified rapidly in an ice bath with rigorous stirring. The final solid mass is then crushed, pulverized, and sieved, which can be compressed into tablets with the help of tableting agents. The melting point of a binary system is dependent upon its composition, that is, the selection of the carrier and the weight fraction of the drug in the system.[22] An important requisite for the formation of solid dispersion by the hot- meltmethod is the miscibility of the drug and the carrier in the molten form. Another important requisite is the thermostability of both the drug and the carrier.

5.2. Solvent Evaporation Method

Tachibana and Nakamura[23] were the first to dissolve both the drug and the carrier in a common solvent and then evaporate the solvent under vacuum to produce a solid solution. This enabled them to produce a solid solution of the highly lipophilic β-carotene in the highly water soluble carrier povidone.

Many investigators studied solid dispersion of meloxicam, naproxen,	and nimesulide using solvent evaporation
technique. These findings suggest that the above-mentioned technique can be improvement and stability of solid dispersions of poorly water soluble drugs.[15,17]	employed

The main advantage of the solvent evaporation method is that thermal decomposition of drugs or carriers can be prevented because of the low temperature required for the evaporation of organic solvents. However, the disadvantages associated with this method are the higher cost of preparation, the difficulty in completely removing the organic solvent (a regulatory perspective), the possible adverse effect of the supposedly negligible amount of the solvent on the chemical stability of the drug, the selection of a common volatile solvent, and the difficulty in reproducing crystal forms.[24]

5.3. Hot-Melt Extrusion

Hot-melt extrusion is essentially the same as the fusion method except that intense mixing of

the components is induced by the extruder. Just like in the traditional fusion process, miscibility of the drug and the matrix could be a problem. High-shear forces resulting in high local temperature in the extruder is a problem for heat sensitive materials. However, compared to the traditional fusion method, this technique offers the possibility of continuous production, which makes it suitable for large-scale production. Furthermore, the product is easier to handle because at the outlet of the extruder the shape can be adapted to the next processing step without grinding.[20]

6. Nanosuspension

Nanosuspension technology has been developed as a promising candidate for efficient delivery of hydrophobic drugs. This technology is applied to poorly soluble drugs that are insoluble in both water and oils. A pharmaceutical nanosuspension is a biphasic system consisting of nano sized drug particles stabilized by surfactants for either oral and topical use or parenteral and pulmonary administration. The particle size distribution of the solid particles in nanosuspensions is usually less than one micron with an average particle size ranging between 200 and 600nm.[25, 26]

Various methods utilized for preparation of nanosuspensions include precipitation technique, media milling, high pressure homogenization in water, high pressure homogenization in nonaqueous media, and combination of Precipitation and high-Pressure homogenization.[27, 28]

6.1. Precipitation Technique

In precipitation technique the drug is dissolved in a solvent, which is then added to anti solvent to precipitate the crystals. The basic advantage of precipitation technique is the use of simple and low cost equipments; but the challenge is the addition of the growing drug crystals to avoid formation of microparticles. The limitation of this precipitation technique is that the drug needs to be soluble in at least one solvent and this solvent needs to be miscible with antisolvent. Moreover, precipitation technique is not applicable to drugs, which are simultaneously poorly soluble in aqueous and nonaqueous media.[29] Nanosuspension of Danazol and Naproxen have been prepared by precipitation technique to improve their dissolution rate and oral bioavailability. The size reduction of naproxen was also associated with an apparent increase in the rate of absorption by approximately 4- fold.[30, 31]

6.2. Media Milling

The nanosuspensions are prepared by using high-shear media mills. The milling chamber

charged with milling media, water, drug, and stabilizer is rotated at a very high-shear rate under controlled temperatures for several days (at least 2–7 days). The milling medium is composed of glass, Zirconium oxide, or highly cross-linked polystyrene resin. High energy shear forces are generated as a result of the impaction of the milling media with the drug resulting into breaking of microparticulate drug to nanosized particles.[28]

6.3. High Pressure Homogenization

High-pressure homogenization has been used to prepare nanosuspension of many poorly water soluble drugs. In this method, the suspension of a drug and surfactant is forced under pressure through a nanosized aperture valve of a high pressure homogenizer. The principle of this method is based on cavitation in the aqueous phase. The cavitations forces within the particles are sufficiently high to convert the drug microparticles into nanoparticles. The concern with this method is the need for small sample particles before loading and the fact that many cycles of homogenization are required.[32] Dissolution rate and bioavailability of poorly soluble drugs such as spironolactone, budesonide, and omeprazole have been improved by reducing their particle size by high pressure homogenization.[33–35]

6.4. Combined Precipitation and Homogenization

The precipitated drug nanoparticles have a tendency to continue crystal growth to the size of microcrystals. They need to be processed with high- energy forces (homogenisation). They are in completely amorphous, partially amorphous or completely crystalline forms which create problems in long term stability as well as in bioavailability, so the precipitated particle suspension is subsequently homogenized which preserve the particle size obtained after the precipitation step.

7. Inclusion Complex

Formation-Based Techniques

Among all the solubility enhancement techniques, inclusion complex formation technique has been employed more precisely to improve the aqueous solubility, dissolution rate and bioavailability of poorly water soluble drugs. Inclusion complexes are formed by the insertion of the nonpolar molecule or the nonpolar region of one molecule (known as guest) into the cavity of another molecule or group of molecules (known as host). The most commonly used host molecules are cyclodextrins. The enzymatic degradation of starch by cyclodextrin-glycosyltransferase (CGT) produces cyclic oligomers, Cyclodextrins (CDs). These are nonreducing, crystalline, water soluble, and cyclic oligosaccharides consisting of

glucosemonomers arranged in a donut shaped ring having hydrophobic cavity and hydrophilic outer surface as illustrated in Figure 1. Three naturally occurring CDs are α-Cyclodextrin, β-Cyclodextrin, and γ-Cyclodextrin.[36] The surface of the cyclodextrin molecules makes them water soluble, but the hydrophobic cavity provides a microenvironment for appropriately sized non-polar molecules. Based on the structure and properties of drug molecule it can form 1 : 1 or 1 : 2 drug cyclodextrin complex as illustrated in Figure 1.. Various technologies adapted to prepare the inclusion complexes of poorly water soluble drugs with cyclodextrins are briefly described below.

9.1. Kneading Method

This method is based on impregnating the CDs with little amount of water or hydroalcoholic

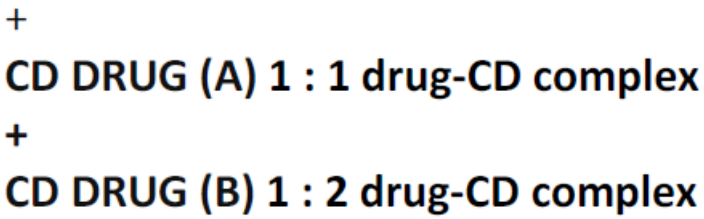


Figure 1: 1:1 and 1:2 drug cyclodextrin complexes solutions to convert into a paste.

The drug is then added to the above paste and kneaded for a specified time. The kneaded mixture is then dried and passed through a sieve if required. In laboratory scale, kneading can be achieved by using a mortar and pestle. In large scale, kneading canbe done by utilizing the extruders and other machines. This is the most common and simple method used to prepare the inclusion complexes and it presents very low cost of production.[38]

9.2. Lyophilization/Freeze-Drying Technique

In order to get a porous, amorphous powder with high degree of interaction between drug and CD, lyophilization/freeze drying technique is considered suitable. In this technique, the solvent system from the solution is eliminated through a primary freezing and subsequent drying of the solution containing both drug and CD at reduced pressure. Thermolabile substances can be successfully made into complex form by this method. The limitations of this technique is the use of specialized equipment, time consuming process, and yield poor flowing powdered product. Lyophilization/freeze drying technique is considered as an alternative to solvent evaporation and involve molecular mixing of drug and carrier in a common solvent.[39]

9.3. Microwave Irradiation Method

This technique involves the microwave irradiation reaction between drug and complexing agent using a microwave oven. The drug and CD in definite molar ratio are dissolved in a mixture of water and organic solvent in a specified proportion into a round bottom flask. The mixture is reacted for short time of about one to two minutes at 60◦C in the microwave oven. After the reaction completes, adequate amount of solvent mixture is added to the above reaction mixture to remove the residual uncomplexed free drug and CD. The precipitate so obtained is separated using what man filter paper, and dried in vacuum oven at 40◦C. Microwave irradiation method is a novel method for industrial scale preparation due to its major advantage of shorter reaction times and higher yield of the product.[40]

8. CONCLUSION

Dissolution of drug is the rate determining step for oral absorption of the poorly water soluble drugs and solubility is the basic requirement for the absorption of the drug from GIT. The various techniques described above alone or in combination can be used to enhance the solubility of the drugs. Proper selection of solubility enhancement method is the key to ensure the goals of a good formulation like good oral bioavailability, reduce frequency of dosing and better patient compliance combined with a low cost of production. Selection of method for solubility enhancement depends upon drug characteristics like solubility, chemical nature, melting point, absorption site, physical nature, pharmacokinetic behavior and so forth, dosage form requirement like tablet or capsule formulation, strength, immediate, or modified release and so forth, and regulatory requirements like maximum daily dose of any excipients and/or drug, approved excipients, analytical accuracy and so forth.

REFERENCES

1. L. Lachman, H. Lieberman, and J. L. Kanig, The Theory And Practise of Industrial Pharmacy, Lea & Febiger, 3rd edition, 1986.
2. M. Clugston and R. Fleming, Advanced Chemistry, Oxford Publishing, Oxford, UK, 1st edition, 2000.
3. P. B. Myrdal and S. H. Yalkowsky, “Solubilization of drugs in aqueousmedia,” in Encyclopedia of Pharmaceutical Technology, J. Swarbrick, Ed., p. 3311, InformaHealth Care, New York, NY, USA, , 3rd edition, 2007.
4. A. Martin, Solubility and Distribution Phenomena, Physical Pharmacy and Pharmaceutical Sciences, Lippincott Williams and Wilkins, 6th edition, 2011.

5. "IUPAC gold book," http://goldbook.iupac.org/S05740.html.
6. M. Aulton, "Dissolution and solubility," in Pharmaceutics: The Science of Dosage form Design, M. E. Aulton, Ed., p. 15, Churchill Livingstone, 2nd edition, 2002.
7. The United States Pharmacopeia, USP 30-NF 25, 2007.
8. British Pharmacopoeia, 2009.
9. G. L. Amidon, H. Lennern¨as, V. P. Shah, and J. R. Crison, "A theoretical basis for a biopharmaceutic drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability," Pharmaceutical Research, 1995; 12(3): 413–420.
10. S. R. K. Yellela, "Pharmaceutical technologies for enhancing oral bioavailability of poorly soluble drugs," Journal of Bioequivalence & Bioavailability, 2010; 2(2): 28–36.
11. K. H. Edward and D. Li, "Solubility," in Drug Like Properties: Concept, Structure, Design and Methods, from ADME to Toxicity Optimization, p. 56, Elsevier, 2008.
12. V. R. Vemula, V. Lagishetty, and S. Lingala, "Solubility enhancement techniques," International Journal of Pharmaceutical Sciences Review and Research, 2010; 5(1): 41–51.
13. D. Sharma, M. Soni, S. Kumar, and G. D. Gupta, "Solubility enhancement— eminent role in poorly soluble drugs," Research Journal of Pharmacy and Technology, 2009; 2(2): 220–224.
14. A. Kumar, S. K. Sahoo, K. Padhee, P. S. Kochar, A. Sathapathy, and N. Pathak, "Review on solubility enhancement techniques for hydrophobic drugs," Pharmacie Globale, 2011; 3(3): 001–007.
15. N. Blagden, M. de Matas, P. T. Gavan, and P. York, "Crystal engineering of active pharmaceutical ingredients to improve solubility and dissolution rates," Advanced Drug Delivery Reviews, 2007; 59(7): 617–630.
16. M. Vogt, K. Kunath, and J. B. Dressman, "Dissolution enhancement of fenofibrate by micronization, cogrinding and spray-drying: comparison with commercial preparations," European Journal of Pharmaceutics and Biopharmaceutics, 2008; 68(2): 283–288.
17. J. C. Chaumeil, "Micronization: a method of improving the bioavailability of poorly soluble drugs," Methods and Findings in Experimental and Clinical Pharmacology, 1998; 20(3): 211–215.
18. K. Sekiguchi and N. Obi, "Studies on absorption of eutectic mixtures. I.A. comparison of the behaviour of eutectic mixtures of sulphathiazole and that of ordinary sulphathiazole in man," Chemical and Pharmaceutical Bulletin, 1961; 9: 866– 872.
19. P. Gupta, V. K. Kakumanu, and A. K. Bansal, "Stability and solubility of celecoxib-PVP

amorphous dispersions: a molecular perspective," Pharmaceutical Research, 2004; 21(10): 1762–1769.

20. A. M. Abdul-Fattah and H. N. Bhargava, "Preparation and in vitro evaluation of solid dispersions of halofantrine," International Journal of Pharmaceutics, 2002; 235(1-2): 17–33.
21. S. Sinha, M. Ali, S. Baboota, A. Ahuja, A. Kumar, and J. Ali, "Solid dispersion as an approach for bioavailability enhancement of poorly water-soluble drug ritonavir," AAPS Pharm- SciTech, 2010; 11(2): 518–527.
22. W. L. Chiou and S. Riegelman, "Pharmaceutical applications of solid dispersion systems," Journal of Pharmaceutical Sciences, 1971; 60(9): 1281–1302.
23. T. Tachibana and A. Nakamura, "A methode for preparing an aqueous colloidal dispersion of organic materials by using water-soluble polymers: dispersion of β-carotene by polyvinylpyrrolidone," Colloid and Polymer Science, 1965; 203(2): 130–133.
24. "Nanosuspension drug delivery technology and application— nanotech— express pharma pulse.htm," http://www.expresspharmapulse. com/.
25. R. H. Muller, C. Jacobs, and O. Kayer, "Nanosuspensions for the formulation of poorly soluble drugs," in Pharmaceutical Emulsion and Suspension, F. Nielloud and G Marti-Mestres,Eds., pp. 383–407, Marcel Dekker, New York, NY, USA, 2000.
26. R. A. Nash, "Suspensions," in Encyclopedia of Pharmaceutical Technology, J. Swarbrick and J. C. Boylan, Eds., vol. 3, pp. 2045–3032, Marcel Dekker, New York, NY, USA, 2nd edition, 2002.
27. K. P. R. Chowdary and B. L. R. Madhavi, "Novel drug delivery technologies for insoluble drugs," Indian Drugs, 2005; 42(9): 557–564.
28. V. B. Patravale, A. A. Date, and R. M. Kulkarni, "Nanosuspensions: a promising drug delivery strategy," Journal of Pharmacy and Pharmacology, 2004; 56(7): 827–840.
29. R. H.Muller, B. H. L. Bohm, and J. Grau, "Nanosuspensions: a formulation approach for poorly soluble and poorly bioavailable drugs," in Handbook of Pharmaceutical Controlled Release Technology, D.Wise, Ed, 2000; 345–357.
30. E. Merisko-Liversidge, G. G. Liversidge, and E. R. Cooper, "Nanosizing: a formulation approach for poorly-watersoluble compounds," European Journal of Pharmaceutical Sciences, 2003; 18(2): 113–120.
31. G. G. Liversidge and P. Conzentino, "Drug particle size reduction for decreasing gastric irritancy and enhancing absorption of naproxen in rats," International Journal of Pharmaceutics, 1995; 125(2): 309–313.

32. C. M. Keck and R. H. M¨uller, “Drug nanocrystals of poorly soluble drugs produced by high pressure homogenisation,” European Journal of Pharmaceutics and Biopharmaceutics, 2006; 62(1): 3–16.
33. P. Langguth, A.Hanafy, D. Frenzel et al., “Nanosuspension formulations for low-soluble drugs: pharmacokinetic evaluation using spironolactone asmodel compound,”Drug Development and Industrial Pharmacy, 2005; 31(3): 319–329.
34. C. Jacobs and R. H. M¨uller, “Production and characterization of a budesonide nanosuspension for pulmonary administration,” Pharmaceutical Research, 2002; 19(2): 189–194.
35. J. M¨oschwitzer, G. Achleitner, H. Pomper, and R. H. M¨uller, “Development of an intravenously injectable chemically stable aqueous omeprazole formulation using nanosuspension technology,” European Journal of Pharmaceutics and Biopharmaceutics, 2004; 58(3): 615–619.
36. K. Uekama, F. Hirayama, and T. Irie, “Cyclodextrin drug carrier systems,” Chemical Reviews, 1998; 98(5): 2045–2076.
37. http://www.nature.com/nrd/journal/v3/n12/fig tab/nrd1576 F3.html.
38. R.K. Parikh, N. S. Mansuri, M. C. Gohel, and M.M. Soniwala, “Dissolution enhancement of nimesulide using complexation and salt formation techniques, ”Indian Drugs, 2005; 42(3): 149– 154.
39. F. Cao, J. Guo, and Q. Ping, “The physicochemical characteristics of freeze- dried scutellarin- cyclodextrin tetracomponent complexes,” Drug Development and Industrial Pharmacy, 2005; 31(8): 747–756.
40. X. Wen, F. Tan, Z. Jing, and Z. Liu, “Preparation and study the 1:2 inclusion complex of carvedilol with β- cyclodextrin,”Journal of Pharmaceutical and Biomedical Analysis, 2004; 34(3): 517– 523.

WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

EATING DISORDER

Nitish Kumar Singh[1], Dr. Hriom Sharma[2], Dr. Gaurav Kumar Sharma[3], Dr.Kaushal Kiashore Chandrul[4]

[1]STUDENT OF B. PHARMA(4TH YEAR),
[2]PROFESSOR (SUPERVISOR),
[3]H.O.D,
[4]PRINCIPLE
DEPAETMENT OF PHARMACY, MEWAR UNIVERSITY CHITTORGRH(RJ),INDIA

ABSTRACT

Serious mental health illnesses include eating disorders. They entail serious issues with your eating habits and food-related thoughts. You might consume far less or far more food than you require.

Eating disorders are not a choice of lifestyle; they are medical diseases. They interfere with your body's capacity to absorb healthy nutrients. Health complications, such as heart and renal problems, or occasionally even death, can result from this. However, there are remedies that can be helpful.

INTRODUCTION

Eating disorders are significant conditions caused by persistent eating patterns that have an adverse effect on your health, your emotions, and your capacity to carry out essential life functions. Anorexia nervosa, bulimia nervosa, and binge-eating disorder are the three most prevalent eating disorders.

The majority of eating disorders are characterised by an unhealthy obsession with food, body image, and weight. These actions can have a serious negative effect on your body's capacity to absorb the proper nutrients. Eating disorders can cause various ailments and affect the heart, gastrointestinal tract, bones, teeth, and mouth.

- Anorexia nervosa
- Bulimia nervosa
- Binge-eating disorder
- Rumination disorder
- Avoidant/restrictive food intake disorder

A psychological eating condition called bulimia causes episodes of binge eating (consuming a large quantity of food in one sitting). You don't feel like you have any control over your food during these binges. After that, you experiment with improper weight-loss methods like:

- Vomiting \sFasting \sEnemas
- excessive bowel movements and use of diuretics
- Obsessive exercise

Bulimia, which is also known as bulimia nervosa, typically begins in late adolescence or early adulthood. Typically, you binge and purge covertly. When you binge, you feel humiliated and ashamed, and when you purge, you feel relieved.

Bulimics typically weigh within the range for their height and age. But they could be quite unhappy with their bodies, fear gaining weight, and wish to lose it.

Anorexia nervosa

A potentially fatal eating disorder known as anorexia nervosa (an-o-REK-see-uh) is characterised by an unusually low body weight, a strong fear of gaining weight, and a skewed sense of weight or shape. Anorexics make tremendous efforts to maintain their weight and shape, which frequently adversely affects their health and daily activities.

When you have anorexia, you severely restrict your calorie intake or employ alternative weight-loss strategies, such as excessive exercise, the use of laxatives or other diet supplements, or vomiting right after eating. Possibly when you are overweight, dieting can have a serious negative impact on your health and even result in fatal self-starvation.

Bulimia nervosa

Bulimia nervosa, often known as bulimia, is a serious eating disorder that may be life-threatening. Bulimia causes binge-and-purge episodes where the person feels like they have no control over their food. The daytime eating restrictions that are common among bulimics frequently result in increased binge eating and purging.

During these episodes, you frequently consume a lot of food quickly and then try to burn off the excess calories in undesirable ways. You might force yourself to vomit, overexert yourself when working out, or use other techniques, like laxatives, to get rid of the calories out of fear of feeling guilty, ashamed, and gaining weight as a result of overeating.

If you have bulimia, you are likely obsessed with your weight and body image and may harshly and critically evaluate yourself for your perceived defects. You can be slightly overweight or at a typical weight.

Binge-eating disorder

With binge-eating disorder, you frequently overeat (binge) and experience a loss of control over your eating. Even when you are not hungry, you may eat rapidly or consume more food than you wanted to, and you may keep eating even after you feel uncomfortable.

Following a binge, you could feel bad about how much food you ate and how you acted. But unlike someone with bulimia or anorexia, you don't try to make up for this behaviour with excessive exercise or purging. Eating by yourself to disguise your bingeing can result from embarrassment.

The average person binges at least once every week. You can be of average weight, an overeater, or obese.

Rationing disorder

Repeatedly and persistently regurgitating food after eating is a symptom of rumination disorder, which is not related to a medical illness or another eating disorder such anorexia, bulimia, or binge-eating disorder. Without feeling queasy or gagging, food is brought back up into the mouth, and regurgitation may not be deliberate. Regurgitated food may occasionally be rechewed, reabsorbed, or spit out.

If the food is spit out or if the person eats much less to stop the behaviour, the problem may cause malnutrition. Rumination disorder may be more prevalent in young children or those who have an intellectual handicap.

Disorder of avoidant/restrictive eating

Due to lack of interest in food, avoidance of food with particular sensory qualities, such as colour, texture, smell, or taste, or worry about the results of eating, such as choking fear, you fail to achieve your basic daily nutritional requirements. Food is not eschewed out of concern for putting on weight.

In addition to substantial weight loss or failure to gain weight in childhood, the disease can lead to dietary deficiencies that may have negative health effects.

NEW RESEARCHES

- New research shows that exercise addiction is nearly four times more common amongst people with an eating disorder.

  These results demonstrate that atypical anorexia nervosa is a true illness and not merely a milder version of "pre-anorexia nervosa," continued Garber. "Even if patients were bigger to begin with and now seem "normal," paediatricians and other primary care providers need to keep a close check on patients who have lost a lot of weight quickly. These patients are just as sick as those who have the conventional anorexia nervosa diagnosis.
- Adolescents and young adults with anorexia nervosa whose weight is in the healthy, overweight or obese ranges face similar cardiovascular and other health complications as their counterparts with low body mass index (BMI), according to a new study led by researchers at UCSF.

Causes and Risk Factors

We don't know the exact cause of bulimia. But research suggests that a mixture of certain personality traits, emotions, and thinking patterns, as well as biological and environmental factors, might be responsible.

Researchers believe this eating disorder may begin with dissatisfaction with your body and extreme concern with your size and shape. Usually, you have low self-esteem and fear becoming overweight. The fact that bulimia tends to run in families also suggests that you might inherit a risk for the disorder.

Other danger signs consist of:

- being a woman
- diseases of anxiety and depression
- diseases caused by drug usage
- traumatic experiences
- Regular dieting under stress

Symptoms

The signs of bulimia can change from person to person. Both your physical appearance and your behaviour could alter. It can be more difficult to diagnose bulimia since, unlike the eating disorder anorexia, a person with bulimia might not lose a significant amount of weight.

Bulimia's physical symptoms can include:

- dental issues
- unwell throat
- enlarged glands in your face and neck
- bloating, indigestion, and heartburn
- irregular cycles
- Weakness, fatigue, and red eyes
- Having calluses on your hands' backs or knuckles as a result of making yourself sick

- frequently gaining and loosing weight. Although your weight is often within the acceptable range, you can be overweight.
- fainting or vertigo
- experiencing constant cold
- issues with sleep
- Dry skin and fragile, dry nails.

Complications

- tooth enamel erosion brought on by frequent contact to stomach acid
- cavities in the teeth and stained teeth
- sensitivity to hot or cold foods in the mouth
- gum diseases
- Your salivary glands are swollen and hurting (from repeated vomiting)
- throat pain and inflammation
- peptic ulcers
- stomach or oesophagus rupturing
- Changing your bowel routine
- Dehydration. Electrolyte imbalances, including those in particular minerals like calcium and potassium, might result from this. Low potassium or sodium levels can result in potentially fatal heart or renal issues. Seizures can also be brought on by abnormal blood sugar levels and abnormal electrolyte levels.
- abnormal heartbeat
- chest pain (in severe cases)
- Reduced sex drive
- heightened danger of committing suicide
- Self-harm, such as self-cutting
- abuse of drugs or alcohol
- Having gastroparesis, where your stomach absorbs

What kinds of eating problems are there?

Eating disorders frequently seen include:

Binge eating is uncontrollable eating. Even after they are full, many who suffer from binge eating disorder continue to eat. They frequently eat past the point of extreme discomfort. They typically experience remorse, shame, and distress afterward. Obesity and weight increase can result from overeating. The most prevalent eating disorder in the United States is binge-eating disorder.

Anorexia nervosa Periods of binge eating are also common in those who have bulimia nervosa. However, they then purge by forcing themselves to vomit or by using laxatives. They could also overwork themselves or fast. People who have bulimia nervosa could be overweight, average weight, or slightly underweight.

Nervosa anorexia. People who have anorexia nervosa skip food, restrict food excessively, or consume small quantities of only certain foods. They may see themselves as overweight, even when they are dangerously underweight. Anorexia nervosa is the least common of the three eating disorders, but it is often the most serious. It has the highest death rate of any mental disorder.

How are eating problems identified?

In light of how serious eating disorders may be, it is crucial to get assistance if you or a loved one suspects that there may be a problem. Your doctor may use a variety of instruments to make a diagnosis, including:

A medical history that asks about your symptoms is included. It's critical to be open with your provider about your food and activity habits so they can support you.

a medical checkup

To rule out additional potential reasons of your symptoms, get a blood or urine test.

other examinations to determine if your eating disorder is causing any more health issues. An electrocardiogram and tests for renal function are examples of these (EKG or ECG).

Treatment

Plans for treating eating disorders are personalised for each patient. A group of healthcare professionals, including doctors, nutritionists, nurses, and therapists, will probably be working with you. The therapies could consist of:

Psychotherapy for individuals, groups, or families. Cognitive behavioural techniques in individual therapy may be used to help you recognise and alter unfavourable ideas. You can also develop coping mechanisms and alter ing behavioural habits with its aid.

medical attention and supervision, including attention for potential side effects of eating disorders

counselling on nutrition. You can achieve and keep a healthy weight with the aid of doctors, nurses, and counsellors by eating a healthy diet.

Some eating disorders may be treated with drugs such mood stabilisers, antipsychotics, or antidepressants. The medications can also assist with the symptoms of despair and anxiety that frequently coexist with with eating disorders.

CONCLUSION

It's critical to address the patients' emotional and psychological demands in addition to their bodily ones when treating eating disorders. Pharmacists are in a perfect position to serve patients who need encouragement to seek and continue therapy. Common disorders like purging and binge eating indicate a variety of negative results. These diseases, which might be underrepresented in eating disorder clinic samples, should be made known to primary care practitioners. The focus of eating disorder prevention initiatives should be on subthreshold severity cases.

REFERENCES

1. https://www.sciencedaily.com/releases/2020/01/200128114642.htm
2. https://www.sciencedaily.com/releases/2019/11/191106130340.htm
3. https://www.webmd.com/mental-health/eating-disorders/bulimia-nervosa/mental-health-bulimia-nervosa
4. https://medlineplus.gov/eatingdisorders.html
5. https://www.everydayhealth.com/eating-disorders/all-articles.aspx
6. https://quillbot.com/
7. https://pubmed.ncbi.nlm.nih.gov/10363466/
8. https://pubmed.ncbi.nlm.nih.gov/22802602/
9. https://www.mayoclinic.org/diseases-conditions/eating-disorders/symptoms-causes/syc-20353603
10. https://pubmed.ncbi.nlm.nih.gov/9603723/
11. https://pubmed.ncbi.nlm.nih.gov/32252365/
12. https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-minute-eating-disorders-affect-all-genders-races/

A NOVEL METHOD FOR DEVICE-TO-DEVICE COMMUNICATIONS

Yahya Mohammed Ali Al-Naamani[1], Mr. Gaurav Sharma[1], Mr. Jitendra Vaswani[2]
Department of Electronics and Communication Engineering, Mewar university,
Chittorgarh, Rajasthan, India.

ABSTRACT:

D2D communications plays a major role in the 5G systems in order to increase the utilize the spectrum efficiently. By using this D2D communications more number of users can share a single range of spectrum by allocating the users to a cellular device. This process provides better results but care should be taken while allocating the resource to the cellular user. Hence, in the proposed method the resources are allocated to the cellular user by using the location and outage probability of the resources. This process is further extended by increasing the number of users in the cell and also by increasing the number of code words that need to be send to the user. This method provides better results when compared to state of art methods in increasing the throughput.

Keywords: Device to Device communications, outage probability.

I. INTRODUCTION:

To accommodate more users in cellular networks sustaining high spectral efficiency, the device-to-device (D2D) communication utilizing spectrum resources, which are already assigned to cellular devices, was introduced. Regarding D2D communications, the resource allocation has been mainly studied for D2D underlay cellular networks in various aspects, such as energy efficiency maximization with joint power control of devices and overall sum rate maximization for multiple D2D pairs, for D2D groups and for vehicle to everything networks. Content dissemination over congested D2D networks was studied from a perspective of medium access control layer where energy efficient strategies using game theory were developed.

Considering the interference between the ordinary cellular transmission and D2D multicast, CR is applied in D2D communications. Many studies have shown that the utilization of licensed spectrum is very low, and CR plays as a promising technology to improve the utilization of licensed spectrum. Secondary users (SUs) sense the spectrum conditions and seek to send their signals by reusing the spectrum of primary users (PUs), which can improve the spectrum utilization. In ordinary D2D communications, D2D users only utilize the temporally idle spectrum to avoid

collisions. It is naturally to think that D2D with CR function is able to improve the spectrum resource utilization more effectively than conventional D2D technology by dynamic establishment of the transmission links with the help of cognitive terminals. In this paper, we focus on multicast treated as a more general transmission mode, and investigate the resource allocation algorithm for cognitive D2D underlay multicast and cellular communications.

II. LITERATURE REVIEW:

L. Wang, H. Tang, H. Wu, and G. L. Stuber [4] studied on the D2D communications in order to allocate the resource to the cellular users. They focused mainly on the heterogeneous networks for reducing noise in which the lowest position consists of the D2D cells. They considered both uplink and downlink conditions. This process increases the performance by reducing the interference. They follow the concept of using the frequency again and again by following some conditions, density of the user, transmitter density, switching frequency. But the obtained results proved that the number of users allocated for the cellular users are reduced.

Antonopoulos and C. Verikoukis [7] performed their studies on the D2D communications They majorly concentrate on the sources which are active in nature. The main contribution of the paper is to minimize the lifetime of the battery and thereby reducing the energy consumption. They have designed a medium access control over the self-centered behavior of nodes. This process involves the best outcomes at each terminal which uses the energy efficiently.

They also studied on the gaming theory which deals with the conservation energy and data the action or fact of spreading something. They formed two type of strategies which forms an equilibrium points on the conserved energy and the data. They are using the ad-hoc networks and coordinating the data in between the cells. In this process they used network coding techniques in order to eliminate the control packets for transformation of data. Though this procedure produces better results in the simulation environment they do not produce the qualitative results in the real time environment.

III. EXISTING METHOD:

The exiting procedure is implemented based on the information obtained from the D2D user. The information may consist of full data or partial data. The full and partial is classified based on the location of the D2D user. The location or the distance of the user is considered as constant in partial data selection. Whereas the location is considered different in the full information data selection.

This allocation is based on the Hungarian algorithm. The Hungarian algorithm is explained in the following way:

The Hungarian algorithm:

The Hungarian algorithm is considered as the best algorithm for allocating the resource without any interference. This algorithm is explained in the step wise manner. In that the first two steps are determined and executed in as per the procedure then the next steps are repeated until the fine results are obtained. The condition is that the matrix on which the algorithm is applied should contain the non-negative numbers.

Step 1: Subtracting the row minima:

In the first step the procedure is to follow is to find the lowest value in the row of the matrix. Then remove this minimum value from all the rows.

Step 2: Subtracting column minima:

The second step also is same as the step in the above process. But in this process the minimum value is obtained from the column and to minimize this value from all the elements in the column.

Step 3: Covering all zeros with a minimum number of lines:

This procedure is implemented until all the lines that are rows and columns in the matrix should be zero free. If this size of matrix is enough to next process, then we stop the process here otherwise the fourth step will start.

Step 4: Creating additional zeros:

In this step the element which is very small is obtained then again the same procedure is carried on until required size if the matrix is obtained to continue the next process.

Then based on the power allocation and the number of transmitting antennas the effective throughput is calculated.

Drawbacks of existing method:

1. Minimum number of cellular users and D2D users are considered with consideration of less transmission area.
2. The throughput is less thereby the interference may increase.

IV. PROPOSED METHOD:

The heuristic dynamic clustering method of [16] is constructed based on the above mentioned procedure. By using this algorithm all the D2D users are divided into different inner cells in the way such that where the interference is less. Let us consider L are the total number of D2D users. The total number of cellular users can be indicated as the D. Each D2D user is equipped with the cellular user and uses the channel by using the reuse concept. The concept of

frequency reuse is used in the way of utilizing the spectrum effectively.

In order to reduce the optimization problem, this Hungarian algorithm is utilized in the better way for the D2D user allocation and channel allocation.

The proposed method is clearly explained in the following block diagram:

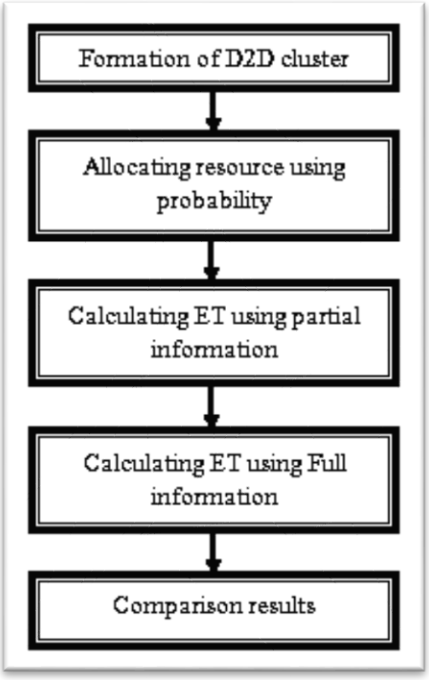


Figure 3: Block Diagram of the Proposed Method

Methodology:

- In the proposed method the number of inner cells are increased.
- By increasing this inner cells, the more number of D2D users can be allocated.
- The cellular users are also increased in the same cell radius.
- The code words which are used to transmit the data from transmitter and receiver without interference are also increased.
- This process involves the Hungarian algorithm for resource allocation.
- This process involves the parameters like power allocation for calculating the throughput.

4. Advantages of proposed method:

1. The sum efficient throughput (ET) is maximized through the cellular link which guarantees a certain level of Qos.
2. As the number of DRxs supported by D2DC grows, the proposed system becomes very efficient.
3. Higher max sum ET is provided because it allows higher transmit power of DTxs.

5. Applications:

- In 5G networks.
- D2D communications regarding public safety applications such as search and rescue missions, coverage extension, and road safety. In search and rescue missions, discovery of devices in impacted areas can be achieved by other devices that have access to the cellular network.

- One of the most valid applications of D2D communication is Mission critical application. The possibility of network may be narrow or non-existent. D2D communication will permit users to link the nearest devices and collaborates each other even if there is no mobile network.
- For Smart Clouds and Low Power Mesh Networking, D2D communication can be enabled in IoT applications.

RESULTS

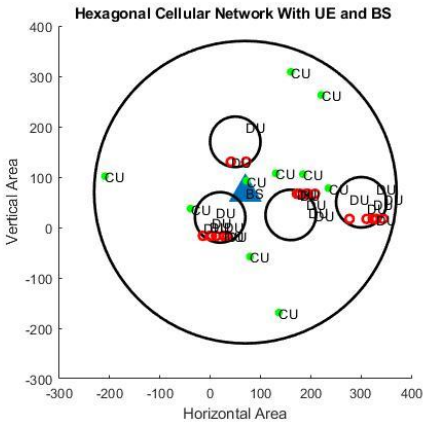


Figure 1: Cellular networks

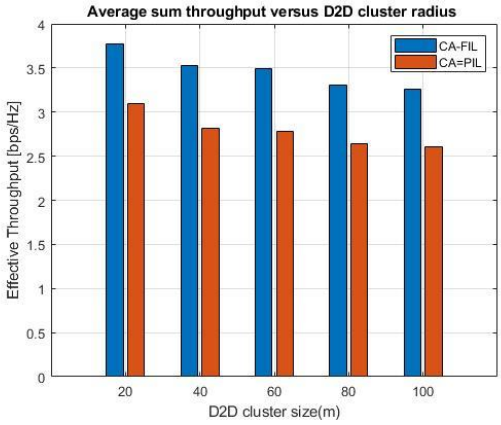


Figure 2: Average sum throughput versus D2D Cluster radius

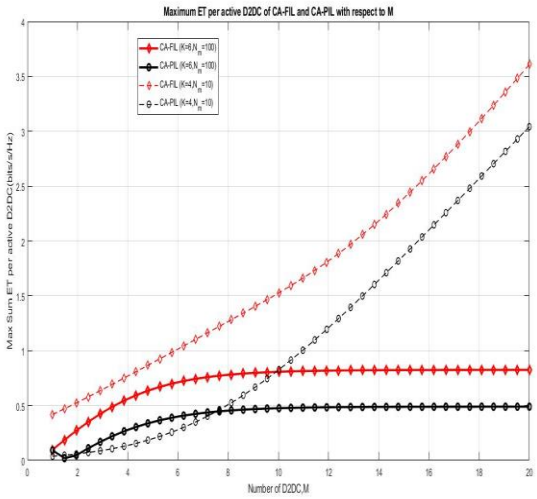


Figure 3: Maximum ET per active D2DC of CA-FIL and CA-PIL with respect to M.

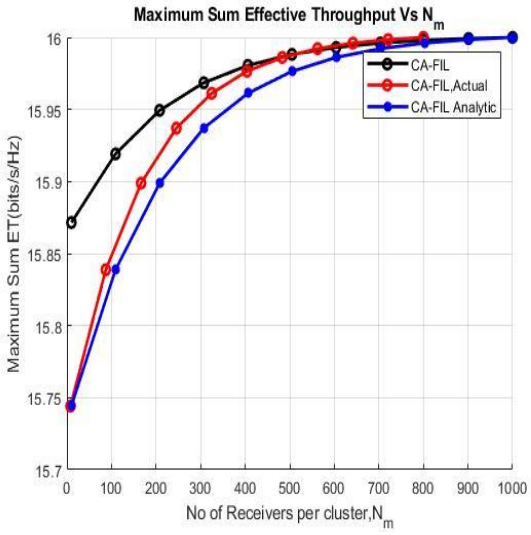


Figure 4: Maximum sum effective throughput Vs Nm

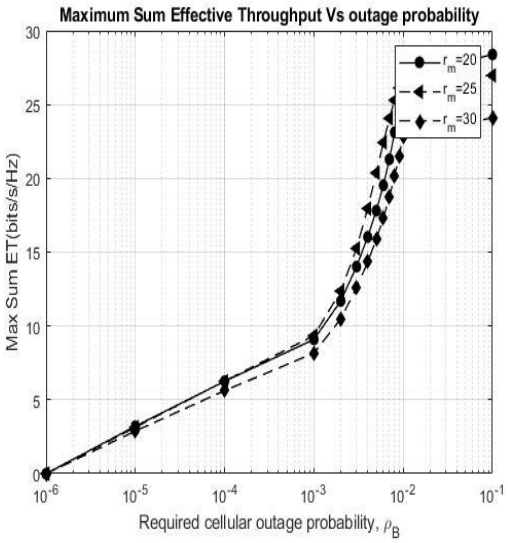


Figure 5: Maximum Sum effective throughput Vs Outage probability.

CONCLUSION

Hence, the proposed scheme intimates that the increment in the number of cellular users in the base station transmission area may increase the throughput of the D2D users.

REFERENCES

[1] K.Doppler, M.Rinne, C.Wijting, C.B.Ribeiro and K.Hugl, "Device-to- Device Communication as an underlay to LTE – advanced networks," IEEE Commun. Mag., vol.47, No12, pp. 42-forty nine Dec. 2009

[2] J. Hu, W. Heng, X. Li, and J. Wu, "Energy-efficient resource reuse scheme for D2D Communications under lying celluar networks, " IEEE Commun. Lett. Vol.21, no.Nine, pp. 2097-2100, Sep. 2017.

[3] T.-P. Low, M.-O. Pun, Y.-W. Hong, and C.-C. J. Kuo, ``Optimized oppor-tunistic multicast scheduling (OMS) over wi-fi mobile networks," IEEE Trans. Wireless Commun., vol. 9, no. 2, pp. 791 801, Feb. 2010.

[4] G. Araniti, M. Condoluci, L. Militano, and A. Iera, ``Adaptive resource allocation to multicast offerings in LTE structures," IEEE Trans. Broadcast., vol. Fifty nine, no. Four, pp. 658 664, Dec. 2013.

[5] J. Liu, N. Kato, J. Ma, and N. Kadowaki, ``Device-to-device communication in LTE-superior networks: A survey," IEEE Commun. Surv. Tuts., vol. 17, no. 4, pp. 1923 1940, 4th Quart., 2015.

[6] A. Asadi, Q. Wang, and V. Mancuso, ``A survey on device-to-device communication in mobile networks," IEEE Commun. Surveys Tuts., vol. Sixteen, no. 4, pp. 1801 1819, 4th Quart., 2014.

[7] S. Andreev, A. Pyattaev, K. Johnsson, O. Galinina, and Y. Kouch-eryavy, ``Cellular visitors of reordering into network-assisted device-to-tool connections," IEEE Commun. Mag., vol. Fifty two, no. 4, pp. 20 31, Apr. 2014.

[8] Y. Pan, C. Pan, H. Zhu, Q. Z. Ahmed, M. Chen, and J. Wang, ``On attention of content preference and sharing willingness in D2D assisted of reodering," IEEE J. Sel. Areas Commun., vol. 35, no. Four, pp. 978 993, 2017.

[9] J. Liu, Y. Kawamoto, H. Nishiyama, N. Kato, and N. Kadowaki, ``Device-to-tool communications gain efficient load balancing in

LTE-advanced network," IEEE Wireless Commun., vol. 21, no. 2,57 65, Apr. 2014.

[10] L. Militano, M. Condoluci, G. Araniti, A. Molinaro, A. Iera, and G. M. Muntean, ``Single frequency-based totally device-to-tool-enhanced video shipping for advanced multimedia broadcast and multicast services," IEEE Trans. Broadcast., vol. Sixty one, no. 2, pp. 263 278, Jun. 2015.

Design and Implementation of Smart Room

Article · May 2020

DOI: 10.22214/ijraset.2020.5327

1 author:

Muhammad Ibrahim
Mewar University
1 PUBLICATION **0** CITATIONS

SEE PROFILE

iJRASET
International Journal For Research in Applied Science and Engineering Technology

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 8 **Issue:** V **Month of publication:** May 2020

DOI: http://doi.org/10.22214/ijraset.2020.5327

www.ijraset.com

Call: 08813907089 | E-mail ID: ijraset@gmail.com

International Journal for Research in Applied Science & Engineering Technology (IJRASET)
ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.429
Volume 8 Issue V May 2020- Available at www.ijraset.com

Design and Implementation of Smart Room

Muhammad Ibrahim Zubair[1], Ritesh Kumar Ojha[2], Abbati Muhammad Ado[3]
[1, 3]*Post Graduate Scholar,* [2]*Assistant Professor, Electronics and Communication Engineering Department, Mewar University, Chittorgarh, India.*

Abstract: ***Our modern life today is simply over dependent on technology and its application. The cornerstone of such development in industrial and commercial sectors of our life is the automation process as a field of modern technology. This paper concerns on commercial residential application of automation technique to design and implement advanced conventional room known as smart room using Arduino UNO as the main microcontroller board .Smart room incorporates room appliances control automation wirelessly using HC-05 Bluetooth module and android application; automatic security alarm system involving buzzer; and a real time weather status display via 16x2 LCD using DHT11 sensor. The user controls all room appliances and also display temperature and humidly status on the LCD by sending numerical character from his Smartphone Bluetooth terminal to the microcontroller wirelessly, furthermore the security system works automatically upon detecting an intruder.***

Keywords: Arduino Uno, LCD, Smart phone, HC-05 Bluetooth module, Sensor

I. INTRODUCTION

Room appliances Automation; security of our rooms; and whether status information; remain vital to our daily day-to-day activities. Elderly and handicapped people find it tedious or are not able to move frequently for controlling room appliances such as: fans, bulbs, television etc. Intruders and thieves continue to invade our rooms, unknowingly to us and as a result we lost our properties, belongings and peaceful mind of a secured room when we are outside our rooms. Similarly, we often look through our windows each morning to understand the weather status which would enable us to know the cloth we will wear, where shall we visit and what we will do over the day etc. With the advancement of technology and our over dependence on our smart mobile phones, The smart room technology will be a much needed extension of our conventional rooms to contains all needs mentioned and to cater for many problem that do affect our residence. Over the years different technologies have evolved for smart room technology implementation among which are: Bluetooth, WIFI and ZigBee for communication purposes and different devices such as: smart phones, laptops etc controlling various appliances. This paper designs and implements smart room using Bluetooth technology and is economically low cost for easier implementation.

II. LITERARUTE REVIEW

In [1] the research paper designs and implement smart home, it consists of an android application which would send control signal via ESP8266 WIFI module to an Arduino microcontroller for automating and controlling of accessories using relay board. [2] The paper presented home automation system (HAS).

Bluetooth HC-05 module was used to establish the communication purposes. Android Application sends signal or voice command to Arduino to control up to four appliances using 4-channel relay board. [3], the paper employs IOT technology; it implemented home automation and home security technique. ESP8268 WIFI module and other sensors are interface with Arduino, the sensors read the condition of the home appliances and upload it to a cloud platform so that user can access it. The microcontroller provided the control.

[4] Home automation and security ware discussed and implemented using GSM module, Arduino and Android application. A counter displays the number of people entering the home on LCD, in automation mode, appliances are turned on/off depends upon if a person is available in the home while in security mode, light and an alarm are turned and SMS message alert is sent upon detecting intruder. Similarly, Smartphone application can be use by residence for appliances automation. [5] Home Automation of appliances cantered on Arduino UNO as the main controller was designed and implemented, features include water level indication using ultrasonic detector and plant irrigation system monitoring using soil moisture detector was used. Bluetooth module HC-06 was used.

[6] The author demonstrated home automation of appliances over the internet as channel of communication. It employs raspberry microcontroller as a server and upon receiving control signal from Smartphone application from any place, it activates the operation of relay to an appliance.

III. PROPOSED DESIGN

From the literature review above, most of the design concern only about automation of appliances in homes and employs WIFI module which relatively is cost high and difficult in implementation, require expertise to handle and monitor, and problem of network connectivity would always remain a setback. The design here gives expansion upon automation of appliances to add intelligent security system and real time weather status in a room and it involves Bluetooth which is easier in implementation than WIFI module and better cost economic.

The figure below shows the block diagram of Smart Room Technology:

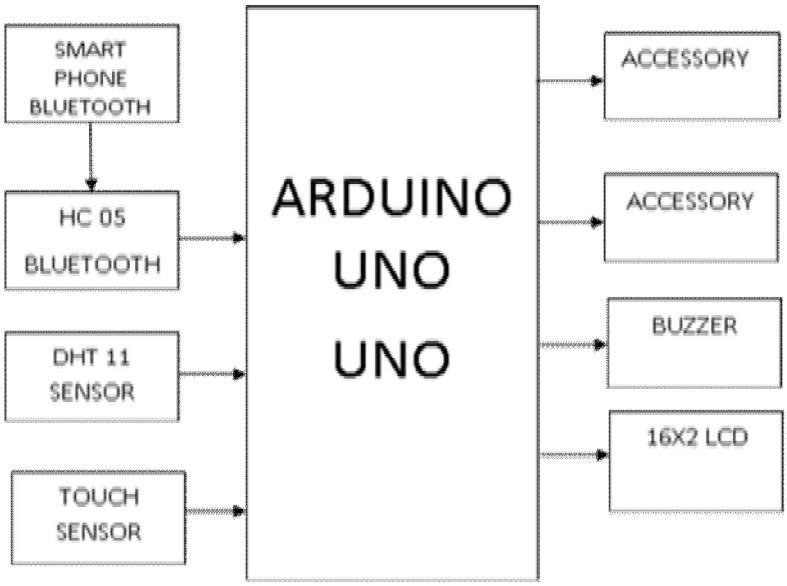


Figure 1: Block Diagram of Smart Room

IV. COMPONENTS AND SPECIFICATIONS

A. *Hardware Used*

1) *Arduino Uno Board:* This is an open source general purpose microcontroller board based on ATMEGA 328 Microcontroller. The board has 14 digital input/output pins, six analog inputs pins, programmable using Arduino UNO IDE and can be powered through USB port or External 7v to 20v power adaptor. The board however can be used in extension with other boards for some applications. The board has other technical specification and other pins of different application.

Figure 2: Arduino Uno

2) *Hc-05 Bluetooth Module:* This is manufactured for wireless communication, it is based on IEEE8802.15.1 standard protocol, through which one can build wireless personal area network. It uses frequency-hopping spread spectrum radio technology to send data. This module can be used in a master and slave configuration. It has 6 pins: Key/EN ;VCC ;GND ;TXD ;RXD and STATE. Similarly, the module has RED LED to show connection status, before user device is connected, the light blinks fast and continuously, after the device is connected it slows down to blink slowly. HC 05 operates on 3.3V voltage supply but can work with 5V supply since it has in-build voltage regulator. Default baud rate is 38400bps.

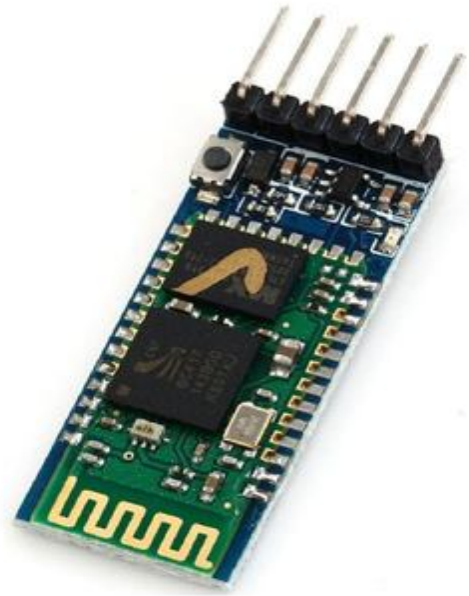


Figure 3: HC-05 Bluetooth module

3) *16x2 LCD:* Liquid crystal display (LCD) is very popular in embedded and IOT projects because of its cheapness, availability and easily to be programmed for display of an image or characters on its flat screen. LCD does not produce their own light rather depends on some reflectors to produce image in a single color. It is named 16x2 because it has 16 columns and 2 rows meaning it can contain 16*2=32 images or characters in total and each is made of 5x8 pixel dots.

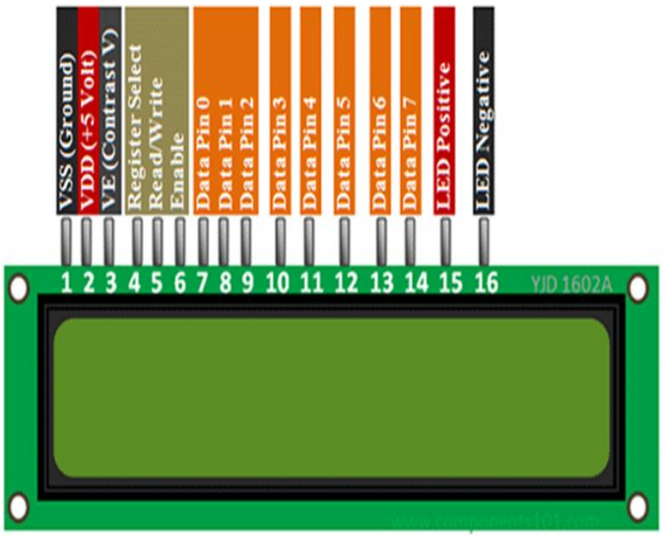


Figure 4: 16x2 LCD Pin Descriptions and Specification[7]

4) *DHT11* Sensor: This consists mainly of resistive humidity measurement component and negative temperature coefficient component. It is a single wire humidity and temperature detector that produce fully calibrated digital humidity and temperature values output serially with a single wire protocol. The sensor is manufactured in a single row of 3 0r 4 pins package and operates from 3.5v to 5.5v supply. It measures temperature range of 0-50^{0}C with an accuracy of +2^{0}C% and humidity ranging from 20-90% with an accuracy of 5%.

Figure 5: DHT11 Sensor

5) *Touch Sensor:* Also known as tactile sensor, it is mostly a proximity sensor reduced to lowest distance. Touch sensors are used to detect and sense touch, they operate as a closed switch upon touched. They perform action similar to human being's skin.

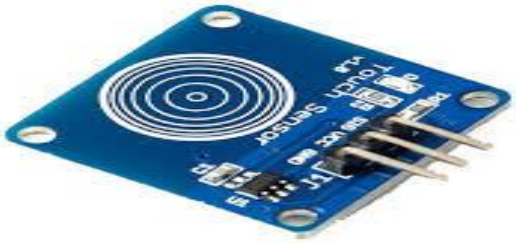


Figure 6: Touch sensor

6) *Relay Module:* This is designed for mostly microcontroller such as Arduino UNO board, PIC, etc. Relay is an electrically operated switch that is used to control or operate both AC and DC output devices upon receiving a pulse signal. A channel relay module has six pins: VCC (+5V), GND, Digital input, normally closed and normally open. The relay output is always connected to normally closed pin, upon receiving pulse it got triggered to normally open.

Figure 7: relay module

V. SOFTWARE ARCHITECTURE

The microcontroller was programmed in an open source ARDUINO UNO IDE, the programmed was written as a sketch and uploaded to the Arduino UNO board. The detail algorithm is below:

A. Automation and Weather status Display Algorithms

1) *Input:* Character "KEY" from android application
2) *Output:* Status of pin
a) Initialize input and output pins
b) If serial available, read and store it in to variable "KEY"
c) Switch "KEY"
d) Case "1": switch ON first accessory
e) Case"2": switch OFF first accessory
f) Case"3": switch ON second accessory
g) Case"4": switch OFF second accessory
h) Case"0": display weather status information on LCD
i) End

B. Automatic security Program Algorithms

1) *Input:* character "INPUTVAL" from android application
2) *Output:* status of pin
a) Initialize input and output pins
b) Declare character ALARM VALUE
c) Analog read input quantity and stores in "INPUTVAL"
d) If INPUTVAL is greater than ALARMVALUE, Set output pin HIGH
e) If INPUTVAL is less than ALARMVALUE, Set output pin LOW
f) Repeat continuously

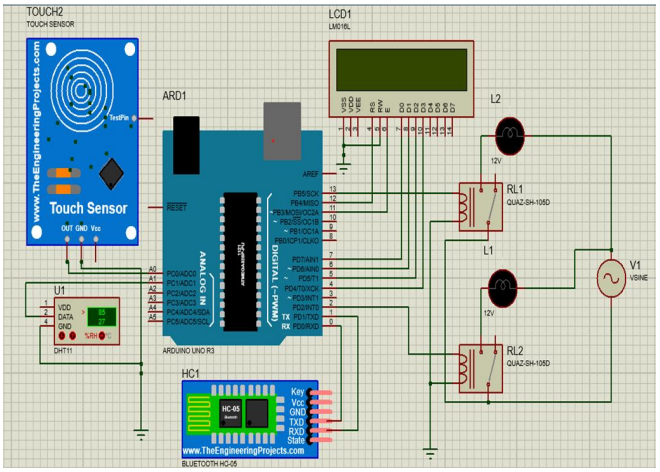


Figure 8: Circuit Diagram

VI. RESULTS

The proposed plan of this paper leads to its real implementation and all the goals required of the smart room was observed and tested. Excellent communication between our smart phone android application and Arduino UNO was obtained first, the accessories were then fully controlled independently and simultaneously by sending the right numerical command also the LCD displayed the real time weather status information on the LCD by sending the appropriate command. Finally, the security system was tested, the touch sensor was touched and buzzer alarm sound was heard. The system is very important for Room residence, economic friendly and easily implemented.

VII. CONCLUSION

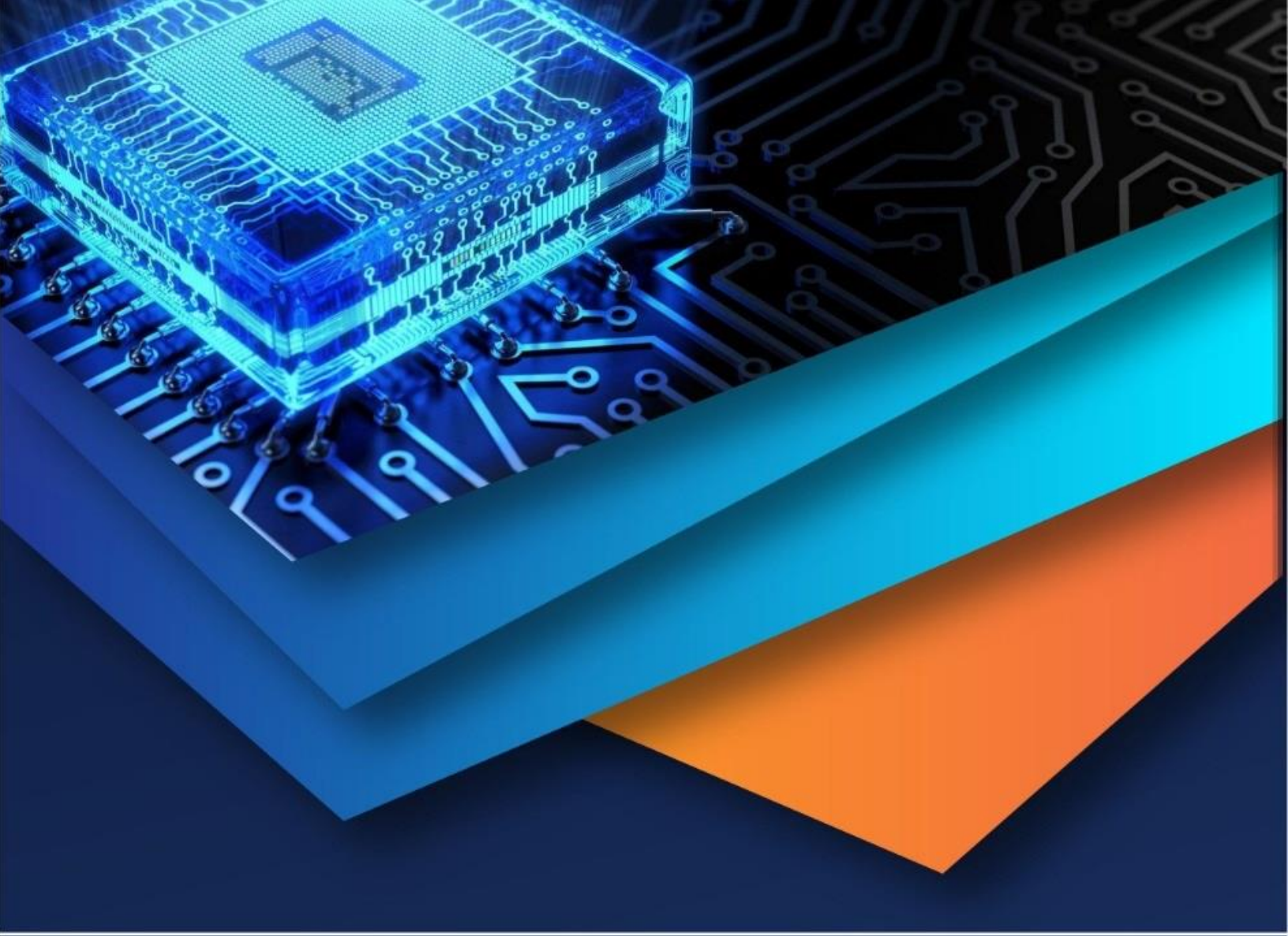
Smart room is an advance extension of commercial room to make life very comport for its residence. In the paper, design of smart room was discussed along with a block diagram and all hardware and software ware discussed appropriately. The system was also implemented and tested and it comprises of room accessories automation, security system and real time weather status display. The Bluetooth module provides the communication channel between the smart phone application and Arduino UNO microcontroller. The project demonstrated the high objective of energy saving needs, cost effectiveness and easily programmed, implemented and maintained.

VIII. ACKNOWLEDGMENT

The research was supported by department of electronics and communication, Mewar University of Rajasthan and presented at the university's EXPO fest competition. we are grateful to Mr. Ritesh ojha for supervising and assisting the project to its completion.
We are also thankful to our colleagues Gurzal, Auwal, Abubakar and Aliyu for their support and encouragement.
Lastly, my deepest appreciation to the head of department Mr. Gaurav for sharing his wisdom, support and making sure the department provided all the needful of the project.

REFERENCES

[1] H.B.Shinde, 312222Abhay Chaudhari, Prafull Chaure, Mayur Chandgude and Pratik Waghmare (2017) " Smart Home Automation System using Android Application" International Research Journal of Engineering and Technology (IRJET) Apr -2017 Volume: 04 Issue: 04, Pp:2408- 2411
[2] Sheetal Prusty (2017) "ARDUINO BASED HOME AUTOMATION USING ANDROID APPLICATION" International journal of Intelligent Computing and Applied Sciences, ISSN (Print): 2322-0031, Vol. 5, Issue 1, 2017, Pp:23-26
[3] Siddharth Wadhwani, Uday Singh, Prakarsh Singh and Shraddha Dwivedi "Smart Home Automation and Security System using Arduino and IOT" International Research Journal of Engineering and Technology (IRJET), e-ISSN: 2395-0056 Volume: 05 Issue: 02, Feb-2018, Pp 1357-1359
[4] Surinder Kaur, Rashmi Singh, Neha Khairwal and Pratyk Jain "HOME AUTOMATION AND SECURITY SYSTEM" Advanced Computational Intelligence: An International Journal (ACII), Vol.3, No.3, July 2016.Pp 17-23.
[5] Muhammad Asadullah and Khalil Ullah 2017 "Smart Home Automation System Using Bluetooth Technology"
[6] Himani Singh Dhami, Nidhi Chandra and Nishank Srivastava. "International Journal of Advance Research, Ideas and Innovations in Technology" ISSN: 2454-132X. Volume:03, Issue:02, 2017. Pp:521-525
[7] https://components101.com/16x2-lcd-pinout-datashee



10.22214/IJRASET

45.98

IMPACT FACTOR: 7.129

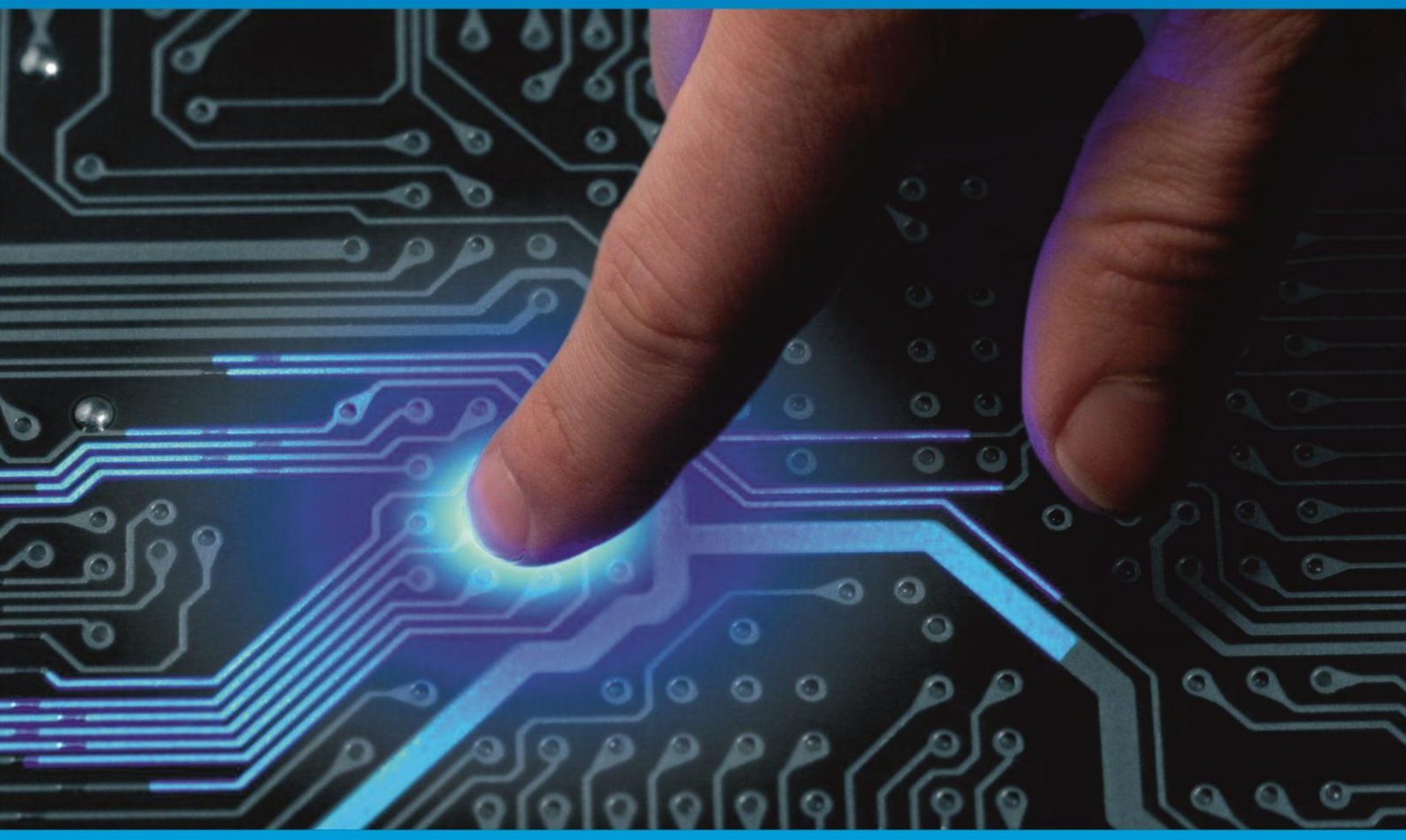
IMPACT FACTOR: 7.429

INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

IJIRCCE

e-ISSN: 2320-9801 | p-ISSN: 2320-9798



INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH

IN COMPUTER & COMMUNICATION ENGINEERING

Volume 8, Issue 11, November 2020

INTERNATIONAL STANDARD SERIAL NUMBER INDIA

Impact Factor: 7.488

International Journal of Innovative Research in Computer and Communication Engineering

| e-ISSN: 2320-9801, p-ISSN: 2320-9798| www.ijircce.com | Impact Factor: 7.488 |

|| Volume 8, Issue 11, November 2020 ||

An Optimized Dual Band Highly Miniaturized Patch Antenna

Ankush Saraswat[1] , Gaurav Sharma[2]

Research Scholar, M.Tech, Mewar University, Chittorgarh, Rajasthan, India

Assistant Professor, Mewar University, Chittorgarh, Rajasthan, India

ABSTRACT: Wireless communication technology is the greatest discovery in advanced modern communication systems in human history. Information between one or more devices requires any physical media. This system efficiently transmits information in the form of radio waves on its antenna system. Modern technological systems like cellular satellites and missile applications have low demands due to their small size, light weight, performance and easy installation. Microstrip patch antenna is a thin antenna, which has many advantages over other antennas. They have the ability to integrate with microwave circuits, so they are very suitable for many applications such as cellular equipment, WLAN applications, navigation systems and so on. It is light and cheap, and electronic products like LNA can be easily integrated with these antennas.

I. INTRODUCTION

An antenna is a type of transducer that converts electrical energy into radio waves (electromagnetic energy) and vice versa. The antenna is used as an electromagnetic wave transmitter or an electromagnetic wave receiver. According to the IEEE standard, "antenna is considered as a means of transmitting and receiving radio waves" [1]. All wireless communication systems that need to be small or portable require antennas that are not bulky and take up less space.

In the public and commercial sector, the latest trend in communications systems is to develop a small, inexpensive, lightweight and compact antenna that can maintain high performance over a wide frequency range. This development has focused a lot of technical energy on the design of microstrip patch antennas. A patch antenna with a simple structure has many advantages over other antennas. For example, they are very light, simple, low profiles and cost effective when manufactured using printed circuit board technology and are compatible with flat and non-planar surfaces [2]. The design changes of the microstrip antenna may exceed any other type of antenna.

However, microstrip patch antennas also have many disadvantages. Some of their main disadvantages are low gain, narrow bandwidth and surface wave excitation with excitation radiation efficiency. To overcome the narrow bandwidth, various methods have been used [3]. A substrate with a low dielectric constant or a thick ferrite composition can provide a wider bandwidth, but the first method does not lead to a low profile design, and the second solution is expensive. The bandwidth of the antenna can be improved by a tight / aperture coupling method, but the manufacturing process is difficult for this technology. The bandwidth can also be improved using a stacked multi-resonator configuration, but it has a larger thickness prototype [4,5]. The electromagnetic band gap design has been used to reduce the surface wave of the antenna. To achieve a high-gain antenna, a number of patch elements are used [2].

II. DEVELOPMENT OF MICROSTRIP PATCH ANTENNA

The microstrip patch antenna (MPA) was first proposed by Deschamps [7] in 1953. Received a patent in France in 1955 under the name Baissinot and Gutton [8]. However, the first actual implementation was completed by Howell [9] and Munson [10] in the early 1970s. In the 1970s, its development accelerated due to the availability of good dielectric substrates. During this time frame, two MPA feeding methods were developed: edge feeding plastics and probe feeding plastics.

Research and development of MPA technology continued until the 1980s. The main contribution comes from the defense industry in the form of direct R&D or grants. Researchers have tried to increase the bandwidth of microstrip antennas. To overcome these limitations, two important methods of voltage for the antenna have been introduced: essentially capacitive aperture coupling supply and proximity coupling plasters. In the 1980s [11], some complex software tools and integrated equation techniques were established. These methods can calculate the antenna more accurately.

| e-ISSN: 2320-9801, p-ISSN: 2320-9798| www.ijircce.com | Impact Factor: 7.488 |

|| Volume 8, Issue 11, November 2020 ||

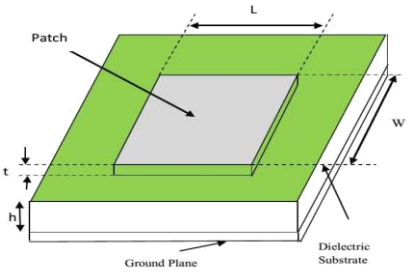


Fig.1- Basic structure of a microstrip patch antenna

ADVANTAGES OF MICROSTRIP PATCH ANTENNA

MPA has many advantages over conventional microwave antennas. The basic benefits are rarely mentioned below.

• They are light, compact and small.
• They can be kept in shape on the host's surface.
• The ease of mass production using printed circuit board technology reduces production costs.

OBJECTIVE

The purpose of this work is to design a dual band patch antenna with different services. By inserting slits or slits in the radiation or ground plane to design a reduced or compact microstrip antenna. Since patch antenna generally show low bandwidth, research has been conducted into the increase in bandwidth. The enhancement of microstrip antennas is also being investigated and some patch antenna with increased gains has been designed. This work also implements multi-frequency operation. Some designs have been developed with the combination of compactness, improved gain and multi-frequency operation. Finally, the use of dual patch antennas in the medical field is being investigated.

III. METHODOLOGY

The dual band patch antenna has a very high antenna quality factor (Q). Q represents the loss associated with the antenna, while a large Q leads to narrow bandwidth and low efficiency. Q can be reduced by increasing the thickness of the dielectric substrate. But as the thickness increases, more and more of the total power that the source delivers enters the surface wave. The contribution of this surface wave can be counted as useless power loss because it eventually propagates in the bend of the dielectric and causes the antenna properties to decrease. As discussed by Qian et al. however, surface waves can be minimized by means of photonic band gap structures. By using the array configuration for the element, other problems can be overcome, such as lower gain and lower power handling function.

IV. PROPOSED SYSTEM

In this work designed a highly miniaturized dual patch antenna. U-shaped grooves are designed on the ground to achieve maximum return loss. By using coaxial feed, the highest performance can be achieved for the designed antenna. A substrate with a dielectric constant of 4.4, which is FR4 material. Finally find the right of return, radiation pattern, VSWR and bandwidth. Simulation using HFSS.13 (High Frequency Structure Simulator)One of the potential uses of WiMAX is to cover the so-called "last mile" (or "last mile") area, which means offering high-speed Internet access to areas that cannot be covered by standard wired technology (such as DSL, cable or dedicated T1). One possibility is to use WiMAX as a backhaul between two local wireless networks (such as wireless local area networks using the WiFi standard). WiMAX will eventually allow two different hotspots to be linked to create a mesh network. This article introduces WLAN broadband antennas and worldwide interoperability for microwave access (WiMAX) applications covering 2.4 / 5.2 / 5.8 GHz WLAN operating frequency bands and 2.5 / 3.5 / 5.5 -GHz WiMAX frequency band. The proposed printed antenna is based on a 1.6 mm thick FR4 epoxy substrate with a size of 25 mm £ 38 mm. It has a rectangular open ring groove enclosed in a rectangular patch. And part of the ground plane will resonate at the other two frequencies. The dimensions of the patch, ground and two slots are optimized to achieve the required functional frequency range. This article proposes a new type of tri-band antenna suitable for WLAN / WiMAX applications. Using the split groove implanted in the rectangular patch and the local ground plane etched by the U-shaped groove, three resonant states with excellent impedance performance can be realized. The compact size, triple band frequency, excellent radiation pattern, good gain and simple structure make this antenna suitable for three different frequency bands 2.4 {2.5, 3 {4, 5.2 {5.9 GHz.}

➢ **Proposed design**

- Length and width of the substrate:**14mm*14mm**
- Substrate material: **FR4**

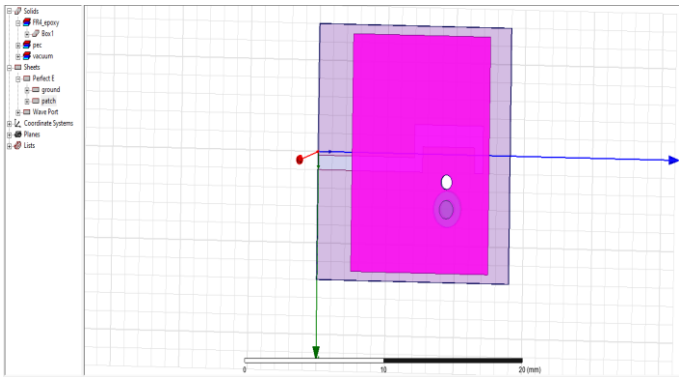


Fig.2 The patch antenna geometry (a) top view,

Fig. 2 shows the proposed patch antenna geometry and the detailed dimensions are listed in Table I. The proposed antenna is simply a patch antenna miniaturized using a shorting post close to the feeding position and a novel DGS. The dual-band property is achieved by etching a U-slot in the ground. As the current goes to the ground through the shorting post, this makes the ground part of the antenna. The patch antenna is fed with an SMA connector acting as a feeding probe at its edge. The antenna is fabricated on a double sided Rogers RO4350 substrate with dielectric constant of 3.48, loss tangent of 0.004 and thickness of 0.76 mm. The total antenna size along with its GND plane is 18.8mm by 20mm by 0.76mm which represents an ESA at 2.45 GHz even when the circle surrounds all the substrate. The radius a of the circle is 13.86 mm so that ka = 0.7 < 1.

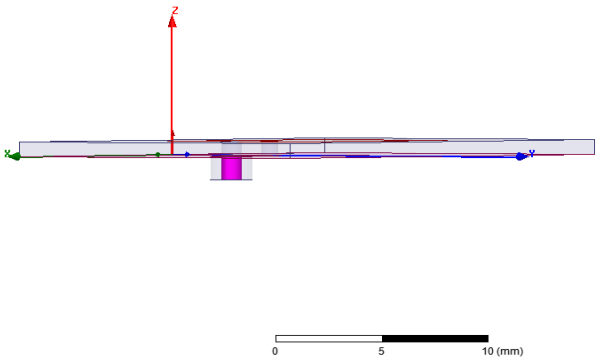


Fig. 3 The patch antenna geometry ,side view,

The proposed patch antenna was modeled, optimized and simulated using HFSSTM (version 15). Fig. 3 show the proposed patch antenna current distributions at 2.43 and 5.2 GHz, respectively. At 2.43 GHz, the highest current intensity traces two of the patch edges. Although the U-slot is etched on the ground, it affects the current on the patch. As the current go around the U-slot position in the ground, its electrical length increases thus explaining the miniaturization rule of the DGS. The current path length is found to be 32 mm which is approximately λ/4. At 5.2 GHz, the current is over two edges of the patch and in the ground is surrounding the DGS. The current path is approximately 23 mm which corresponds to about λ/2

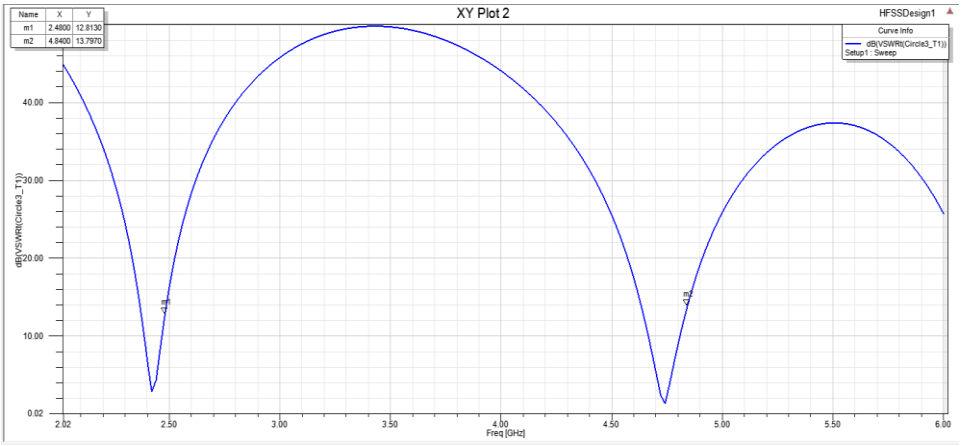


Fig4 radiation pattern

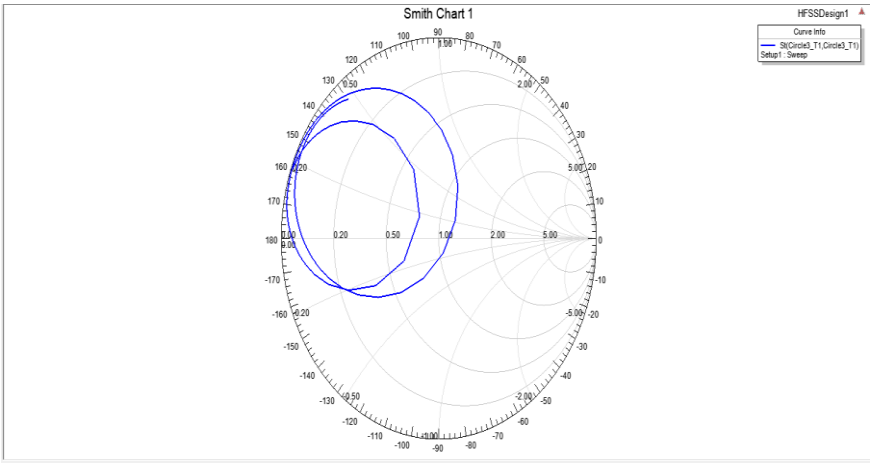


Fig 5 smith chart

V. CONCLUSIONS

It has been proven that the proposed antenna is a highly dual-band patch antenna, and the same antenna can be used in two dimensions. Due to the simple design of the design, the antenna is designed to be easier to design. Compared to other state-of-the-art antennas, the proposed antenna shows high antenna gain and high bandwidth. Finally, the antenna is designed to show better radiation patterns, better return losses and lower VSWR characteristics. Because two suitable dielectric requirements are required moreover, the thickness of the antenna increases. In research, there are always more aspects that can be investigated than what is presented. Here also, there are some aspects of both the new antenna and parameter calculation that can be extended. The new designed presented in this thesis open up the scopes for high gain, wide band and miniaturized microstrip patch antennas for wireless applications. The controlling tools like slot length, width, angle can be further exploited to achieve tunable parameters of micros trip patch antenna

REFERENCES

1. Jian Wang Wei-Bing Lu Zheng-Guo Liu A Hybrid Graphene-Metal IFA Antenna with Dynamically Tunable Operating Frequency at Microwave Freauencies 2018 IEEE International Conference on Computational Electromagnetics (ICCEM) Year: 2018 ISBN: 978-1-5386-1241-5 DOI: 10.1109/ IEEE Chengdu, China
2. Yu-Ze Jiang Lin-Sheng Wu Bin Xia Jun-Fa Mao Dual-Band Fabry-Perot Resonator Antenna Based on Hybrid Graphene-Metal Structure 2019 IEEE Asia-Pacific Microwave Conference (APMC) Year: 2019 ISBN: 978-1-7281- DOI: 10.1109/ IEEE : Singapore, Singapore, Singapore3517-5
3. Huang Yong Wang Wenjie Zhu Tianting Lai Jiankun Peng Dajuan Lyu Donglai Guo Yinquan Yuan Elfed Lewis Minghong Yang Graphene–Gold–Au@Ag NPs-PDMS Films Coated Fiber Optic for Refracti ve Index and Temperature Sensing IEEE Photonics Technology LettersYear: 2019 | ISSN: 1041-1135ve DOI: 10.1109/: IEEE

| e-ISSN: 2320-9801, p-ISSN: 2320-9798| www.ijircce.com | Impact Factor: 7.488 |

|| Volume 8, Issue 11, November 2020 ||

4. Junyi Ren Shuxi Gong Wen Jiang Low-RCS Monopolar Patch Antenna Based on a Dual-Ring Metamaterial Absorber IEEE Antennas and Wireless Propagation Letters Year: 2018DOI: 10.1109/ IEEE
5. Miroslav J. Veljovic Anja K. Skrivervik Patch Antenna System for CubeSats in L band 2019 13th European Conference on Antennas and Propagation (EuCAP) Year: 2019ISBN: 978-88-907018-8-7 IEEE Krakow, Poland, Poland
6. Sayeed Sajal Saeed I. Latif Edmund Spencer Circularly Polarized Small-Footprint Hybrid Ring-Patch Stacked Antenna for Pico-Satellites 2018 IEEE International Symposium on Antennas and Propagation & USNC/URSI National Radio Science Meeting Year: 2018 ISBN: 978-1-5386-7102-3 DOI: 10.1109/ IEEE Boston, MA, USA
7. M. Y. Mat Zain M. T. Ali A. N. H. Hussin B. Baharom 2.4GHz Patch Antenna on Bio-Composite Substrate Using Quarter Wave Transmission Line 2018 International Symposium on Antennas and Propagation (ISAP) Year: 2018 ISBN: 978-89-5708-304-8 IEEE Busan, Korea (South), Korea (South)
8. Neng-Wu Liu Lei Zhu Wai-Wa Choi Jin-Dong Zhang A Low-Profile Differentially Fed Microstrip Patch Antenna With Broad Impedance Bandwidth Under Triple-Mode Resonance IEEE Antennas and Wireless Propagation Letters Year: 2018 DOI: 10.1109/ IEEE
9. Hong-Wei Yu Yong-Chang Jiao Complementary Magneto-Electric Coupling Feeding Methods for Low-Profile High-Isolation Dual-Polarized Microstrip Patch Antenna 2019 International Symposium on Antennas and Propagation (ISAP) Year: 2019 ISBN: 978-7-9009-1404-0 Publisher: IEEE Xi'an, China, China

INNO SPACE

SJIF Scientific Journal Impact Factor

Impact Factor:
7.488

ISSN INTERNATIONAL STANDARD SERIAL NUMBER INDIA

निस्केयर NISCAIR

INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH

IN COMPUTER & COMMUNICATION ENGINEERING

9940 572 462 6381 907 438 ijircce@gmail.com

www.ijircce.com

Scan to save the contact details