ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

# A REVIEW ON NOVEL CORONA-VIRUS AND ITS TREATMENT THERAPIES

**Yogita Ale[1], Mansi Butola[1], Bikash Gupta[2*], Nitish Chib[2,] Amandeep Singh[3]**
[1]Assistant Professor, Dev Bhoomi Institute of Pharmacy & Research, Dehradun.
[2]Research Scholars, Dev Bhoomi Institute of Pharmacy & Research, Dehradun
[3] Professor, Dev Bhoomi Institute of Pharmacy & Research, Dehradun

**ABSTRACT**
The objective of this study is to review a current goal of all the researchers to look in-forward. As per the all-current research no accurate treatment out-there but since from the date SARS-COV-2 is declared as a Pandemic the use of Re-purposed drug as per the clinical data have proven effective in some case but It's not a permanent treatment to treat. Researchers are dealing to find the permanent regimen to treat the Covid-19 by developing a vaccine which are in different phases. This Review has an Eagle Eye on the treatment used to treat the SARS-COV-2 since from the starting. It contains the information on structure of Covid-19, lethality along with the description of re-purposed drug with its mechanism and the efficacy as per data and the vaccines which are currently approved till date and are employed for the treatment globally.
**Keywords:** SARS-COV-2, Covid-19, Pandemic, Re-purposed drugs, vaccine, Lethality.

## INTRODUCTION

### PANDEMIC INTRODUTION

This 21st century has faced various disease since from starting as we humans are facing till date. This is not the very first time that we humans have heard the term Corona-virus. Corona virus is mainly associated with the Respiratory Diseases may be of Acute respiratory disease or may be severe respiratory disease. Since in this 2 decade corona-virus took many more life by its disasteous out-break , starting from 2002 it made its approach on human very first time and been named as the Severe Acute Respiratory Syndrome (SARS or SARS-COV-1), it out-break in China very first time ,later on after the decade in 2012 we human heard about the Middle East Respiratory Syndrome (MERS ) which is also a respiratory disorder that out-break in Middle East Region and made its threat in humans.**{1}** And now recently in 2019, again Corona-virus in the name of SARS-COV-2 which is a Nobel Corona-virus we are facing has made a globally threat and being registered as Pandemic globally ( i.e. in many Countries and Territories respectively ). Or we can saythis is the third time in a just 2 Decade we are attacked by Corona-virus earlier in 2002 by SARS-COV , 2012 by MERS and now 2019 originated SARS-COV-2. . COVID-19 is declare as a Pandemic on 11 March 2020 by W.H.O. SARS-COV-2 name was given by Int. Committee on Taxonomy of Virus.

- Nidovirus
  a. Ronivirus
  b. Arteriviridae
  c. Coronaviridae
     i. Torovirinae
     ii. Coronavirinae

Corona-virus actually belong to *CoronaViridae* family which is divided in subfamily *Coronavirinae* which is further classified as into Alpha , Beta , Gamma and Delta corona-virus which are mainly affecting respiratory disease as like of SARS & MERS **{2,3 }** in which 229E Alpha Corona-virus , 0C43 Beta Corona-Virus , NL63 alpha Corona-Virus and HKU1 Beta Corona-virus cause mild clinical symptoms in infected patient **{ 4}.**

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

**STRUCTURE OF SARS-COV-2:**

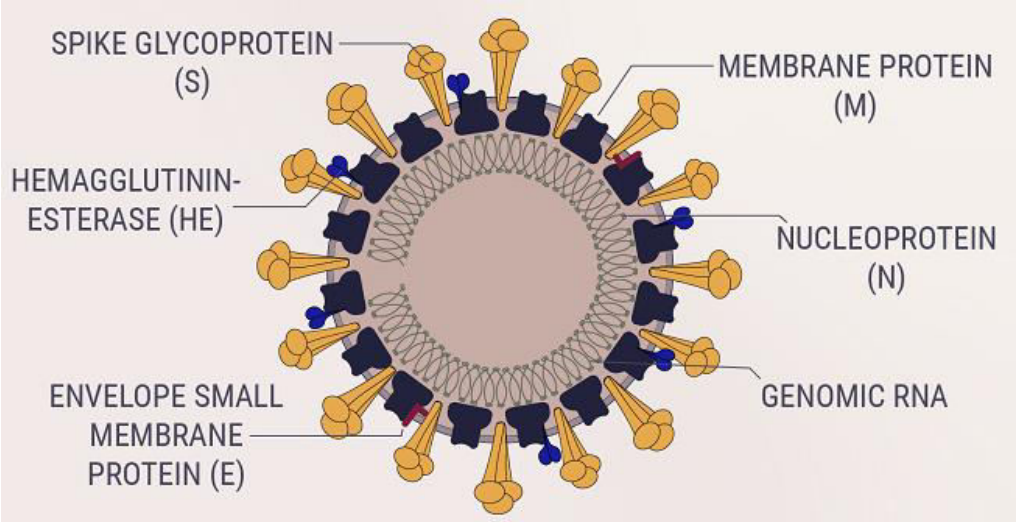



**Figure. 1**

The Severe Acute Respiratory Syndrome Corona-virus 2 (SARS-COV-2) is a novel corona-virus that is newly identified. It is a Retro-Virus with spikes resembling *CROWN* in its surface (through which its name is been resembled or given by researchers). The name Corona-Virus is given by International Committee on Taxonomy of viruses. **{2,3,4}** . This corona-virus has made a global threat to public health hence a result W.H.O. made a global health emergency on 31$^{st}$ of January of very next year, i.e. 2020 .

Corona-virus are Positive-sense RNA un-segmented, single, stranded RNA Genome around 30kB , enclosed by a 5'-cap and 3'-poly (A) tail . These virus are encircled with an envelope containing viral nucleocapsid. The nucleocapsids in Corona-Virus are arranged in helical symmetry resembling positive (+ve) sense virus mainly affecting to humans in a range from Common-Cold to more severe respiratory disease like SARS and MERS did in 2002 & 2012 respectively. The emerging SARS-COV-2 making its disastrous Mortality rate ever in any of pandemic that we human race have faced till date.

Corona-virus encodes 4 structural proteins like:

1. Spikes(S)
2. Membrane(M)
3. Envelope (E)
4. Nucleocapsid (N)

**a) Spikes Glycoprotein (S):** Corona virus S protein is a large , multifunctional class 1 viral transmembrane protein . The size of this S- protein ranges in terms of amino-acids from 1160 amino-acids (IBV Infectious Bronchitis Virus) to 1400 amino-acids (feline corona-virus). It is basically present on the surface which provides a *Crown like resemblance* or can say appearance and hence providing its name as ' A Corona-Virus '. It mainly function for entry of virus into the cell while attachment with the host receptors **{1}**

**b) Membrane Protein ( M) :**The M protein is the most abundant viral protein in the virion particle which provides a round shape to virus envelope . It majorly binds to the host cell ; M structure is diversed amino-acid having amino group at outer-side where as carboxy group at inner-side of virion .

**c) Envelope ( E ) :**The corona-virus E protein is the most mysterious and smaller in all structural protein which plays a major and multi-role in pathogenesis, assembly and release of virus . It is a small integral membrane poly-peptide that acts as a viro-porin (ion channel ) . The E protein consists of 3 domain that are a short hydrophilic amino terminal, a large hydrophobic trans-membrane domain and an efficient C-Terminal domain. Since, SARS-COV-2 has similar arrangement without any substitution.

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

d) **Nucleo-capsid ( N-protein ) :**N-protein is one of the vital organ of the virion since it plays a vital role in virion mechanism like of genetic coding takes place here , also initiate M-protein in viral assembly formation. It majorly contain 3 domain that is NTD , Linkers Region (LKR ) or RNA binding domain and a CTD . The Linker region is responsible for interaction/approach with in-vitro RNA interaction and is directly responsible for Cell-Signaling . It also play an important role in antagonizing the activity of Anti-viral interaction and RNA interference . Since SARS-COV-2 have extra amino-acid two in Intrinsically Dispersed Region ( IDR ) one each in NTD ,LKR and CTD .

e) **Nsp and accessory protein:** SARS-COV-2 also contain 15 nsps along with main structural protein i.e. nsp-1 to nsp-10 and nsp-12 to nsp-16 and around 8 accessory protein ( 3a, 3b, p6 , 7a , 7b ,8b , 9b and ORF 14 ) where it lacks 8a protein . { **1** }

**CLASSIFICATION OF PHASES OF SEVERITY OF SARS-COV-19 DISEASE ON THE BASIS OF SYMPTOMS:**

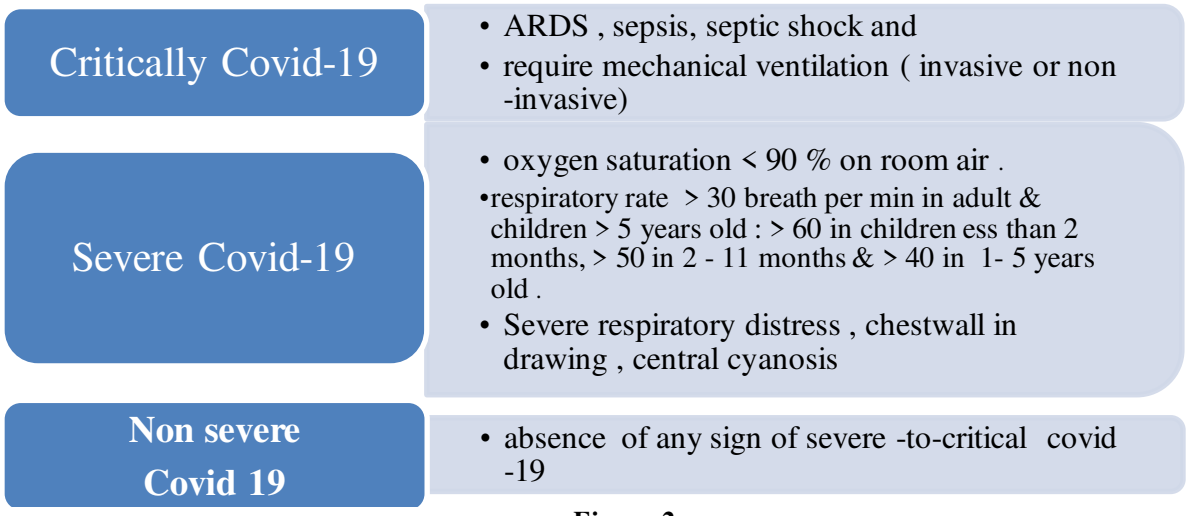



**Figure. 2**

**ORIGIN OF THE CORONA-VIRUS:**

This corona-virus which is in its dead-least form have emerged from Wuhan City of Hubai Province of People Republic Of China in 2019. Wuhan city has started to report the increment in a Severe Pneumonial cases suddenly and which have been reported in different hospitals. Upon on diagnostic report suggest about the new strain of Corona-Virus which started to spraed in nerby district and soon in the entire nation. Therefore, the first case officially reported in China in 2019 **{ 6 }** and the various report suggest the origination from the sea-foods from the nearby market in Wuhan City **{5}.**Very interesting to know that the report suggest that the genome of SARS-COV-2 is quite similar to with bat COV-RaTG13 of about 96.2% and as well similarities with SARS-COV-1 by 79.5% . Along with the report suggest that SARS-COV-1 as one of the ancestor of SARS-COV-2 and the natural host of this deadly SARS-COV-2 may be BAT through it transmission to human cause the spread **{8}.**

Mainly the virus is transmitted by in form of nasal droplets , oral droplets , close contacts and also the environment loaded with huge concentration of virion by infected patient ( when patient sneeze or cough in open environment without use of conopy/cover/mask ).

**LETHALITY AND TRANSMISSION " ZOONOTICS"**

Spike of a corona-virus plays a key role in attachment of a virion to the host cell. It's Spike protein mainly has two domain namely S1 and S2 Domain. Initial step starts from binding of spike protein with Receptor Binding protein(RBD) of Host (i.e ACE-2). S1 binds with receptor where as S2 facilitate the fusion of virion in host cell . In the late 2019 , a huge number of Pneumonial cases were reported in Wuhan Provience , China's hospital . The Human-To-Human transmission was rapidly started to spread and causing severe Pneumonial like condition in the patient , mostly patient were having the problem in lower respiratory tract as similar is seen in MERS ( Middle East Respiratory Syndrome )**{1}**

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

**MECHANISM OF CONJUGATION**

I. Entry of Virus though droplet in nasal region.
II. Attachment of virion to the ACE-2 receptor which is co-aided by TMPRSS-2.
III. SARS-COV-2 down regulate the activities of ACE-2 .

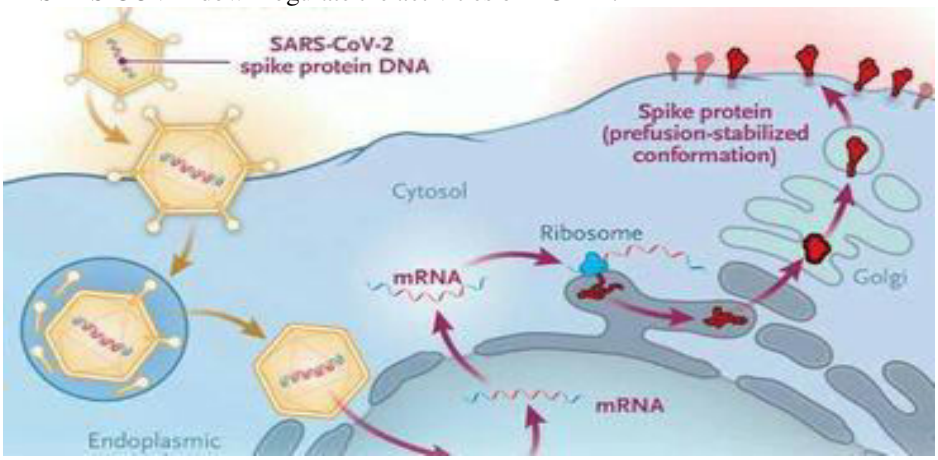
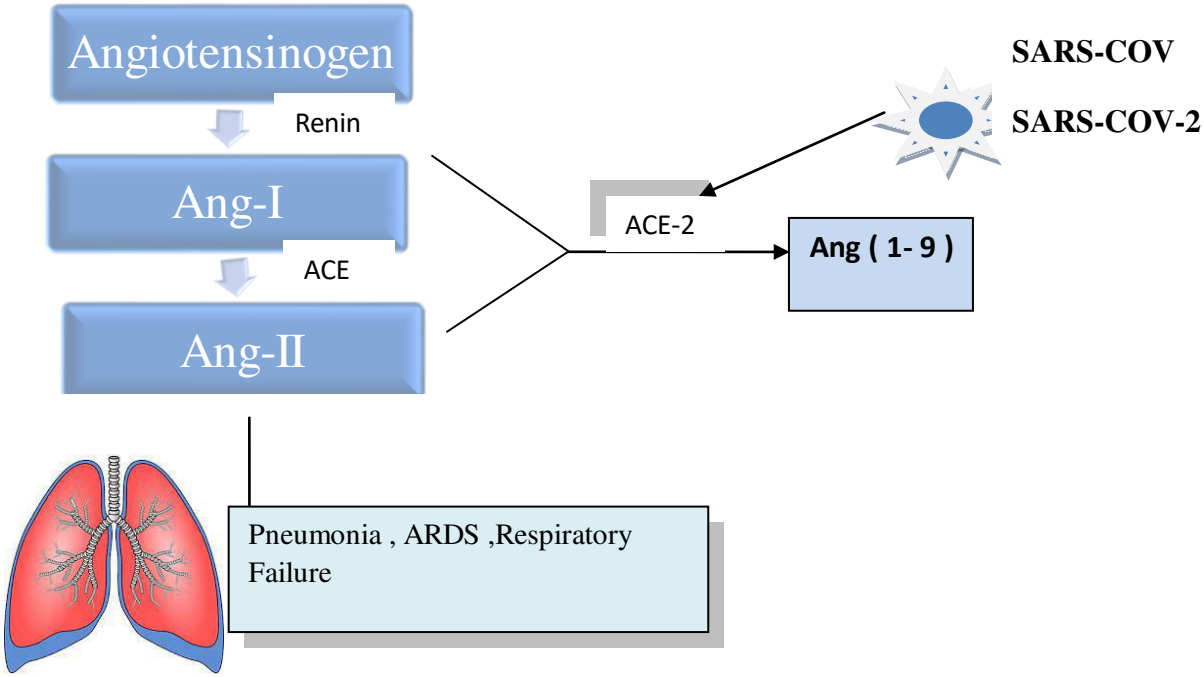



**Figure. 3**

IV. Which increase the amount of Ang-II which cause pulmonary fibrillation , emphysema , acute lung.
V. SARS-COV-2 activate the immune response which further facilitate the Cytokine Storm



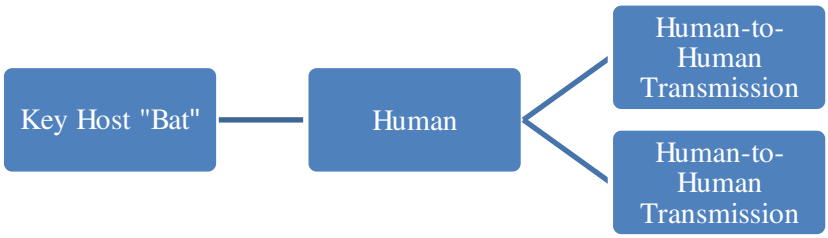




**Figure. 4**

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

Mainly the virus is transmitted by in form of nasal droplets , oral droplets , close contacts and also the environment loaded with huge concentration of virion by infected patient ( when patient sneeze or cough in open environment without use of conopy/cover/mask ).

**CURRENT RE-PURPOSED MEDICATION INVOLVE WITHIN THE TREATMENT OF COVID-19**

Millions of people have lost their life due to of SARS-COV-2 from late 2019's to 2021 up-to date.Covid-19 has spread globally to 219 countries. To treat out the out-break various Re-purposed drugs have been employed as per their clinical response whether they kill the virion or they decrease the severity **{ 9 , 10 ,14 }.**

**1. HYDROXY-CHLOROQUINE ( HCQ ) AND CHLOROQUINE ( CQ )**

HCQ and CQ are both 4- aminoquinoline derivatives with having similar chemical structure and quite similar mode of actions. CQ is available in salt-form of phosphate where as HCQ is present in the form of Sulphate, the absorption window ( i.e. main site of absorption ) of CQ and HCQ is upper-intestinal tract. HCQ is been named as Drug of Choice (DoC) and also been used in Rheumatoid arthritis (R.A.) **{ 4, 10 }**

**MODE OF ACTION:**

CQ and HCQ binds with the ACE-2 receptor which prevent the binding of Virion to the receptor of host cell. It increase the pH of acidic cellulase organelles which ultimately prevent endocytosis which inhibit the post viral RNA synthesis and virion transport. It also block viral protein synthesis and virion assembly (protease inhibitor) **{12}.** HCQ also down-regulate the pro-inflammatory cytokines namely IL-1 , IL-6 , Interferons ( INF-α and INF-Y ) ,Tumor Necrosis factor (TNF ), β-cell Activating Factor ( BAFA ) which intern down-regulate auto-antigen presentation ( i.e. MHC-II ) , T-cell activation , differentiation and expression of co-stimulatory molecule ( CD-154 ) and release of Cytokine **{ 11 }.**

In a randomized clinical trial (RCT), suggest the dose of dose 500mg bid , 15 days were work efficiently and **}** where as an another study of low dose (450 mg bid for 1 day followed by 450mg , 4 day ) and high dose ( 600mg bid ,10 day ) in a combination with AZM & OTV ( Oseltamavir ) were in-effective and induce mortality **{27 }.** And unfortunately , FDA issued Emergency Use Authorization (EUA ) for CQ and HCQ against COVID-19 on March 28, 2020 and revoked on June 15 ,2020 due to many side-effects **{9}.**

Side-effects seen associated with CQ and HCQ were , vomiting , diarrhoea and abdominal discomfort and majorly cause Cardio-toxicity , myopathy and Ratinopathy . As in cardio-toxicity ,it prolong the QT interval as it blocks blocks the Potassium (K+ ) ion channel and cause Ventricular repolarization and prolongs the QT interval and leads to Torsade-de-points resulting ventricular Trachycardia **{11,13}**

**2. LOPINAVIR / RITONAVIR**

Lopinavir/Ritonavir is mainly an approved anti-viral drugs that mainly target the HIV PROTEASE i.e Protease Inhibitor(P.I.). Ritonavir potentiate the activity of Lopinavir during combination. On a trial , many clinician were doing the use/employment of Lopinavir/Ritonavir for treatment of Covid-19. Consequently it shows that the trial didn't shown or failed to any improvement for the patient receiving the Lopinavir/ritonavir **{15}** Infact , Lopinavir were given in combination with Ribavirin ($C_8H_{12}N_4O_5$ ) shows the positive effect on diagnosis both early and later in course of Lopinavir/Ritonavir with Ribavirin (RBV), INF-α shows no clinical response.

LPV/RTV shows adverse gastro-intestinal effects such as Diarrhoea , Nausea and vomiting , QT prolongation and Torsade-de-point in some patients . Therefore, it made difficult to suggest the employment of LPV/RTV as an anti-covid drug rather than anti-retroviral drug **{9}**

Currently, 74 clinical trials have been registered for LPV/RTV for COVID-19 up-to the date of 25 July, 2021 (**ClinicalTrials.gov)**

**3. REMEDESIVIR ( RDV )**

Remedesivir is a Pro-drug of an Adenosine Tri-phosphate (ATP) analog. Remedesivir was developed by Gilead sciences with $70 M in U.S. Government Funding.

**Mode of action:** Remedesivir is either it terminate or inhibit RNA Transcription. Remedesivir which is a RNA dependent RNA polymerase (RdRp ) inhibitor result in termination of replication resulting in decrease in viral manufacturing **{28 }** It was basically clinically approved for Ebola Virus. It's active metabolite was effective against Yellow Fever , Dengue virus Type-2 , influenza A ,Para-influenza and Delta-CoVs and also shows the activity against α-CoV, MERS-CoV and Delta-CoVs.**{9 }**

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

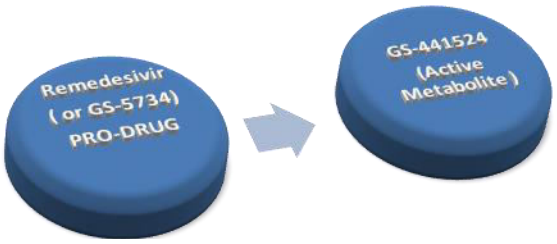



**Figure. 5**

Remedesivir is the first drug which is approved by Food and Drug Administration (FDA) as an Emergency Use Administration (as an anti-viral ) treatment for Covid-19, the US-FDA approved it and it gained approval in October, 2020 **{26}.**

Based on a randomized, double-blind placebo controlled trial, patieof nt with94% oxygen saturation within symptoms of 12 days by the dose of 2:1 to placebo shows effective , dose received either I.V. of dose about 200mg on day-1 followed by 100mg on day 2-10 daily shows clinical improvement **{16 }.**. Also, in a study by Gilead science among 53 patients, shows efficacy in reduction in mortality rate {**17}**

## 4. AZITHROMYCIN(AZM)

Azithromycin is a semi-synthetic Anti-biotic drug which belongs to a Macrolide category .It shows Bactericidal activity (i.e kill the bacteria ) **{9 ).**

**MODE OF ACTION:** The AZM bind with 23s rRNA of 50s ribosome of bacteria and inhibit bacterial protein synthesis.

**Mode of action In terms of Covid-19:**AZM shows immune-modulatory the activity by inhibiting Cytokine which are involved in SARS-COV-2 virion infection , Azithromycin down-regulated the production of IL-1β ,IL-6 , IL-10 , IL-8 , IL-12 and IFN-α . Azithromycin is also seen in inducing the Memory T-cell. AZM decrease level of IL-8 where as HCQ decrease level of IL-2 . IL-8 cause neutrophill chemo-taxis which facilitate the lung infiltration and macrophage activation in severe patient **{19}.**

A case report of AZM with HCQ shows effective treatment in Pregnant women infected by SAR-COV-2 infection and shows reduced Mortality **.** A study conducted on ventilated patient with a combination of AZM/HCQ >3gm of HCQ and >1gm AZM shows significant result and increased chances of survival. A doses shows efficacy on ~500mg Q.D.. for 3 days then 250mg Q.D. on day2-5 , 1000mg for remaining 10 days and for more than 20 days 500mg Q.D. for 10days **{18,19}**

## 5. CORTICO-STEROIDS

Cortic-steroid is an analog of Glucocorticoid and mineralocorticoid. The gluco-corticoid produce the anti-inflammatory effects and hyperglycemia in relation with steroid whereas in sense with mineralo-corticoid ,it affect the RAS system and cause Na- retention and Aldosterone secration resulting increase in blood volume and $Na^+$ ion concentration (Hypernatremia )

**MODE OF ACTION:** In the way of Genomic or in low dose GC bind with Glucocorticoid Receptor (GR) then enters in-to the nucleuswhere it binds with genetic material where it either stimulate or suppress the gene transcription

In a way of Non-Genomic or in high dose bind with GR on cell and mediate T-Lymphocytes signal transmission and decrease the inflammation **{20}**

Definitely, to employ Dexamethasone in-to the Covid-19 patient were a challenging concern. Therefore, for the immune response control , the corticosteroid was seen as one of the best approach and served as a magical remedy in recent times for the treatment of Covid-19, earlier it was also given for the treatment of SARS-COV-1 , MERS, also in severe Pneumonia and now been served to cured SARS-COV-2 Pandemic to control the immune-mediated change **{22 }.**

In a randomized, Controlled , Open -Clinical Trial study over 2104 patient out of 4321 recieving Dexamethasone confirmed with Covid-19 orally or IV 6mg/day dose upto 10 days shows decrease in mortality rate by 22.9% v/s 25.7%. the incidence of death was also lowered in Invasive Mechanical Ventilator (I.M.V.) receiving Dexamethasone v/s alone care (29.3% v/s 41.4%) and in patient receiving oxygen without I.M.V (23% v/s 26,23%) **{50}.** In a multi centre , randomized controlled trial in Spain of 17 ICU patients given I.V. 20mg O.D. from day 1 to

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

day5 , which was later reduce to 10mg from day 6 to day 10 once a day (OD) . this high dose treatment in ventilated patient showed the recovery in mortality and also decrease the viral load in SARS-COV-2 confirmed patient.
Also based on clinical data , European agency (EMA) suggest the use of corticosteroid to the confirmed covid 19 patient being severe to critical who require oxygen therapy (from supplemental to mechanical ventilation ) in adults and adolencence (above 12 year and weight at-least 40 kg ) and administered orally or given I.V. i.e. 6mg once daily for up-to 10 days **{21}.**

**OTHER POTENTIAL THERAPIES SEEN TO BE EFFECTIVE IN COVID-19 TREATMENT**

**CONVALESCENT PLASMA THERAPY ( AS AN ANTI-VIRAL THERAPY )**
Along with use of Convalescent Plasma Therapy ,many of Re-purposeddrug have been use to treat the Covid-19 as per the clinical data like Anti-viral , Anti-biotic , Cortico-steroid , Anti-helmentic etc. Convalescent Plasma obtained from the patient who is finally recovered or recently recovered from Covid-19, there plasma have generated/contain the virus binding specific anti-bodies with effective potential activity which shows the similar activity like Memory B-cell.**{23 }**

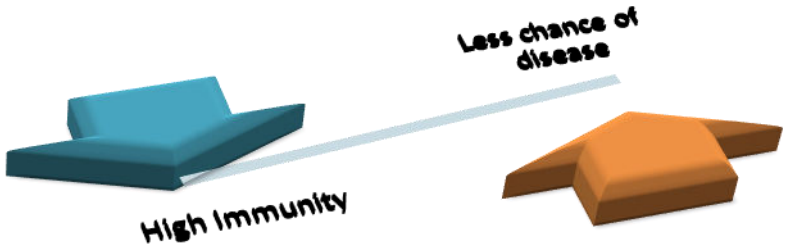



**Figure. 6**

**MODE OF ACTION:** Convalescent Plasma is mostly consider neutralizing Anti-bodies (IgG antibody) against SARS-COV-2 binding protein. Convalescent Plasma generate the passive innate immunity as it is transfused into the patient , it is transfused to those who are not able to generate immunity . Hence, Convalescent Plasma provide Passive immunity, along with CCP activate anti-body dependent cellular toxicity and phagocytosis in response to vorion **{25}**
Although on August 23, 2020 , The Food and Drug Administration (F.D.A) issued an Emergency Use Authorization to use Convalescent Plasma for the treatment in hospitalized patient**{24}.** As per the clinical trial conducted ,a low titer of CCP is not much effective in hospitalized patient whereas high titer of CCP shows efficacy in patient who is hospitalized due to Covid-19 also having 83% neutralizing anti-body within a symptoms of 8 days in RCT. Also in a CCP in Non-invasive patient (oxygen supplement) containing anti-body titer .1:320 dilution showed the survival improvement (Hazard Ratio 0.19 (95% CL 0.05~ 0.72 ) : P=0.015) but wasn't potential against intubation patient. Also the study performed which include the transfusion of high Anti-body IgG ( having specific binding with Virus S-Protein Receptor ) with-in 72 hours of symptoms appearance which conclude with the decrement in mortality (P= 0.0047 )with-in 28 days analysis.**{9}**

**VACCINATION STRATEGY**
Well the term Corona-virus that we are listening past from 2 years has made we human to think about the Healthy life-style , immunity balance , cleanliness/sanitization/hygiene, physical distancing. Earlier in 2002 SARS-COV-1 had shown its out-break resulting infection in more more than 8,000 people over 29 countries and the casualties of around 774 death world-wide, this out-break was first originated in Foshan, Guangdong, China but some how we human shave deaqlt with it by prevention and treatment , just after a decade in 2012 ,we dealt MERS (Middle East Respiratory Syndrome ) which is also a type of Corona-virus , it was more possibly affected in Middle East , the case-fatality ratio was 34.4% with over 2,500 cases of virus and over 900 deaths, the primary host were a Dessert Animal ( i.e. from Dromedaries Camel ) than a Zoonotic transmission to human.
This deadliest Corona-virus ( SARS-COV-2 ) has harmed to humans with total number of cases 199,0,27,698 with the casualties about 42,40,451and recovered patient were17,96,38,585 by date of 2nd August, 2021 this time due to of the continue variation in gene shown by virion which is the reason behind for the researcher to stick for the search of proper medication regimen identification to dealt with the virus as per the situation. In the search of proper vaccination we use various re-purposed drugs with a development of vaccine across the globe. For the Covid-19

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

vaccine development to the date, *Whole Microbe Approach ( i.e. Viral Vector-Based vaccines , Attenuated Vaccine, Inactivated vaccine ), Genetic ( DNA , m-RNA based) Vaccines, Sub-unit Type Vaccines , Protein Based Vaccines*are majorly tested vaccines in a Clinical Trial runned by various Company Authorities . Currently, in all over the world more than 60 SARS-COV-2 vaccines are being under development at different Clinical Trial Phases. Normally for the vaccine development it took 6-10 years to complete its task but for the shake of people in Covid-19 scenario Researchers serving as a task force to develop vaccine as quick as possible

I. **Phase-0 :** Pre-clinical phase , Animal Testing ( Non-Clinical Phase )
II. **Phase-1** : Among few people to determine vaccine safety, determine dosage form and Identify side-effects.
III. Phase-2: Trial among 100-1,000 people to determine safety and efficacy.
IV. **Phase-3:** Trial on 1,000-1,00,000 people to confirm effectiveness.
***NDA approval***
V. **Phase-4:**Trial on more than 1,00,000 people, Post-Marketing Phase(Pharmacovigilance).

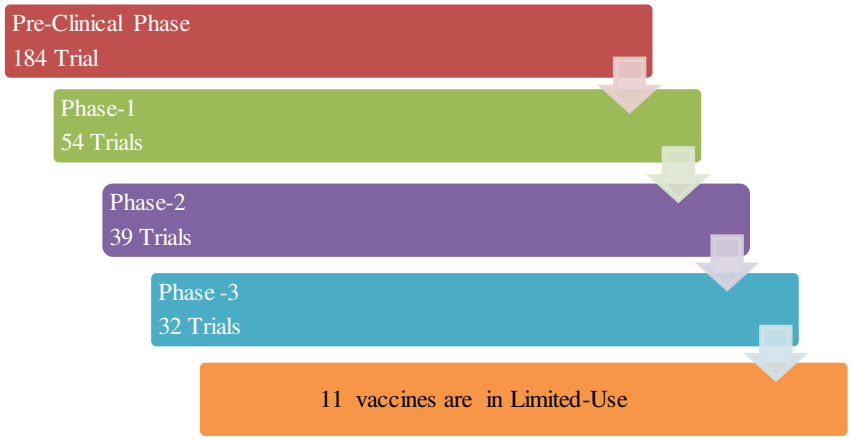



**Figure. 7**

By the date of 2nd August,2021 , there are 184 vaccine in Pre-clinical Trial and 136 vaccine in Clinical Trial and 8 vaccines are under Approved for wide use in humans https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

**MODE OF ACTIONS OF VACCINES:** As vaccine contain antigen where it mimic the activity as antigen cause disease and represented by antigen presenting cell on its surface where it stimulate the T-Cells and Macrophage and correspondence to Immune response .

**1. Whole Microbe Approach**

**I. In-Activated vaccines:**

This vaccines are mainly known as Killed vaccine. This vaccine contain the viral antigen or whole virus which have lost its activity to cause disease ( it's natural activity) by the application of either Chemically , by Radiation or by Temperature alteration where nucleic acid is destroyed keeping the viral antigen intact.**{29}.**

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

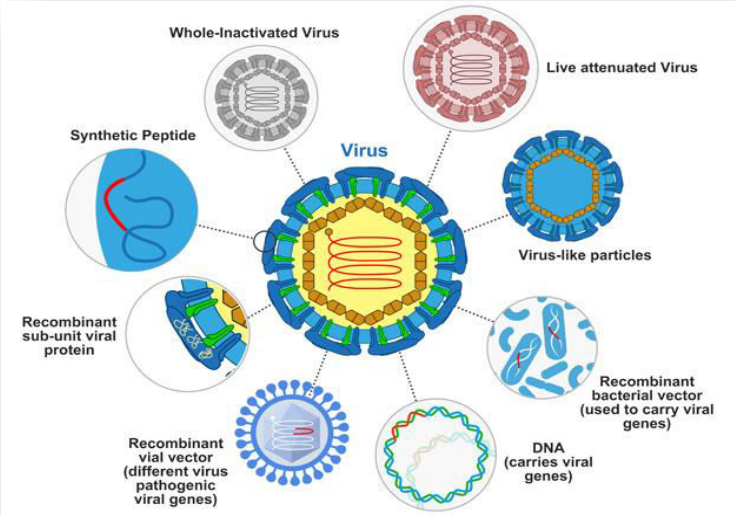



**Figure. 8**

**II. Live-Attenuated vaccine:**

These are those vaccine which consist of a virus activity is weakened under the laboratory se condition such that when injected into the host they only infect the cells rather of causing any **disease** or just causing Mild Pathogenesis**.** Live-attenuated vaccines are not suitable for immune-compromised Patient,if the cellular or hummoral immunity is not in normal range **{29}.** Codegenix and Serum Institute of India initiate dosing in Phase-1 Trial of Live-attenuated vaccine named as *CoVI-VAC* which is a single dose vaccine for Covid-19 , it is administered by Intra-Nasal Route **{30}**

**III. Viral-Vector based vaccine:** It is a vaccination technique where viral gene is implemented by the help of vector rather they don't actually contain antigen. A modifier virus (the vector) is used to deliver the genetic material . In a vector, there is a done a deletion of gene that encodes a viral structural protein which prevent the viral assembly in infected cells. Vector virus mainly used are Adeno Virus , Measles Virus and Vaccinia Virus. **{32}**

**TYPES OF VIRAL VECTOR VACCINE**

- **Non-Replicating Vector vaccine**: It only produce antigen which don't infect the cells.
- **Replicating Vector Vaccine:**Produce other viral particle along with antigen which may infect cells too.

***Note :***Normally, Viral Vector Vaccines are Non-Replicating Vector Vaccine.

**IV. Recombinant Covid-19 Vaccine:**

- **DNA Vaccines:** It is a Recombinant vaccine where DNA as a genetic material of S-Protein which carries a genetic information is inserted in a recombinant with plasmid .Plasmid is a a small, extra, circular double stranded DNA which has a power of self-replicating. DNA upon transcription followed by translation produce antigen which stimulate immune response.
- **RNA Vaccines:** Here mRNA is introduced which carries genetic information which is encapsulated in Lipid Nano-particle delivery System. mRNA is translated in antigen S-protein in cytosol which stimulate immune response.

**V. Protein sub-unit vaccines**

These vaccine are Protein based vaccine as it contain viral protein antigen which stimulate immune response. They utilize either S-Protein or its receptor its Receptor Binding domain(RBD) as an antigen .This antigen are in-capable to cause disease and safer than other vaccines.

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

The approved vaccines by date of 2nd of August, 2021 are given below **{31}**

| Vaccines | Vaccine Type | Manufacturer | Country of origin |
|---|---|---|---|
| **BNT162b2** | mRNA-based vaccine | Pfizer, BioNTech; Fosun Pharma | **US, Germany** |
| **MVC-COV1901** | Protein subunit vaccine | Medigen Vaccine Biologics Corp.; Dynavax | Taiwan |
| **CoviVac** | Inactivated vaccine | Chumakov Federal Scientific Center for Research and Development of Immune and Biological Products | Russia |
| **QazVac** | Inactivated vaccine | Research Institute for Biological Safety Problems | Kazakhstan |
| **COVIran Barekat** | Inactivated vaccine | Shifa Pharmed Industrial Group | Iran |
| **Soberana 02** | Conjugate vaccine | Finlay Institute of Vaccines; Pasteur Institute | Cuba, Iran |
| **CIGB 66** | Protein subunit vaccine | Center for Genetic Engineering and Biotechnology | Cuba |
| **ZIFIVAX** | Recombinant vaccine | Anhui Zhifei Longcom Biopharmaceutical, Institute of Microbiology of the Chinese Academy of Sciences | China, Uzbekistan |
| **WIBP-CorV** | Inactivated vaccine | Wuhan Institute of Biological Products; China National Pharmaceutical Group (Sinopharm) | China |
| **Covaxin (BBV152)** | Inactivated vaccine | Bharat Biotech, ICMR | India |
| **EpiVacCorona** | Peptide vaccine | Federal Budgetary Research Institution State Research Center of Virology and Biotechnology | Russia |
| **Ad5-nCoV** | adenovirus type 5 vector | CanSino Biologics | China |
| **Sputnik Light** | adenovirus vaccine (rAd26) | Gamaleya Research Institute, Acellena Contract Drug Research and Development | Russia |
| **mRNA-1273 (Moderna Covid-19 Vaccine)** | mRNA-based vaccine | Moderna, BARDA, NIAID | US |
| **Janssen (JNJ-78436735; Ad26.COV2.S)** | Non-replicating viral vector | Johnson & Johnson | Netherlands, US |
| **CoronaVac** | Inactivated vaccine | Sinovac | China |
| **Comirnaty (BNT162b2)** | mRNA-based vaccine | Pfizer, BioNTech; Fosun | Multinational |

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021

| | | | |
|---|---|---|---|
| | | Pharma | |
| **Sputnik V** | Recombinant adenovirus vaccine (rAd26 and rAd5) | Gamaleya Research Institute, Acellena Contract Drug Research and Development. | Russia |
| **BBIBP-CorV** | Inactivated vaccine | Beijing Institute of Biological Products; China National Pharmaceutical Group (Sinopharm) | China |
| **Covi-Shield (AZD1222) ; AstraZeneca Vaccine** | Adenovirus vaccine | BARDA, OWS | UK ,India |

**Table. 1**

## CONCLUSION

Since from the review we can sharply conclude that the structure of SARS-COV-2 is complicated as the S-Protein binds with the ACE-2 receptor , the drugs which can inhibit from the bindings to the receptor is used effectively as per the clinical trial conducted. The proper use of a re-purposed drugs are seen effective in the symptoms as per the trial, CCP was seen effective in early symptoms. Also, various vaccines are used to prevent from transmission of SARS-COV-2. Since, more than 20 vaccines are approved for the wide use globally with different efficacy as per the trial performed.

## REFERENCE


1. Coronavirus Disease 2019–COVID-19,Dhama et.al, ClinMicrobiol Re33:e00028 20. https://doi.org/10.1128/CMR.00028-20.
2. Current Situation of Coronavirus Disease:(COVID-19) Review Article, Albaraa A Milibari , DOI: 10.36648/1791-809X.S1.005.
3. A Review of Coronavirus Disease-2019 (COVID-19), Tanu Singhal , https://doi.org/10.1007/s12098-020-03263-6
4. The Coronavirus Disease of 2019: Prevention, Management and Treatment Strategies , Edde et.al. , DOI: 10.9734/jabb/2021/v24i130193 , ISSN: 2394-108
5. Melika Lotfi, Michael R. Hamblin, Nima Rezaei , COVID-19: Transmission, prevention, and potential therapeutic opportunities, https://doi.org/10.1016/j.cca.2020.05.044
6. Huihui Wang & Xuemei Li & Tao Li & Shubing Zhang & Lianzi Wang & Xian Wu & Jiaqing Liu, The genetic sequence, origin, and diagnosis of SARS-CoV-2 , https://doi.org/10.1007/s10096-020-03899-4
7. Omkar Indari, Shweta Jakhmola, Elangovan Manivannan and Hem Chandra Jha, An Update on Antiviral TherapyAgainst SARS-CoV-2: How Far Have We Come? , DOI: 10.3389/fphar.2021.632677
8. Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan-Yang Tan, Shou-Deng Chen, Hong-Jun Jin,Kai-Sen Tan, De-Yun Wang and Yan Yan, The origin, transmission and clinicaltherapies on coronavirus disease 2019(COVID-19) outbreak – an update on the status , https://doi.org/10.1186/s40779-020-00240-0
9. Saghir et.al. , Chloroquine and Hydroxychloroquine for the Prevention and Treatment of COVID-19: A Fiction, Hope or Hype? An Updated Review, DOI https://doi.org/10.2147/TCRM.S301817.
10. Mohammad Sultan Khuroo, Chloroquine and hydroxychloroquine in coronavirus disease 2019 (COVID-19). Facts, fiction and the hype: a critical appraisal, appraisal https://doi.org/10.1016/j.ijantimicag.2020.106101.
11. Maximilian Große , Natalia Ruetalo , Mirjam Layer , Dan Hu , Ramona Businger , Sasch Rheber ,Christian Setz , Pia Rauch , Janina Auth , Maria Fröba , Ekkehard Brysch , Michael Schindler,and Ulrich Schubert, Quinine Inhibits Infection of Human Cell Lines with SARS-CoV-2, https://doi.org/10.3390/v13040647
12. Dr. Aarushi Kataria, Dr. Naveen Nandal and Dr. Ritika Malik, Shahnaz Husain -A Successful Indian Woman Entrepreneur, International Journal of Disaster Recovery and Business ContinuityVol.11, No. 2, (2020), pp. 88–93
13. Senthil Nachimuthu, Manish D. Assar and Jeffrey M. Schussler, Drug-induced QT interval prolongation: mechanisms and clinical management, DOI: 10.1177/2042098612454283

ISSN:0975-3583,0976-2833 VOL12,ISSUE05,2021


14. Adewale Bayode Owa, Olufunke Tolulope Owa, Lopinavir/ritonavir use in Covid-19 infection: is it completely non-beneficial? https://doi.org/10.1016/j.jmii.2020.05.014
15. A Trial of Lopinavir–Ritonavir in Covid-19, DOI: 10.1056/NEJMc2008043
16. Wang et.al. Remdesivir in adults with severe COVID-19: a randomised,double-blind, placebo-controlled, multicentre trial , https://doi.org/10.1016/S0140-6736(20)31022-9
17. Umesh Devappa Suranagi, Harmeet Singh Rehan, Remdesivir: Remedy the world is waiting for? https://doi.org/10.1016/j.mjafi.2020.07.003
18. Giovanni Sisti, Antonio Schiattarella, Andrea Sisti, Treatment of COVID-19 in pregnancy with hydroxychloroquine and azithromycin: a case report, DOI: 10.23750/abm.v91i4.10216
19. Nathalie Bleyzac, Sylvain Goutelle, Laurent Bourguignon, Michel Tod, Azithromycin for COVID-19: More Than Just an Antimicrobial? https://doi.org/10.1007/s40261-020-00933-3
20. Qing Ye, Bili Wang, Jianhua Mao, The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19, https://doi.org/10.1016/j.jinf.2020.03.037
21. Corticosteroids in COVID-19: one size does not fit all, https://doi.org/10.1183/13993003.00224-2021
22. Tang et.al. , Early Use of Corticosteroid May Prolong SARS-CoV-2 Shedding in Non-Intensive Care Unit Patients with COVID-19 Pneumonia: A Multicenter,Single-Blind, Randomized Control Trial , DOI: 10.1159/0005120
23. Robbiani et.al. ,Convergent antibody responses to SARS-CoV-2 in convalescent individuals, https://doi.org/10.1038/s41586-020-2456-9
24. FDA (2021a). FDA EAU letter –Convalescent plasma. Available at httpswww.fda.govmedia141477download
25. Massimo Franchini Giancarlo Maria Liumbruno, Convalescent Plasma for the Treatment of Severe COVID-19.
26. Benedette Cuffari, How do RdRp Inhibitors Combat SARS-COV-2?, https://www.news-medical.net/health/How-Do-RdRp-Inhibitors-Combat-SARS-CoV-2.aspx
27. Mayla Gabriela Silva Borba ET.AL. , Effect of High vs LowDoses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection A Randomized Clinical Trial, doi:10.1001/jamanetworkopen.2020.8857
28. K. Lo et.al., Remdesivir targets a structurally analogous region of the Ebola virus and SARS-CoV-2 polymerases, doi:10.1073/pnas.2012294117/-/DCSupplemental.
29. Jun Zhoua, Wei Wang , Qiong Zhong, Wei Houa, Zhanqiu Yang, Shu-Yuan Xiao ,Runqing Zhub, Zhijiao Tang, Yong Wang, Qiaoyang Xian, Hongbing Tan, Li Wen , Immunogenicity, safety, and protective efficacy of an inactivated SARS-associated coronavirus vaccine in rhesus monkeys , doi:10.1016/j.vaccine.2004.11.075
30. https://www.gavi.org/vaccineswork/what-are-whole-virus-vaccines-and-how-could-they-be-used-against-covid-19
31. https://www.prnewswire.com/news-releases/codagenix-and-serum-institute-of-india-initiate-dosing-in-phase-1-trial-of-covi-vac-a-single-dose-intranasal-live-attenuated-vaccine-for-covid-19-301203130.html
32. https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html