# Review Article
# Recent Approaches of Drugs and Vaccines Used in Covid 19 – A Review

**ABSTRACT**:

A novel SARS-CoV-2 coronavirus developed in December 2019, triggering a life-threatening pneumonia outbreak in China, and has since expanded worldwide, producing a pandemic. Because of the urgent need to control the disease and the dearth of specific and effective treatment options, FDA-approved medicines that have proven efficacy against comparable viruses are being used. In vitro, chloroquine, remdesivir, lopinavir/ritonavir or ribavirin have been found to be effective at inhibiting SARS-CoV-2. The preliminary findings of a variety of clinical trials utilising various chloroquine or hydroxychloroquine delivery procedures all indicate to a positive outcome. They may not be effective in cases of consistently high viremia, and data on ivermectin (another antiparasitic medication) is currently unavailable. Intriguingly, azithromycin, a macrolide antibiotic, in conjunction with hydroxychloroquine may provide therapeutic benefit. Favipiravir, tocilizumab, and azithromycin types are among the other treatment options being investigated.

*Keywords: SARS-CoV 2, MOA, Drugs, Vaccines*

## 1. INTRODUCTION:

Coronavirus sickness, a highly communicable virus because of the SARS, has made a huge impact on global demography; killing over 3.8 People around the world have died because of the pandemic, causing it the worst worldwide health disaster since the 1918 disaster. After the first cases was it was found in Dec 2019 in Wuhan, Hubei Province, China. The disease increases quickly, prompting the WHO to declare it a global pandemic on March 11, 2020. Since it was COVID disease has ravaged the world and has been declared a global pandemic in several countries throughout the world, and it has overloaded several medical care systems. Covid disease continues too many nations are experiencing a second or third wave of infections, which can be linked in large part to the rise of variant versions of this virus. The fact that significant Clinical research has contributed to a better understanding of covid disease and Has turned into a problem growing concern, as Covid disease continues to cause problems around the world, with most nations are in the early stages of a second or third wave of breakouts[1]. Since the outbreak began, four SARS-CoV-2 VOCs have been detected, according to a current WHO epidemiological statement as of June 22, 2021: Alpha was UK reported the first variation of concern in late Dec 2020; Beta was first shown in South Africa in Dec 2020; Gamma was first identified in early Jan 2021 in Brazil. In Dec 2020, Delta for the first time, it was discovered in India. This review research aims to give a comprehensive summary of the most recent pharmacological treatment options for Covid disease. The efficacy of different existing COVID-19 and variant vaccines is also briefly discussed in this review (1).

## 2. COVID19 SYMPTOMS:

Different persons are affected by the coronavirus in different ways. The majority of infected patients will experience mild to moderate symptoms and will recover without the need for hospitalisation. The following are the most common signs and symptoms:

- Fever/cough
- Tiredness
- A change in flavour or odour

### 2.1 Less common symptoms include:

- Sore throat pains and aches cause a headache.
- Diarrhoea,

- The appearance of a rash on skin or irritated eyes, or coloration of the fingers or toes
- Breathing difficulties, shortness of breath, speech or mobility loss, and confusion are all serious signs.
- Chest discomfort

Mildly symptomatic people who manage their symptoms at home. When a person is infected with the virus, symptoms appear after 5–6 days, but it can take up to 14 days [2].

### 2.2 Risk factors:

- Chronic kidney disease is a condition that affects the kidney sl Possessive
- Obesity
- Heart failure or coronary anery disease are serious heart disorders.
- Sickle cell disease is a type of sickle cell illness.
- Diabetes type 2

The following some of the conditions that can cause severe COVID-19 illness:

- Asthma ranges from mild to severe.
- Diseases that influence your brain's blood arteries and blood flow
- Cystic fibrosis is a disease that affects the lungs.
- Blood pressure that is too high
- A compromised immune system as a result of a blood or bone marrow transplan or corticosteroid prescription
- Dementia
- Hepatitis is a disease of the liver.
- Pregnancy
- Lung tissue that has been damaged or scarred (pulmonary fibrosis)
- Smoking
- Thalassemia
- Kind 1 diabetes is a type of diabetes in which the body
- Depression
- Anxiety
- Schizophrenia

Some COVID-19-infected children and teenagers develop an inflammatory illness know multisystem inflammatory syndrome in children, according to doctors. Doctors believe it anything to do with the virus. It has symptoms that are comparable to toxic shock and illness, which causes inflammation in the blood vessels of children [3].

According to experts, the following symptoms were the most common in COVID-19 patients
:

- 99.9% fever
- 70% exhaustion
- 59 percent of coughing
- 40% suffer from a lack of appetite
- 35% of body aches
- 31% of people experience shortness of breath.
- 27% mucus/phlegm



### 3. DRUGS:

### 3.1 Remdesivir:

Remdesivir is a medication that is a nucleoside analogue. It is justified to employ a broad-spectrum antiviral with invitro coronavirus action. The action mechanisms of remdesivir is the Remdesivir-triphosphate (RDV-TP) is a monophosphoramidate prodrug of remdesivir that inhibits RNA-dependent RNA polymerases (RdRps) [4]. Adenosine triphosphate is used by Remdesivir-TP to incorporate into viral RNA strands. Once fused to viral RNA at location I, RDV-TP terminates the RNA combination at position i+3. Because RDV-TP does not produce rapid chain termination, it appears to resist viral exoribonuclease editing. In Table No.1 .Remdesivir's method of action it has been shown in vitro to work against the Arenaviridae, Flaviviridae, Filoviridae, Paramyxoviridae, Pneumoviridae, and Coronaviridae virus families, indicating that it has broad antiviral activity [4]. Remdesivir's activity against the Coronaviridae family was initially demonstrated in 2017, sparking interest in the drug as a potential covid disease treatment [8]. Remdesivir has been confirmed as a non-obligate chain terminator of RdRp from corona virus and similar corona viruses, as well as MERS-CoV, in a number of clinical trials for covid disease [12, 13].

### 3.2 Chloroquine and hydroxychloroquine:

Its anti-SARS-CoV-2 efficacy in vitro and immunomodulatory features justify its use. Through their method of action, chloroquine and hydroxychloroquine block viral enzymes [14]. Inhibition of the ACE2 cell receptor, acidification of the cell membrane's outer surface to impede viral combination, and immunomodulation of cytokine discharge are all options [15]. Based on hydroxychloroquine's in vitro antiviral activity, the optimal dose design as the therapy of Coronavirus 2 SARSCoV-2 was predicted. However, preliminary results from randomised controlled studies in hospitalised patients comparing hydroxychloroquine with or without azithromycin to placebo indicated no difference in clinical status or overall mortality [16, 17].. According to the findings of randomised controlled studies, using hydroxychloroquine as a postexposure preventative infection with the covid virus or symptoms of covid sickness was not prevented [18].

### 3.3 Lopinavir/Ritonavir:

Classification of Lopinavir/Ritonavir is Inhibitor of HIV protease. Additional coronaviruses may be active, according to in vitro and animal model research. In Table No.1 it works by inhibiting covid virus reproduction and activity [20]. Lopivir/ritonavir is an FDA-approved HIV medication combination, was recommended as an antiviral treatment against covid disease in the early phases of the pandemic. A randomised control pilot research found no advantage from the drug therapy compared to a minimum standard of care in individuals hospitalized has severe covid disease. In both hospitalized and non-hospitalized patients, it is currently not advised for covid disease treatment [21].

### 3.4 Ivermectin:

Classification of Ivermectin is Antiparasitic. Rationale for use of Ivermectin is it prohibits covid virus replication in cell cultures.

In any case, pharmacokinetic and pharmacodynamic studies suggest that dosages up to 100 times higher than those approved in people would be required to achieve the plasma focuses required for the antiviral effect seen in vitro [23].

In Table No.1 Ivermectin is transport within the cell protein that virus employ to increase infection by inhibiting the antiviral response of the host. Ivermectin is an anti-parasitic medicine that has been licensed by the FDA and is used to take care of Covid disease all over the world. It was created after an in vitro investigation showed that it could prevent corona virus proliferation [24]. A randomised controlled experiment in which 476 adult Covid disease patients were randomly assigned Ivermectin 300mcg/kg body weight or placebo for five days did not result in substantial improvement or the desired symptom relief. Both hospitalised and non-hospitalized individuals should avoid ivermectin treatment for Covid disease [24].

### 3.5 Favipiravir:

Favipiravir is an inhibitor of RNA polymerase that is dependent on RNA currently being researched. The following rationale for its use favipiravir is a broad-spectrum antiviral that has been discovered effective in the laboratory against RNA viruses.

Favipiravir acts by blocking the RNA polymerase that is RNA-dependent enzyme, which prevents synthesis of viral RNA [25]. China's NMPA has included this drug to a list of potential covid virus treatments. Favipiravir group participant's lab tests for covid virus were negative after the treatment was administered [26]. In addition to interferon is 5 million U twice daily via aerosol inhalation, 35 patients with a median age of 43 years were given 1600mg twice day as a loading dosage and 600mg twice daily. In a study conducted, 45 patients were given lopinavir 400mg or ritonavir 100mg (RTV) everyday twice by aerosal inhalation, as well as 5 million U IFN-a twice a day (middle age was 49 a long time). They noticed a short timeme for the virus to be cleared and a considerable imaging of the chest has improved in the FPV group with low ADRs. In a study conducted, 45 patients were given lopinavir 400mg or ritonavir 100mg (RTV) twice day by aerosal inhalation, as well as IFN-a 5 million U twice daily. They noticed a short In the FPV group; there was a significant improvement in chest imaging and a minimal rate of adverse effects. The results of a recent trial with 120 corona virus patients in Wuhan, China [27].

### 3.6 REGN-COV2 (Casirivimab and Imdevimab)

Classification of Casirivimab is a monoclonal antibody. Casirivimab is a recombinant human IgG1 monoclonal antibody that binds to the corona virus spike protein's receptor binding domain, which is involved in viral connection, combination, and cell entry. The coronavirus spike protein is destroyed by casirivimab in conjunction with imdevimab [28]. In Table No.1 Casirivimab is a cocktail of two non-competing IgG1 antibodies that have been shown to reduce viral load in vivo by targeting the RBD on the corona virus spike protein, preventing virus infection (14). In a break analysis of 275 patients from a continuous double blinded test including non-hospitalized patients with corona disease who were given a placebo, 2.4g of casirivimab, or Imdevimab at random. The safety profile of this cocktail antibody was also evaluated in this investigation. According to early data from a Phase 3 trial of REGN-COV, corona disease resulted in a 70% decrease in hospitalization or a 70% reduction in non-hospitalized patients. There is in vitro data available on the impact of REGN-COV2 on the two novel corona virus variants of concern that demonstrate retained activity [29].

### 3.7 Glucocorticoids:

Dexamethasone is a glucocorticoid hormone. Corticosteroids decrease Leukocyte migration to inflammatory regions, as well as vasodilation and capillary permeability. Corticosteroids bind to the glucocorticoid receptor, causing gene expression alterations with a wide range of downstream effects that might take hours to days to manifest . In Table No.1 Glucocorticoids inhibit phospholipase A2, which prevents the formation of arachidonic acid derivatives, as well as Death and demargination of neutrophils they inhibit the transcription factors NF-Kappa B and other inflammatory transcription factors while boosting the production of anti-inflammatory genes like interleukin-10. Corticosteroids at lower amounts are anti-inflammatory, however higher doses suppress the immune system. Sodium levels rise and potassium levels fall when high amounts of glucocorticoids bind to the mineralocorticoid receptor over time [30]. Corona disease has been associated to cytokine-induced inflammatory lung damage, which is characterised by an increase in inflammatory markers. Glucocorticoid effectiveness in covid disease patients was not thoroughly reported in the early phases of the epidemic. The recovery preliminary study found that giving dexamethasone to hospitalized people was given to patients with clinically suspected or lab-confirmed corona virus. Dexamethasone or frequent consideration for patients who received intrusive mechanical breathing or oxygen support for clinically suspected or lab-confirmed corona virus had a reduced 28-day death rate than those who did not. Dexamethasone, alone or in combination with remdesivir, is used in hospitalized patients who require supplementary oxygen or non-obtrusive or invasive mechanical respiration is currently regarded the standard of therapy, depending on the severity of the condition [31].

### 3.8 Azithromycin

Classification of Azithromycin is Macrolide Antibacterials and the Rationale for use is macrolides may have immunomodulatory characteristics, and azithromycin may prevent bacterial super infection, making them suitable for adjuvant therapy.
To grow, Bacteria require a unique protein synthesis pathway that is facilitated by ribosomal proteins [32, 33]. It obstructs bacterial protein synthesis by preventing the movement phase the binding of the 50S ribosomal subunit as well as protein synthesis Label. As a result, various bacterial illnesses have been brought under control. Macrolides In pulmonary inflammatory illnesses, they exhibit immunomodulatory effects [34]. They may aid in reducing cytokine overproduction associated with respiratory virus infections. Preventing cytokines from prompting neutrophils (PMNs) to chemotaxis to the lungs is one example of immunomodulatory approaches. Mucus hypersecretion is inhibited (20).In Table No.1 Azithromycin is a macrolide antibiotic is a type of antibiotic that is used to treat bacterial infections [35]. This macrolide possesses antibacterial, antiviral, and immunomodulatory properties, making it potentially useful in viral infections such as corona virus. The high tissue accumulation compensates for the poor absorption, resulting in a 37 percent oral bioavailability. Azithromycin is 400 to 1,000 times more concentrated in epithelial cells, fibroblasts, lymphocytes, and alveolar macrophages than in blood [36, 37]. Chemotactic drug delivery raises local drug concentrations by releasing stored azithromycin through blood phagocytes and other cells that move to inflamed and dirty tissues. As a result of this, azithromycin has a half-life of 68–79 hours. This medication has an amazing ability to permeate lung tissue and keep medication concentrations stable [38].

### 3.9 Tocilizumab:

Tocilizumab is a monoclonal antibody that has been shown to target the interleukin-6 receptors alpha receptor demonstrated to be useful in the treatment of rheumatoid arthritis. The information on how this agent was utilized is distorted. When compared to placebo, Tocilizumab did not result in a significant change in clinical status or a decrease in 28-day mortality in a randomised controlled trial comprising 438 hospitalised patients with severe corona virus pneumonia, 294 of them were given tocilizumab and 144 were given placebo [39]. Another randomized, two-fold visually impaired fake treatment controlled trial involving persons with confirmed extreme corona disease that comprised A study of 243 patients who were randomly assigned to receive tocilizumab or a placebo discovered that it was ineffective in preventing death [40]. The REMAP-CAP and RECOVERY preliminary (not yet released) showed a mortality advantage in individuals with fast respiratory decompensation [41]. Interleukin 6 is a pro-inflammatory cytokine produced by T cells, B cells, lymphocytes, monocytes, and fibroblasts. Antibody synthesis, cytotoxic T-cell isolation, and development are all steps in the cytotoxic T-cell process are all boosted by IL-6. By binding to IL-6 receptors in the solvent and on the membrane layer, tocilizumab suppresses IL-6-mediated inflammation. C-reactive protein, serum amyloid A, fibrinogen, haptoglobin, and -1-antichymotrypsin are all blood markers for inflammation and all produced in response to IL-6, but not fibronectin, egg whites, or transferrin [42].

### Table.1 Covid Drugs

| Drugs | Classification | Rationale for use | Brand name | Generic name | Mechanism of action | Route of Administration |
|---|---|---|---|---|---|---|
| Remdesivir | Antiviral - Nucleoside Analogue | Broad spectrum | Veklury | Remdesivir | Mono phosphoramidate prodrug of (RDV - TP) | Intravenous |
| Chloroquine and Hydroxychloroquine | Antimalarial | Invitro against corona virus | Aralen | Chloroquine | Inhibition of viral enzymes. Acidification of the surface of the cell membrane. | Intramuscular or Subcutaneous. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Lopinavir or Ritonavir | Inhibitor of HIV protease | Other coronaviruses may have activity based on in vitro and animal model investigations | Kaletra | Lopinavir/Ritonavir | Suppress corona virus replication | Oral |
| Ivermectin | Antiparasitic | Inhibits the replication of corona virus | Sklice, Soolantra, Stromectol | Ivermectin | Suppress the virus infections. | Oral, IV, Topical route |
| Favipiravir | Antiviral | Antiviral having broad spectrum efficacy in vitro against RNA viruses. | Avigan | Favipiravi | RNA polymerase (RdRp) inhibitor that inhibits viral RNA synthesis. | Oral, IV |
| Azithromycin | Macrolide antibacterial | Macrolides may have immunomodulatory characteristics and can be used as an adjuvant therapy to prevent bacterial infection.. | Azasite | Azithromycin | Immunomodulatory properties in pulmonary Inflammatory disorders, Inhibit cytokine production, accelerating neutrophil apoptosis. | Iv, Oral |
| Casirivimab and Imdevimab | Monoclonal antibody | Cytokine release syndrome | REGEN-COV, Ronapreve | Casirivimab and Imdevimab | Inactivation of spike protein | Iv, Subcutaneous |
| Tocilizumab | Monoclonal antibody | Cytokine release syndrome | Actemra, RoActemra | Tocilizumab | T-cell activation | Iv, Subcutaneous |

## 4. VACCINES;

### 4.1 Covishield: (ChAdOx1 nCoV-19 antibody):

In Table No.2 After two doses, a preliminary evaluation of an on 70.4% clinical efficacy and a favourable safety profile have been proven in a multinational randomised control trial to 64% protect to avoid corona disease. In various places throughout the world that have not yet gotten formal approval, the Covishield has been approved to prevent corona disease. The FDA has granted emergency use authorisation or approval in the US [43].

### 4.2 Moderna (mRNA-1273):

People receiving 2 doses of Moderna antibody 28 days apart in a trial 3 randomly selected, observer blinded, placebo-controlled trial were found to be 94.1% effective in preventing corona disease, with no safety concerns other than short-term local and systemic reactions(26). Based on the results of

this vaccine effectiveness preliminary trial, the FDA issued a EUA for the use of the moderna antibody to prevent corona disease on December 18, 2020. Up to seven distinct Vaccines were developed natively by Covaxin (India), Sputnik V (Russia), and CoronaVac (China), incorporating protein-based and inactivated antibodies certified for crisis use in various countries throughout the world to prevent corona disease [43].

**Table.2 Covid Vaccines**

| Vaccines | Scientific name | Firm | Dosing schedule | Route of Administration | Storage |
|---|---|---|---|---|---|
| **COVISHIELD** | ChAdOx1nCoV-19 | M/s Serum Institute of India Pvt. Ltd. | Two doses Day 01& Day 84 | Intramuscular | 2-8°C |
| **COVAXIN** | Whole-Virion Inactivated SARSCoV-2 Vaccine | M/s Bharat Biotech | Two doses, Day 0& 28 | Intramuscular | 2-8°C |
| **MODERNA** | mRNA-1273COVID-19vaccine | M/s Cipla Ltd.(Importer) | Two doses, Day 0& 28 | Intramuscular | -25˚Cto-15˚C |
| **JOHNSON AND JOHNSON** | Ad26.COV2-S (recombinant) | M/s Johnson& Johnson Pvt. Ltd. (Importer) & Biological Limited | Single dose | Intramuscular | -25˚Cto-15˚C& 2-8°C |
| **SPTUNIKV** | Recombinant Adenovirus vector Based SARS-CoV-2 liquid vaccine Gam COVID Vac | M/s Dr.Reddy's Lab. Ltd.(Importer) | Two doses, Day 0& Day21 | Intramuscular | -18°C |
| **ZYCOV-D** | Novel CoronaVirus-2019-nCov Vaccine (recombinant DNA) | Cadila Healthcare Limited | Three doses(Day 0, 28 And 56) | Intradermal | 2-8°C |

## 5. CONCLUSION:

COVID-19 has been tested using a variety of antiviral medications, both separately and in combination, that have previously been used against SARS and MERS, as well as FDA-approved and laboratory tests. Despite extensive research, no viable COVID-19 antiviral medication or vaccine is currently available. While many innovative therapeutic techniques are being developed more clinical trials are essential during these key periods to ensure the safety and efficacy of innovative medications. While many medications have been found to be successful against a variety of respiratory viral infections, including influenza and some coronavirus strains, building resistance to existing antiviral medications remains a significant concern.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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