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Clinically available/under trial drugs and vaccines for treatment of SARS-COV-2

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20.1 Introduction

COVID-19, a unique COVID disorder, was initially found within the Chinese town of Wuhan center at the end of December 2019. On January 7, 2020, a progression of respiratory illness frequencies was accounted for by the China National Health Commission at the initiation of the affliction. Thus comparative cases directly contact the world, inciting the World Health Organization (WHO) to step in. Then WHO broadcasted the circumstance of a worldwide pandemic on March 11, 2020 (Tahir ul Qamar et al., 2020). Around 57 million Affirmed cases and over 1.3 million passings are accounted for in 220 countries and domains throughout the world as of November 22, 2020. The International Committee on Taxonomy of Viruses has named COVID-19 contributive specialist extreme intense respiratory illness [severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2)] since it shares 89% nucleotide likeness with bat SARS-like CoVZXC21 and 82% with human SARS-like CoVZXC21 (Abd El-Aziz & Stockand, 2020). Researchers are currently carrying out different trials to foster control measures and medicines to cope with the pandemic as quickly as time permits, to keep away from the death toll and economic harms caused by COVID-19 (Tahir ul Qamar et al., 2020). In the Republic of China, the United States (US), the United Kingdom (UK), and the European Union, clinical preliminaries of antiviral medications, as an example, remdesivir (Beigel et al., 2020), hydroxychloroquine, and azithromycin (Gautret et al., 2020), favipiravir (Cai et al., 2020), ritonavir, and lopinavir (Hung, Ke et al., 2020; Hung, Lung et al., 2020), methylprednisolone, epoprostenol, sirolimus, sarilumab, and anakinra (Wu et al., 2020) are in

progress. Remdesivir, as an example, is active against COVID connected to the SARS, Middle East respiratory syndrome (MERS) (Amanat & Krammer, 2020), and therefore the Ebola fever infection, anyway it's less powerful than alternative treatments (Mulangu et al., 2019). Likewise, COVID-19 patients are being treated with chloroquine (malarial drug) and hydroxy-chloroquine (antiinflammatory), which have antiviral character towards the human immunological disorder infection and AIDS (Viveiros Rosa & Santos, 2020). Along with this, lopinavir, ritonavir, arbidol, etc. are mostly being tried throughout the world, despite the very fact that their viability still cannot appear to be resolved, and many preliminaries are all over as a result of patient disappointment (Tahir ul Qamar et al., 2020). On the other hand, some of the antibodies (mRNA-1273, measles, mumps, and rubella (MMR), ChADOx1, nCoV-19) have been employed in its third and fourth preliminary stages, and an outsized variety of volunteers are registered, none has been found affirmed to be powerful towards COVID-19 on these lines far. Some notable antiviral meds, like nucleoside analogs, polymer-subordinate RNA enzyme (RdRp), Human Immunodeficiency Virus (HIV) proteolytic enzyme inhibitors, and angiotensin-changing over catalyst 2 pair of [angiotensin-converting enzyme 2 (ACE2)], were used as the potential for COVID-19 treatment (Enayatkhani et al., 2021; Shah et al., 2020). Statins, a category of cholesterol-bringing medicine that is notable right down to impede the SARS-CoV-2 important proteolytic enzyme (Mpro) chemical, might likewise be a possible treatment target. Statins such as pitavastatin, rosuvastatin, lovastatin, and fluvastatin have the limiting power to restrain COVID-19, as indicated by Reiner team (Reiner et al., 2020). In addition, in silico studies have shown that peptide-like small proteins such as (cobicistat, ritonavir, lopinavir, and darunavir), are conceivably compelling inhibitors of the SARS-CoV-2 protease (Pant et al., 2020; Shah et al., 2020). Besides, nonconventional medication revelation apparatuses like processed reasoning (AI) and AI have shown guarantee within the advancement of COVID-19 elective medicines and cures (Omolo et al., 2020). Coronavirus is being focused on by analysts from all over the world with expectations of discovering a fix. Beforehand, there have been solely some audits, as an example, the SARS-CoV-2 immunization pipeline (Abd El-Aziz & Stockand, 2020; Chan et al., 2020; Huang et al., 2020) were delivered. As of currently, this section is focused on totally different medications and immunizations pertinent to COVID-19.

Vaccines against viruses come in a variety of forms, depending on the technical platforms that were utilized to create them. Inactivated or live attenuated viral particles, virus-like particles lacking the viral genome, recombinant viral proteins or peptides, viral nucleic acids encapsulated in delivery vesicles such as liposomes or inserted in plasmid vectors, and viral vectors that may or may not replicate in host cells are examples of these. Several attempts are being conducted globally to develop vaccines for each of these platforms against SARS-CoV-2. According to one estimate, there are over a 100 candidate vaccines in development and at various phases of clinical trials, some of which have proceeded to phase 3/4, and a few of which have recently been licensed in several countries for immunization of adults aged 18 and above.

A COVID-19 vaccine was created utilizing an adenovirus type 5 (common cold virus) vector incorporating partly Coronavirus genetic material that encodes the spike protein in one of the first human trials. Only one dosage of the Ad5-nCoV vaccine was shown to produce specific T-cells and antibodies against the Coronavirus, and it was also proven to be safe. SinoVac Biotech, a Chinese firm, stated that their inactivated Coronavirus vaccine

candidate generated neutralizing antibodies in a preclinical model using rhesus macaque monkeys and was proven to be safe. Inovio Pharmaceuticals, Inc., a US-based business, has developed INO-4800, a DNA vaccine for COVID-19. The firm claimed that the vaccine generated “robust neutralizing antibody and T-cell immune responses against Coronavirus SARS-CoV-2” in preclinical research involving mice and guinea pigs. In the US, a phase 2 clinical study of its proposed vaccine (ClinicalTrials.gov Identifier: NCT04447781) is underway.

Clinical studies for at least three potential vaccines are also ongoing in India. The National Institute of Virology of the Indian Council of Medical Research (ICMR) has teamed up with Bharat Biotech International Ltd (BBIL), an indigenous biotech business, to create COVAXIN, a whole-virion inactivated SARS-CoV-2 vaccine. This candidate, coded BBV152, is now undergoing a randomized, double-blind, multicenter phase 1/2 trial to assess its safety, reactogenicity, tolerability, and immunogenicity in healthy volunteers. Zydus Cadila, an Indian pharmaceutical firm, has developed a plasmid DNA vaccine called ZyCoV-D for the prevention of COVID-19, which was proven to be safe in phase 1 clinical study in healthy volunteers. The firm has started a multisite, prospective, randomized, adaptive phase 2 study to assess the vaccine candidate’s safety and immunogenicity.

20.2 Structure, symptoms, and remedies

SARS-CoV-2 from the *Coronavirinae* taxonomic group belongs to the Coronaviridae family. In subfamily, there are four genera available: Alpha (α), Beta (β), Gamma (γ), and Delta (δ). Coronavirus had a solitary abandoned positive-sense ribonucleic acid that was additional noteworthy than that of another ribonucleic acid viral infection. The capsid present outside the genome is created by the nucleocapsid protein, and also additionally pressed by an envelope that’s comprised of three underlying proteins: film, spike, and envelope protein as shown in Fig. 20.1. Four underlying proteins and sixteen nonprimary proteins form up SARS-CoV-2 (Wang, Zhao, Gao et al., 2020; Wang, Cao et al., 2020; Wang, Zhao, Chen et al., 2020).

The underlying passageway of COVID-19 in human body cells is helped by the protease enzyme which supports the binding of spike protein with ACE2 compound (Guo et al., 2020). SARS-CoV-2 S1 and S2 areas facilitate the combination between cell layers (Ashour et al., 2020). Since ACE2 receptors are well expressed in the heart, respiratory, digestive, urinary organs, and different inward parts, the virus affects the functioning of multiple organs (Wrapp et al., 2020).

20.2.1 Symptoms

From day 2 to 14, after exposure to the COVID-19 virus, the following symptoms can be found. The incubation period can be defined as the time interval between virus exposed time and symptoms occurring (Zhu et al., 2020):

Major symptoms are as follows:

- mild fever along with dry cough;

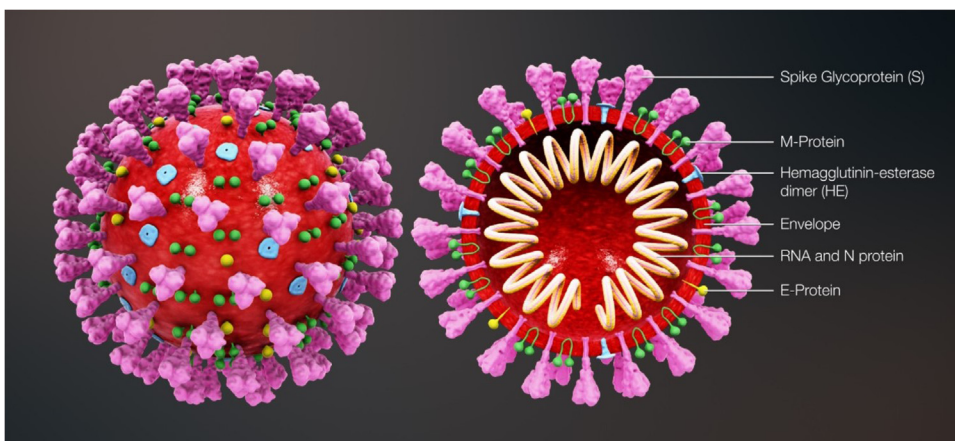


FIGURE 20.1 Structure of severe acute respiratory syndrome-Coronavirus-2. This figure is adapted from an open-access journal. Reference: Wu, David, Raghuram Koganti, Upendra P. Lambe, Tejabhiram Yadavalli, Shyam S. Nandi, and Deepak Shukla. 2020. "Vaccines and Therapies in Development for SARS-CoV-2 Infections" *Journal of Clinical Medicine* 9, no. 6: 1885. <https://doi.org/10.3390/jcm9061885> (Wu et al., 2020).

- body tiredness;
- loss of taste and smell.

Other signs and symptoms include can be found in some patients (Holshue et al., 2020; Xiao et al., 2020):

- difficulty in breathing or shortness of breath;
- muscle pain;
- body chills;
- throat irritation;
- a stuffy nose;
- mild or severe headache;
- chest stiffness;
- pink eyes, known as conjunctivitis;
- vomiting, along with diarrhea;
- skin rashes.

Asymptomatic humans operate as viral transmission vectors and are responsible for SARS-CoV-2 rapid proliferation. SARS-CoV-2 is commonly detected via oral and anal swabs, as well as blood tests. In the initial stage, SARS-CoV-2 can be detected through oral swabs, in the later stage during illness it can be found through anal swabs (Zhang, Du et al., 2020; Zhang, Lin et al., 2020; Zhang, Wu et al., 2020). Patients in China have been shown to have a variety of symptomatology, including inducing coagulation of blood, decreasing cellular immunity, kidney-related problems along with secondary bacterial infections. To summarize, COVID-19 mostly affects older males along with related manifestations that cause's acute respiratory distress

disorders in them, which leads to worsening of the patient's condition and death within a short period (Chen, Zhang, Huang et al., 2020; Chen, Zhang, Wang et al., 2020; Chen, Zhou et al., 2020).

20.2.2 Remedies

Following are a couple of cures that help in forestalling just as a fix to the patients who are asymptomatic and in gentle condition (Abd El-Aziz & Stockand, 2020). Anyway hospitalization and medicine will be the lone path if there should arise an occurrence of extreme condition.

- usage of N-95 covers;
- washing hand regularly with cleanser and water;
- following social separating;
- self-segregation;
- maintaining satisfactory hydration;
- steaming;
- doing proactive tasks like exercise and yoga;
- taking protein-rich food.

20.3 Important drug target of SARS-COV-2

The spike protein could be a type 1-transmembrane (TM) protein (macromolecule) with a clove structure. The ectodomain (ED), the TM space, and the intracellular short tail phase, are the three parts of the spike protein. The ED is comprised of the receptor-restricting S1 space (three S1 heads) and combination part S2 (trimeric tail) on the C-terminal (Belouzard et al., 2012). Spike proteins cluster along in a very trimeric structure on the virion's external cover, giving it the state of a crown, therefore the name CoV. The spike protein is imperative for infection (Li, 2016). Starting communications between the S1 space and its host receptor (ACE2 on account of SARS-CoV and PP4 on account of MERS-CoV) and succeeding S2 portion intervened combination of the host and infective viral agent layers allow the CoV-RNA order to enter the cells, creating these proteins vital medication revelation targets. The spike macromolecule triggers the host cell's immunologic reaction to CoV. SARS-CoV-2 spikes show 10–20 times more limiting fondness with ACE2 comparative with different Coronavirus (Huang et al., 2020; Wrapp et al., 2020). The medications and immunizations currently being tried in clinical preliminaries throughout the world have specific focuses within the host cells (Huang et al., 2020; Wrapp et al., 2020). Moreover, continuous treatment tests in human cells are zeroing in on intruding/inactivating the SARS-CoV-2 replication cycle, polymer discharge, proteolytic enzyme chemical execution, provocative pathway enactment, and therefore the age of cytokine storms (Sohag et al., 2020).

20.4 Various therapeutic approaches

20.4.1 Antiviral approaches

Various therapeutic approaches will be discussed in this section. The mechanism of antiviral medicines against SARS-CoV-2 is depicted in Fig. 20.2. In this figure, RDV is for remdesivir; FVP stands for favipiravir; RBV stands for ribavirin; IFN stands for interferon; sIL-6R stands for soluble IL-6 receptor; mIL-6R stands for membrane IL-6 receptor; TCM stands for traditional Chinese medicine. The mechanism for antiviral approaches with the antiviral medicines will be discussed in detail in the coming subsections of this chapter.

20.4.1.1 Peptides

SARS-CoV-2 spike glycoprotein uses its receptor-binding domain (RBD) to connect and bind to the ACE2 cell receptor (Tang et al., 2020). The receptor limiting region of S1 is severed at the S1 and S2 subunits by cell-derived TMPRSS2 catalyst, cathepsin L, and furin after limiting to ACE2 (Hofmann & Pöhlmann, 2004). Hence, S protein turns into the quality objective for immunizations and restorative medications to repress infective viral agent passage (Walls et al., 2020). Primary comprehension of the RBD–ACE2 interface (Yan et al., 2020) could be a very important advance for the inhibitor plan. Aside from peptides, monoclonal antibodies and tiny atom inhibitors are as yet the likable intercession methodology as far as value, dose, strength, pharmacology, and coordination against this virus.

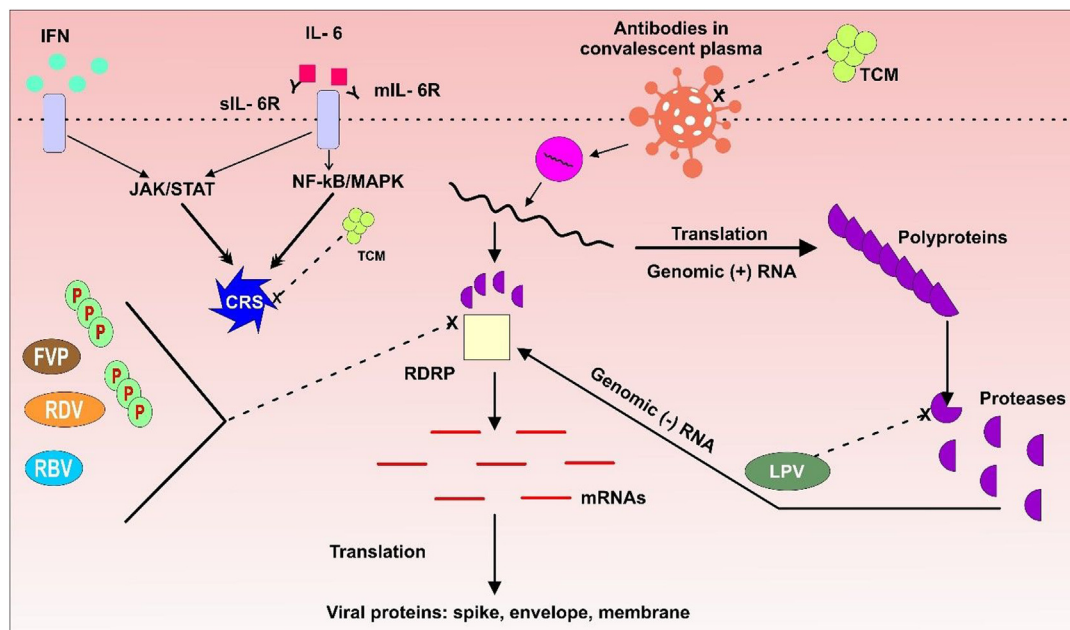


FIGURE 20.2 The mechanism of antiviral drugs against severe acute respiratory syndrome–Coronavirus-2. FVP, Favipiravir; IFN, interferon; mIL-6R, membrane IL-6 receptor; RBV, ribavirin; RDV, remdesivir; sIL-6R, soluble IL-6 receptor; TCM, traditional Chinese medicine.

To acknowledge very few particle inhibitors against RBD, virtual in silico screening of 1582 Food and Drug Administration (FDA)-endorsed medicine was done that confirmed that Simeprevir and Lumacaftor tie RBD and forestall angiotensin-changing over the catalyst-2 association. Lumacaftor and Simeprevir are COVID-19 Mpro inhibitors with the notion of multitarget sedate that repress many proteins at the same time, according to virtual screening and in vitro investigations of comparable medicines (Trezza et al., 2020). Moreover, almost any conventional items were shown to be viable in restricting the collaboration of spike compound protein with its receptor when tested across the RBD of SARS-CoV-2 (ACE2). Moreover, barely any particles, for instance, Thebaine, Withaferin A Nimbin, Curcumin, Mangiferin, Piperine, etc., were seen compelling in clogging the association of spike protein along with its receptor ACE2 (Maurya, Kumar, Bhatt, et al., 2020; Maurya, Kumar, Prasad, et al., 2020). During this specific situation, chloroquine, an anti-protozoal drug, was accounted for to impede COVID-19 infection unwellness, with an IC50 worth of 1.13 μ M and a CC50 greater than 100 in Vero E6 cells. Chloroquine is accepted to hinder fatal glycosylation of ACE2 aboard distended endosomal pH level needed for combination prompting a diminished binding virus S protein to ACE2. Chloroquine is known for its potential to improve antiviral effectiveness through immunomodulation, in addition to its antiviral effects (Wang, Zhao, Gao et al., 2020; Wang, Cao et al., 2020; Wang, Zhao, Chen et al., 2020). Another kind of chloroquine, hydroxychloroquine, has shown to be far safer and more popular in vitro than chloroquine (Yao et al., 2020). However, these repurposed medicines cause bodily cavity arrhythmias, QT prolongation, and alternative cardiovascular connected poison levels in seriously sick patients (Chen et al., 2006). Even so the accessibility of ACE2 inhibitors, its restraint is certifiably not an affordable restorative methodology because it assumes vital physiological components together with respiratory organ injury defensive job in adult respiratory distress syndrome (Imai et al., 2008) and its weakening could exasperate oxidant fiery reactions (Prestes et al., 2017). Clinically supported TM protease serine 2 inhibitors are protected and prospering medications thought-about to support the regulation of the infection by clogging host-cell section. Nafamostat, an FDA authority-supported medicament drug in Japan for persistent urinary organ substitution, was recently answered to indicate 15-fold higher repressing strength than Camostat with 0.5 viable focus (EC50) within the low-nanomolar concentration against COVID-19 combination (Bestle et al., 2020; Bojkova et al., 2020; Yamamoto et al., 2020). In correlation, Gabexate mesylate is the least dynamic in the repressive COVID-19 S-driven host-cell section (Hoffmann et al., 2020). Further, cathepsin L acts as antimicrobials, immunomodulators, antimalarials, hostile to sick, against HIV, cancer interference agent, and was viewed as a repurposed drug for COVID-19. But these medications have their undesirable loads on patients (Idris et al., 2020; Liu, Liu et al., 2020; Liu, Luo et al., 2020; Liu, Zhou et al., 2020; M et al., 2021). Also, an Abelson nonreceptor cystosine (aminoalkanoic acid) enzyme (Abl) advances cathepsin L discharge that demonstrates that drug led to decrease in Abl cystosine kinases could in a very detour fill as cathepsin emission inhibitors and restrain section/combination of SARS-CoV-2 (Tripathi et al., 2018). Another drug imatinib has been flaunted to restrain COVID-19 in an in vitro investigation (Weston et al., 2020). In addition, some kinase inhibitors as mitigating immunomodulators for protein concealment are projected as the probably remedial way to deal with SARS-CoV-2 (Xia et al., 2019; Xia, Liu et al., 2020; Xia, Zhu et al., 2020).

20.4.1.2 *Papine like protease inhibitors*

Advanced components in human body cells drive fiery flagging pathways that are coordinated by unambiguous ubiquitin signals (Xia, Liu et al., 2020; Xia, Zhu et al., 2020). Papine like Protease Inhibitors, that is, PLpro, hold a more amino corrosive arrangement in ubiquitin area and lost each interferon-irritating and deubiquitinase exercise (Klemm et al., 2020). COVID-19 encoded PLpro harbors two different dynamic spaces; a labile Zn-restricting space and an exemplary drug cytosine cleavage space that assume an indispensable part in infective viral agent replication. After PLpro addresses a prominent objective for arranging of PLpro inhibitors it hinders viral multiplication either by the specific discharge of zinc particles from the labile zinc space or probably by obstructive the cytosine buildup at the drug area (Kneller et al., 2020). Many mixtures, such as ritonavir, Chloromycetin, levodropropizine, phenformin, and traditional things, such as platycodin D, cryptotanshinone, quercetin, etc. have shown potential against COVID-19 (Maiti, 2020; Wu et al., 2020; Yuen et al., 2020). Nonetheless, not several of those medications aren't acceptable for the oral organization due to pharmacokinetic limitations and few have limited activities on physiological capacities (Kandeel et al., 2021). However, pharmacokinetic limitations can be settled utilizing nanoembodiment approach.

20.4.1.3 *The 3C-like proteinase [Mpro] inhibitors*

COVID-19 ribonucleic acid encrypted for two huge polyproteins, pp1a and pp1ab, which remain inert till the viral chymotrypsin-like protease enzyme separates them into 12 nonunderlying proteins together with RdRp and helicase. Hindrance of Mpro would keep the infection from multiplication. Consequently, making it a tempting medication focus for SARS-CoV-2 (Naidoo et al., 2020). The high-throughput virtual screening was done utilizing 10,000 complete mixtures together with supporting medication, regular things, and medicine competitors in medical preliminaries. Ebselen, Disulfiram, Tideglusib, Carmofur, Shikonin, PX-12, and TDZD-8 were the most important hits, with IC₅₀ values ranging from 0.67 to 21.4 M. Ebselen was the first grounded inhibitor of Mpro activity (Naidoo et al., 2020). Ebselen is a combination of organoselenium that has antioxidant, relaxing, and cytoprotective effects. Initially, it was given as a chemical mimic that catalyzed the antioxidant response (Cao et al., 2020; Naidoo et al., 2020). Besides, Ebselen weakens the production of ROS, cytokines, and white corpuscle penetration to balance pneumonic and vascular structure aggravation (Jin et al., 2020). Additionally, Ebselen has likewise been accounted for its movement to repress the arrival of IL-6 beneath delayed drive (Müller et al., 1984). Further, its defensive adequacy in microbic or compound boosts prompted liver brokenness (as seen in serious instances of SARS-CoV-2) has in addition been accounted for (Ali et al., 1999; Carroll et al., 2020; Feng et al., 2020; Kono et al., 2001; Koyanagi et al., 2001; Liu et al., 2021; Sies & Parnham, 2020; Su et al., 2020). A characteristic item, Baicalein, maybe a nonpeptidomimetic substance of COVID-19 Mpro with hindrance capability of IC₅₀ = 0.94 μM. Besides, it provided powerful portion subordinate hindrance (EC₅₀ = 0.69 μM) of infective viral agent multiplication in COVID-19 contaminated Vero E6 cell measures. Not in the least like Ebselen, Baicalein, and its subsidiaries upsets each substrate acknowledgment and adjustment of proteolytic response by obstructing the substrates from moving toward the drug website instead of

covalently limiting with cytosine (Ali et al., 1999; Feng et al., 2020). Until now, some potential COVID-19 Mpro inhibitors are accounted for from compound library screening, traditional setup, and regular things together with ketoamide analogs, peptidomimetics, N-subbed isatin compounds, organo-mercuric mixtures, and some resupported medications and medicine up-and-comers with various substance structures (Ali et al., 1999; Dai et al., 2020; Feng et al., 2020; Kono et al., 2001; Koyanagi et al., 2001; Liu et al., 2021; Su et al., 2020). In silico screening projected that Maraviroc may be a doubtless substance for inhibition of Mpro (Li & Kang, 2020) and presently this medication is being assessed in clinical preliminaries for COVID-19 treatment. In addition, a hepatitis infection (HCV) NS3/4 A antiviral drug known as Glecaprevir is also in list (Liu, Liu et al., 2020; Liu, Luo et al., 2020; Liu, Zhou et al., 2020). Glecaprevir's Mpro restraint has also been evaluated in silico (Li & Kang, 2020), suggesting that Glecaprevir might be very feasible for inhibiting Mpro. Similarly, in vitro ($EC_{50} = 26.63 \text{ M}$) and in silico outputs indicated that a peptidomimetic antiretroviral aspartate antiviral drug, known as Lopinavir would block the Mpro of SARS-CoV-2 (Cherrak et al., 2020; Coelho et al., 2020; Kneller et al., 2020). Comparably, Darunavir/Cobicistat may be a fixed-portion mixture of 800 mg of the Humano Deficiency virus antiviral drug Darunavir and 150 mg of Cobicistat, a CYP3A4 substance, that is shown in the mix with alternative antiretroviral specialists for the therapy of HIV contamination. Remdesivir, shown powerful antiviral action ($EC_{50} = 0.38 \mu\text{M}$). GC376, (dipeptidyl bisulfite) a wide selection substance of picornavirus-like supercluster, may be a powerful inhibitor for the COVID-19 Mpro with IC_{50} of $26.4 \pm 1.1 \text{ nM}$ and hinders viral multiplication with EC_{50} of $0.91 \pm 0.03 \mu\text{M}$. In any case, speed up clinical exploration on GC376 for the treatment of SARS-CoV-2 is needed (Choy et al., 2020). In the examination, repurposed medications, Atazanavir and Danoprevir have displayed positive outcomes over SARS-CoV-2. Atazanavir is a federal agency-supported antiretroviral drug that seriously hinders the HIV aspartate enzyme. Nevertheless, as of late, Atazanavir has been accounted to repress COVID-19 multiplication via Mpro hindrance with $EC_{50} = 2 \pm 0.12$ in Vero and human pneumonic vegetative cell lines (Wang, Zhao, Gao et al., 2020; Wang, Cao et al., 2020; Wang, Zhao, Chen et al., 2020). The Danoprevir in combination with protease inhibitor alleviated the aspect effects in SARS-CoV-2 patients and sped up their convalescence in 4–12 days (Liu & Wang, 2020).

20.4.1.4 RNA-dependent polymerase inhibitors

A multisubunit complex of an infectious viral agent which is a nonfunctional protein, includes the middle half, nsp12, and flounce cofactors, nsp7 and nsp8, that increase RNA-dependent polymerase (RdRp) function and processivity, and help in SARS-CoV-2 genome replication (Jang et al., 2020). RdRp may therefore be a critical target for preventing infectious viral agent growth, which is inhibited by a class of antivirals known as “nucleotide analogs,” such as remdesivir (Jang et al., 2020). The triphosphate matter acts as a cutthroat matter of RdRp, causing chain stretching to halt and the infectious agent's RNA replication to end (Cao et al., 2020). Remdesivir was shown to be effective against COVID-19-infected Vero E6 cells, with an EC_{50} of $0.77 \mu\text{M}$ (De Meyer et al., 2020). Presently, remdesivir alone or in the mix with completely different medications, for instance, tocilizumab, merimepodib, or baricitinib is being assessed as a therapy for the treatment of SARS-CoV-2 infection (Hung et al., 2020). Nonetheless, there is inadequate clinical evidence to support the use of remdesivir in SARS-CoV-2 patients.

The FDA has issued a warning against using remdesivir with antimalarials or HCQ at the same time, since these medicines may reduce remdesivir's antiviral effect (Fintelman-Rodriguez et al., 2020). In a study conducted on coronavirus patients ($n = 80$) found that favipiravir (1600 mg orally right from the beginning, then, at that time 600 mg orally doubly day by day for thirteen days) in the mix with IFN- α has shown promising results (Chen, Zhang, Huang et al., 2020; Chen, Zhang, Wang et al., 2020; Chen, Zhou et al., 2020). Favipiravir (1600 mg orally doubly day by day right from the beginning, then, at that time 600 mg orally doubly day by day for 7–10 days) had a convalescence pace of 71.43% once contrasted with management bunch (umifenovir 200 mg multiple times day by day for 7–10 days) with convalescence pace of 45.86% (Yin et al., 2020). Still, it's contraindicated in girls with the proverbial or suspected physiological state. Moreover, an FDA agency-supported deoxyguanosine nucleoside, Ribavirin, maybe a big selection basic antiviral prodrug for persistent hepatitis C infection (Eastman et al., 2020) and infectious agent viral hemorrhagic fevers (VHF). It obstructs the replication of infection within the wake of obtaining utilized to its triphosphate ester. Similarly, clevudine named NCT04347915 can be a deoxythymidine nucleoside antiviral drug that expects phosphorylation to create the relating dynamic ester triphosphate (Cai et al., 2020). Besides, a prophylactic mix of emtricitabine (cytosine nucleoside simple) and tenofovir alafenamide (adenine-based mostly noncyclic ester simple) against SARS-CoV-2 contamination is being assessed in a colossal irregular, twofold visually impaired, controlled clinical preliminary study (NCT04405271) on medical services laborers bestowed to SARS-CoV-2 suffers (Dienstag & McHutchison, 2006). One of the most well-known therapeutic methods is the FDA-approved medication ivermectin, which has been shown to inhibit the importin/receptor, which controls the entry of human infectious agents into the human cell. In various clinical contexts, the drug is effective as a regulatory and medical specialty. The use of ivermectin regularly has been shown to reduce the risk of contracting SARS-CoV-2.

20.5 Drugs being used

Clinics and exploration labs all over the globe try a large variety of treatments on COVID-19 positive patients with a finish goal to trace down a possible COVID-19 treatment. The medical aid framework is increasingly stressed while providing help and compelling medical care for COVID-19 patients.

20.5.1 Potential drugs

The potential drugs available so far for the treatment of COVID-19 are enlisted in Table 20.1 which shows the comparisons of available drugs against SARS-CoV-2. The important drugs which are approved for emergency use are remdesivir, hydroxychloroquine/chloroquine, lopinavir-ritonavir, umifenovir, favipiravir, and oseltamivir. The details of each drug will be discussed in the following subsections.

TABLE 20.1 Commonly available drugs with additional information on dosage, usage, and precautions.

Drugs	AHFS class	Rationale	Dosage	Remarks
<i>Antiviral agents</i>				
Baloxvir	8:18.92 Antiviral	Active against influenza viruses as an antiviral. There are conflicting reports on potential in vitro antiviral efficacy against SARS-CoV-2.	In one open-label COVID-19 trial in adults in China, a baloxavir marboxil dosage of 80 mg on days 1 and 4, and another dose of 80 mg on day 7 (as required; not to exceed 3 total doses) was utilized.	Although it was examined as a possible therapy during the early stages of the COVID-19 pandemic, in vitro antiviral efficacy against SARS-CoV-2 was not established, and there is no evidence to support the use of baloxavir in COVID-19 treatment.
Chloroquine phosphate	8:30.08 Antimalarial	Active in vitro against SARS-CoV-1 and MERS-CoV. Known pharmacokinetics and toxicity profile based on use for other indications.	300 mg chloroquine base is comparable to 500 mg chloroquine phosphate. 500 mg twice daily for 7 days (adults 18–65 years weighing >50 kg); 500 mg twice daily on days 1 and 2, then 500 mg once daily on days 3–7 (adults weighing <50 kg).	Efficacy and safety of chloroquine for <i>treatment</i> or <i>prevention</i> of COVID-19 not established. Data from various published randomized, controlled clinical trials and retrospective, cohort studies have not substantiated initial reports of the efficacy of 4-aminoquinoline antimalarial for treatment of COVID-19. IDSA recommends against use of chloroquine (with or without azithromycin) for the <i>treatment</i> of COVID-19 in hospitalized pts.
Favipiravir (Avigan, Avifavir, Favilavir)	8:18.3 Antiviral	Nucleoside analog prodrug; RNA polymerase Inhibitor. Broad-spectrum antiviral with in vitro activity against various viruses, including coronaviruses.	A favipiravir dosage of 1600 mg twice daily on day 1, then 600 mg twice daily thereafter for 7–10 or 14 days was used in several open-label COVID-19 studies in adults and adolescents ≥ 16 years of age in other countries. Protocols in many registered trials generally specify a favipiravir dosage of 1600 or 1800 mg twice daily on day 1, then a total daily dosage of 1200–2000 mg in 2, 3, or 4 divided doses for 4–13 days for treatment of COVID-19 in adults.	Given the lack of pharmacokinetic and safety data for the high favipiravir dosages proposed for treatment of COVID-19, the drug should be used with caution at such dosages. There is conflicting evidence as to whether favipiravir is associated with QT prolongation. Some have suggested close cardiac and hepatic monitoring during treatment, as well as monitoring of plasma and tissue concentrations of the drug and, if possible, the active metabolite. Some data suggest that favipiravir exposure may be greater in Asian populations. Early embryonic deaths and teratogenicity observed in animal studies. Favipiravir is contraindicated in women with known or suspected pregnancy and precautions should be taken to avoid pregnancy during treatment with the drug.

(Continued)

TABLE 20.1 (Continued)

Drugs	AHFS class	Rationale	Dosage	Remarks
Hydroxychloroquine (Plaquenil)	8:30.08 Antimalarial	In vitro activity against various viruses, including coronaviruses In vitro activity against SARS-CoV-2 in infected Vero E6 cells reported; may be more potent than chloroquine in vitro, but some data are conflicting and additional study needed.	Oral hydroxychloroquine sulfate dosage used or being investigated in clinical trials: 400 mg once or twice daily for 5–10 days or 400 mg twice daily on day 1 then 200 mg twice daily on days 2–5.	Efficacy and safety of hydroxychloroquine for <i>treatment</i> or <i>prevention</i> of COVID-19 not established. Data from various published randomized, controlled clinical trials and retrospective, cohort studies have not substantiated initial reports of efficacy of 4-aminoquinoline antimalarial (with or without azithromycin) for the treatment of COVID-19. The benefits and risks of hydroxychloroquine (with or without azithromycin) should be carefully assessed; diagnostic testing and monitoring are recommended to minimize risk of adverse effects, including drug-induced cardiac effects.
Remdesivir (Veklury)	8:18.32 Antiviral	In vitro evidence of activity against SARS-CoV-2 in Vero E6 cells; antiviral activity against SARS-CoV-2 in human airway epithelial (HAE) cells. In vitro activity against SARS-CoV and MERS-CoV; active in animal models of SARS and MERS; prevented MERS in Rhesus macaques when given before infection and provided benefits when given after animal already infected.	Loading dose of 200 mg by IV infusion on day 1, followed by maintenance doses of 100 mg by IV infusion once daily from day 2. For pts not requiring invasive mechanical ventilation and/or ECMO, recommended total treatment duration is 5 days; if pt does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total treatment duration of 10 days). For those requiring invasive mechanical ventilation and/or ECMO, recommended total treatment duration is 10 days.	The only direct-acting antiviral (DAA) currently approved by FDA for treatment of COVID-19 in certain populations. Remdesivir clinical drug interaction studies have not been performed to date. In vitro studies indicate remdesivir is a substrate for cytochrome P-450 (CYP) isoenzyme 3A4, organic anion transporting polypeptide (OATP) 1B1, and P-glycoprotein (P-gp), and is an inhibitor of CYP3A4, OATP1B1, OATP1B3, and multidrug and toxin extrusion transporter (MATE) 1. The clinical relevance of these in vitro assessments has not been established.

20.5.1.1 Remdesivir (Veklury)

Remdesivir is a drug that is anticipated to cure SARS-CoV-2. The chemical structure of remdesivir is shown in Fig. 20.3. It's a phosphoramidite prodrug of adenosine C-nucleoside with a wide range of antiviral specialists. The Gilead Sciences developed this in 2017 as a cure for Ebola hemorrhagic fever infection contamination (Chen, Zhang, Huang et al., 2020; Chen, Zhang, Wang et al., 2020; Chen, Zhou et al., 2020). Remdesivir is employed in its dynamic structure that inhibits infective agent ribonucleic acid enzyme (Belouzard et al., 2012). Wang and their team discovered that remdesivir powerfully impedes COVID-19 contamination at the low micromolar concentration (Li, 2016). Holshue and their team elaborated that IV organization of remdesivir produced positive outcomes within the SARS-CoV-2 patient recuperating from the respiratory illness within the US. The present doses for remdesivir incorporate a 10-day routine of remdesivir care: 200 mg stacking portion on day 1, trailed by 100 mg once-day by day support dosages for nine days within the two examinations. This routine of remdesivir treatment is like that of previous irregular clinical preliminary against the hemorrhagic fever infection (Hofmann & Pöhlmann, 2004; Tang et al., 2020). Almost 70% of patients who had remdesivir through compassionate use in the US improved in terms of atomic number 8 requirements, and various individuals who were precisely ventilated were extubated, according to a study. Because this study did not consist of a control group, generalizing the outcomes is challenging. It should not be good to say if remdesivir's rapid antiviral effect on better getting free of infective agent loads inside the metabolic process tone is conclusive, but it's a hopeful restorative consequence of remdesivir (Walls et al., 2020).

20.5.1.2 Hydroxychloroquine and chloroquine

Chloroquine (antimalarial) and hydroxychloroquine (antiinflammatory) are antimalarial and antiinflammatory medicines commonly used to treat lupus, arthritic joint inflammation, and viscus disease (Yan et al., 2020; Trezza et al., 2020). Chloroquine found to be repressed COVID-19 and prevent infection by interfering with ACE2 receptor glycosylation and its binding with spike protein, implying that chloroquine treatment decreases ACE2 articulation and thereby SARS-CoV-2 (Li, 2016; Maurya, Kumar, Bhatt, et al., 2020; Maurya, Kumar, Prasad, et al., 2020; Wang, Zhao, Gao et al., 2020; Wang, Cao et al., 2020;

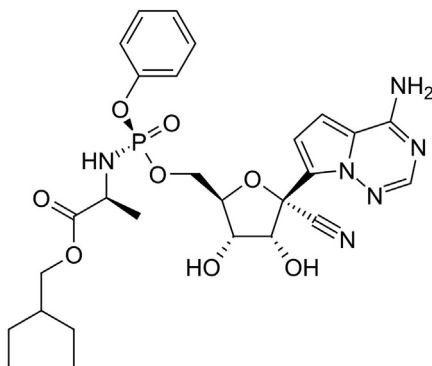


FIGURE 20.3 Chemical structure of remdesivir. Adapted from Wikipedia. Source: <https://commons.wikimedia.org/wiki/File:Remdesivir.svg>.

Wang, Zhao, Chen et al., 2020). In healthy people, as well as people with lupus and arthritic joint pain, hydroxychloroquine has a calming effect on Th17-related cytokines (IL-6, IL-17, and IL-22) (Yao et al., 2020). Chloroquine and hydroxychloroquine have been shown to reduce cytokine storms. According to one study, the primary cause of mortality in SARS-CoV-2 patients is the initiation of a cytokine storm, which leads to severe metabolic process distress (Chen et al., 2006). It's been accounted for that antiinflammatory drug is viable in restraining COVID-19 contamination in vitro (Imai et al., 2008; Prestes et al., 2017; Tahir ul Qamar et al., 2020; Wang, Zhao, Gao et al., 2020; Wang, Cao et al., 2020; Wang, Zhao, Chen et al., 2020; Yamamoto et al., 2020). In this capability, change of integrity metal with the antimalarial or antiinflammatory drug is fascinating and is at the moment being scrutinized. Typically speaking, a lot of clinical trials are ongoing to assess the safety and viability of antiinflammatory drugs as a prophylactic and care for SARS-CoV-2. The US agency has given crisis approval for the use of the antimalarial and antiinflammatory drug for the care of SARS-CoV-2. A report by Tang et al. discovered that antiinflammatory drugs did not prompt developed adverse transformation rates but had diminished medical aspect effects over the calming properties and healing of lymphocytopenia (Bestle et al., 2020). It's likewise been accounted for that prime parts of antimalarial (600 mg doubly on daily for 10 days or all-out portion of 12 g) could be connected with heart hazards and ought not to be suggested for curing SARS-CoV-2 (Bojkova et al., 2020). Therefore, due to absence of proof about the well-being and adequacy of these specialists in treating COVID-19 makes their use questionable (Hoffmann et al., 2020).

20.5.1.3 Lopinavir–ritonavir

Lopinavir is an antiviral that inhibits the HIV-1 proteolytic enzyme. Lopinavir is showcased and directed solely in the mix with protease inhibitor. This mix was initially promoted by Abbott under Kaletra name in 2000. Lopinavir is a peptidomimetic particle, consists of a hydroxy ethylene platform that impersonates the bond normally targeted on by the HIV-1 proteolytic enzyme. Lopinavir-ritonavir was examined in association to open-mark, severally irregular, controlled clinical trial, wherever SARS-CoV-2 patients got either lopinavir-ritonavir 400/100 mg, orally doubly daily additionally to plain care. No advantage was seen with the use of lopinavir–ritonavir past commonplace thought. Loose bowels, sickness, and frailness were the foremost frequently proclaimed antagonistic impacts in patients obtaining lopinavir-ritonavir-based routines. Curiously, during a report from the Korea, the lopinavir–ritonavir organization diminished SARS-CoV-2 titers with no or very few viral titers were seen within the succeeding investigation (Idris et al., 2020).

20.5.1.4 Umifenovir (Arbidol)

Umifenovir (Arbidol), was initially used in 1988 in Russia and then recommended to use in Russia and China for the prevention and treatment of respiratory illness A and B, as well as other arboviruses (Liu, Liu et al., 2020; Liu, Luo et al., 2020; Liu, Zhou et al., 2020; M et al., 2021). Its significant factor of activity is to impede the infection by inhibiting endosome fusion (Tripathi et al., 2018; Weston et al., 2020). Blaising et al. reported that umifenovir was effective against SARS-CoV-1 and SARS-CoV-2 in vitro (Abd El-Aziz & Stockand, 2020; Weisberg et al., 2020; Xia et al., 2019). A review companion observation has declared that the mix of umifenovir and lopinavir-ritonavir has presented swollen

negative transformation pace of COVID-19 and increased chest CT examine results (Xia, Liu et al., 2020; Xia, Zhu et al., 2020). In another study, examination results contrasted the use of favipiravir and umifenovir has shown substandard lead to clinical healing rate and alleviation of fever and headache (Xia, Liu et al., 2020; Xia, Zhu et al., 2020). In the Republic of China, unit 2 randomized and open-name clinical trial is being conducted to govern the feasibility and success of umifenovir against SARS-CoV-2. The impact of umifenovir additionally to plain treatment versus lopinavir–ritonavir to plain treatment currently being assessed in trial NCT04252885, and therefore the impact of umifenovir customary in addition to comparison with traditional treatment are being clinically trialed in NCT04260594.

20.5.1.5 Favipiravir

Favipiravir (Avigan) was developed in Japan by Fujifilm Toyama Chemical in 2014 for the treatment of avian infection resistant to neuraminidase inhibitors. It has, however, a guanine simple pyrazine carboxamide structure, and its antiviral activity is reduced when purine nucleosides are present on to the opposition (Klemm et al., 2020). The antiviral medication favipiravir enters infected cells by endocytosis and subsequently undergoes phosphoribosylation and phosphorylation to become active favipiravir ribofuranosyl phosphates (Yuen et al., 2020). The antiviral action is displayed specifically that specializes in traditionalist chemical space of polymer-subordinate RNA enzyme (RdRp). The dysregulation in microorganism polymerase inhibits growth (Klemm et al., 2020). Favipiravir has been employed for the therapy of irresistible sicknesses induced by ribonucleic viral infections like Ebola and norovirus (Wu et al., 2020). Later in vitro and in human investigations has repurposed favipiravir for COVID-19. Clinical preliminaries testing favipiravir over SARS-CoV-2 are completed energetically in numerous nations including China and Japan. A randomized management trial has reported that SARS-CoV-2 infected persons when treated with favipiravir have an unmatched recovery rate of 71.43% than umifenovir treatment (55.86%) (Xia, Liu et al., 2020; Xia, Zhu et al., 2020). Up to 2020, there are eight probing clinical preliminary studies in China and two in Japan looking at favipiravir's capacity to resist COVID-19. These preliminaries incorporate nonrandomized controlled trials assessing the effectiveness of favipiravir alone or associated with baloxavir marboxil tocilizumab, interferon- α , or antimalarial phosphate.

20.5.1.6 Oseltamivir (Tamiflu)

Oseltamivir can be used as medication supported for therapy of respiratory illness associated in nursing. The neuraminidase sent on the surface of the respiratory illness infection is targeted by oseltamivir to prevent the respiratory illness infection from spreading within the individual (Wu et al., 2020; Zhang, Du et al., 2020; Zhang, Lin et al., 2020; Zhang, Wu et al., 2020). However, this study in urban center declared that no positive results were seen within the wake of obtaining antiviral therapy with oseltamivir (Kandeel et al., 2021). A couple of clinical preliminary trials are now assessing the efficacy of oseltamivir in treating COVID-19 contamination (Naidoo et al., 2020).

20.5.2 Supporting agents

Without immunization or explicit antiviral medications being demonstrated over COVID-19, numerous adjunctive treatments are utilized and are under consideration for treating SARS-CoV-2 infection in patients. The ideal planning of an organization is yet to be recognized. Theoretically, hindering cytokine creation before it reaches to dangerous level could appear to be the most unthinkingly thought. Raised serum centralization of IL-6 is related to more awful results in COVID-19 and hindering the movement of this supportive of incendiary go-between with coordinated treatments might be a main objective of studies (Quimque et al., 2021). Different assistants are aimed at viral multiplication, viral section, or via any other elective components. A comparison of supporting agents is tabulated in Table 20.2.

20.5.2.1 Azithromycin

Azithromycin is an antimicrobial that will be utilized to battle varied types of infections, like skin and throat infections, and physically communicated sicknesses (Rut et al., 2021). Besides this, also used against Zika and viral hemorrhagic fever infections (Jin et al., 2020; Müller et al., 1984; Zhang, Du et al., 2020; Zhang, Lin et al., 2020; Zhang, Wu et al., 2020). It binds to the bacterial organelle's 50S subunit, inhibiting the ribonucleic acid-mediated translation (Carroll et al., 2020). Beforehand, azithromycin has been utilized as a connected treatment to convey medicinal drug inclusion and potential immunomodulatory and mitigating impacts within the treatment of flue (Ali et al., 1999; Sies & Parnham, 2020). At present, varied preliminaries are attempting the impact of azithromycin combination with antiinflammatory during illness in COVID-19 patients. Pfizer, for example, has reportable positive evidence for the use of azithromycin in a SARS-CoV-2 clinical trial conducted in France. Especially, Gautret and his team proclaimed a 100% viral infection recovery in bodily cavity swabs in their six suffers once cotreated with antiinflammatory and azithromycin (Sies & Parnham, 2020). However, the discoveries disclosed by Molina and their team stay apparently with those proclaimed by Gautret team. Molina and their team reported 8 of 11 patients had vast comorbidities. Because of these outcomes, data introduced to this point has uncertainties and deficiencies to assess conceivable clinical advantages of azithromycin in SARS-CoV-2 patients (Kono et al., 2001). Moreover, one ought to believe the added substance heart poisonousness of hydroxyl chloroquine and azithromycin. The two specialists are noted to delay the QT stretch and should raise the danger for heart problems in a very world noted to cardiovascular connected comorbidities.

20.5.2.2 Vitamin C (ascorbic acid)

Vitamin C could be a basic supplement and essential element within the body. (Koyanagi et al., 2001). Vitamin C showed some antiviral effects, notably against contagious disease infections where *Scutellaria baicalensis* extract and baicalein had been used as a source of vitamin C (Liu et al., 2021). Various examinations showed that vitamin C unquestionably influences the flip of events and the development of T lymphocytes and NK (normal executioner) cells engaged with the immune reaction to infectious agents. It enhances the production of reactive oxygen species and the modification of the cytosine network (Su et al., 2020). A stage 2 clinical trial (NCT04264533) was started in China to

TABLE 20.2 Commonly available supporting agents with additional information on dosage, usage, and precautions.

Drugs	AHFS class	Rationale	Dosage	Remarks
<i>Supporting agents</i>				
Anakinra (Kineret)	92:36 Disease-modifying antirheumatic drug	Recombinant human interleukin-1 (IL-1) receptor antagonist. IL-1 levels are elevated in patients with COVID-19; anakinra may potentially combat cytokine release syndrome (CRS) symptoms in severely ill COVID-19 patients.	Various dosage regimens are being studied. A retrospective cohort study in Italy compared high-dose anakinra by IV infusion (5 mg/kg twice daily) and low-dose anakinra (100 mg twice daily) given subcutaneously. In a French case series and a French cohort study, anakinra was given subcutaneously in a dosage of 100 mg twice daily (i.e., every 12 hours) on days 1–3, then 100 mg once daily from day 4–10.	Safety profile: Well established in adults with sepsis and has been studied extensively in severely ill pediatric patients with complications of rheumatologic conditions; pediatric data on use in acute respiratory distress syndrome/sepsis are limited. Pregnancy: Limited evidence to date: unintentional first trimester exposure considered unlikely to be harmful.
Azithromycin	8:12.12 Macrolides	Some evidence of in vitro activity against SARS-CoV-2 in infected Vero E6 and Caco-2 cells; clinical importance unclear. Has immunomodulatory and antiinflammatory effects, including effects on pro-inflammatory cytokines; precise mechanisms of such effects not fully elucidated.	Adjunctive treatment in certain viral infections: 500 mg once daily has been used: 500 mg on day 1, then 250 mg once daily on days 2–5 or 500 mg once daily for 7 days has been used in conjunction with a 5-, 7-, or 10-day regimen of hydroxychloroquine.	Only limited information available regarding the frequency and microbiology of bacterial pulmonary coinfections or superinfections in pts with COVID-19. Empiric coverage for bacterial pathogens has been used but is not required in all pts with confirmed COVID-19-related pneumonia. If bacterial pneumonia or sepsis is strongly suspected or confirmed, empiric antibacterial treatment should be administered.
Baricitinib (Olumiant)	92:36 Disease-modifying antirheumatic drug	Janus kinase (JAK) 1 and 2 inhibitor; disrupts regulators of endocytosis [AP2-associated protein kinase 1 (AAK1) and cyclin G-associated kinase (GAK)], which may help reduce viral entry and inflammation; also may interfere with intracellular virus particle assembly. Inhibits JAK1 and JAK2-mediated cytokine release; may combat cytokine release syndrome (CRS) in severely ill patients. Ability to inhibit a variety of pro-inflammatory cytokines, including interferon, has been raised as a possible concern with the use of JAK inhibitors in the management of hyper-inflammation resulting from viral infections such as COVID-19.	4 mg orally once daily for 14 days or until hospital discharge, whichever comes first. For pediatric patients 2 to <9 years of age, 2 mg orally once daily for 14 days or until hospital discharge, whichever comes first. Not authorized for pediatric patients <2 years of age. Dosage adjustment is necessary for laboratory abnormalities, including renal and hepatic impairment. Consult the baricitinib EUA fact sheet for healthcare providers for additional dosage adjustment information.	NIH COVID-19 Treatment Guidelines Panel states that there is insufficient evidence to recommend either for or against use of baricitinib for the treatment of COVID-19 in children. Emergency use authorization (EUA) for baricitinib in combination with remdesivir.

(Continued)

TABLE 20.2 (Continued)

Drugs	AHFS class	Rationale	Dosage	Remarks
Colchicine	92:16 Antigout agents	Exerts broad antiinflammatory and immunomodulatory effects through multiple mechanisms, including inhibition of NOD-like receptor protein 3 (NLRP3) inflammasome assembly and disruption of cytoskeletal functions through inhibition of microtubule polymerization. May combat the hyper-inflammatory state of COVID-19 (e.g., cytokine storm) by suppressing pro-inflammatory cytokines and chemokines.	Dosage in NCT04326790 (GRECCO-19): Colchicine loading dosage: 1.5 mg followed in 1 h by 0.5 mg (reduced to a single 1-mg dose in those receiving azithromycin); maintenance dosage: 0.5 mg twice daily (reduced to 0.5 mg once daily in those weighing <60 kg) until hospital discharge or maximum of 21 days. Dosage in NCT04322682 (COLCORONA): Colchicine 0.5 mg orally twice daily for 3 days, then 0.5 mg once daily for 27 days.	The potential for toxic doses of colchicine to affect alveolar type 2 pneumocytes (which may inhibit surfactant release and contribute to ARDS) and increase the risk of multiple-organ failure and disseminated intravascular coagulation (DIC) has been raised as a possible concern with the use of colchicine in COVID-19 patients. Pregnancy: Limited data are available on use of colchicine during pregnancy; data are lacking on use in pregnant women with acute COVID-19. Fetal risk cannot be ruled out. Pediatric use: Colchicine use in children is limited mainly to treatment of familial Mediterranean fever; data are lacking on use for treatment of acute COVID-19 or multisystem inflammatory syndrome in children (MIS-C).

assess high-portion IV vitamin C in intensive care unit (ICU) patients with extreme SARS-CoV-2-related respiratory disease (Dai et al., 2020). Several emergency rooms have announced that infected patients would be treated with 1500 mg of vitamin C daily. In China, 50 mild to serious SARS-CoV-2 patients received high-portion IV vitamin C as part of their treatment (Li & Kang, 2020; Liu, Liu et al., 2020; Liu, Luo et al., 2020; Liu, Zhou et al., 2020).

20.5.2.3 Corticosteroids

As a powerful calming and hostile to the fibrotic drug, low parts of methylprednisolone will presumably forestall a panoptic protein reaction and should speed up the goal of aspiratory and elementary aggravation in respiratory illness (Coelho et al., 2020; Kneller et al., 2020). As of late, various clinical scientists settle that corticosteroids, significantly methylprednisolone could improve dysregulated resistant reaction caused by infection (conceivable inconvenience of unwellness with COVID-19) and increment pulse once it's low (Cherrak et al., 2020). An investigation on 201 patients with Affirmed COVID-19 by WHO found that adult respiratory distress syndrome was cared with methylprednisolone using 1–2 mg/kg daily IV for 57 days and therefore the outcomes resulted that caring with methylprednisolone may be useful for sufferers. WHO results show promising effects for the treatment of adult respiratory distress syndrome in terms of the decrease of the danger of death (MacArthur & Novak, 2008). In another examination, 46 patients with serious COVID-19, utilization of methylprednisolone was connected with progress in clinical manifestations such as fever and hypoxia (Shamsi et al., 2020). Additionally, as indicated by the master agreement articulation from the Chinese body part Society, the dose routine of methylprednisolone got to be low to direct such as ≤ 0.5 –1 mg/kg day by day (Choy et al., 2020). Additional clarity is required for the correct measures (low portion vs higher portion), treatment timing (early vs late), and corticosteroid job (cytokine tempest or comorbidities the CEOs). There is concern that using corticosteroids in SARS-CoV-2 patients might have negative consequences (i.e., inhibiting safe response and bug freedom) (Coelho et al., 2020). The use of corticosteroids had no effect on mortality and reduced microbial load, according to one study (Zhu et al., 2020). Furthermore, the Yankee Infectious Diseases Society (IPS) advises in contrast to using corticosteroids in SARS-CoV-2 patients. (Wang, Zhao, Gao et al., 2020; Wang, Cao et al., 2020; Wang, Zhao, Chen et al., 2020). In any case, they furnish a proposal to the employment of corticosteroids in patients with adult respiratory distress syndrome recognizing the feeble degree of proof. Antiinflammatory has exhibited utility on adult respiratory distress syndrome by decreasing ventilator days and mortality on serious adult respiratory distress syndrome in patients while not SARS-CoV-2 (Jang et al., 2020). Despite whether or not the employment of corticosteroids furnishes comparable advantage in SARS-CoV-2 patients and adult respiratory distress syndrome is still unclear.

20.5.2.4 Nitric oxide and epoprostenol

Because patients who have previous respiratory disease history are more susceptible to SARS-CoV-2 and should be carefully supervised, pneumonic vasodilator specialists are also employed for treating hypoxemia in addition to standard medications, but no research has been done precisely on SARS-CoV-2 patients. A preliminary study on

aspiratory vasodilator strategy is proposed as salvage treatment in precisely ventilated grown-ups with SARS-CoV-2, serious acute respiratory distress syndrome, and hypoxemia notwithstanding upgraded ventilation and other salvage techniques. Participants with acute respiratory distress patients have shown that iNO may significantly reduce aspiratory pressure in nitric oxide and enhance oxygenation in patients. Furthermore, the evidence of COVID-19 direct antiviral movement was studied in vitro and its probable adequacy against COVID-19 is suggested by hereditary proximity between SARS-CoV and SARS-CoV-2. Doses of up to 50 ng/kg were used for iEPO at each time (Cao et al., 2020; Chen, Zhang, Huang et al., 2020; Chen, Zhang, Wang et al., 2020; Chen, Zhou et al., 2020; De Meyer et al., 2020; Fintelman-Rodrigues et al., 2020; Hung et al., 2020; Yin et al., 2020). According to previous research, the optimum and safe measurement for a clinically meaningful rise in PaO₂ and decrease in pneumonic course pressure in adults is 20–30 ng/kg each moment, and 30 ng/kg each moment in pediatric patients (Yin et al., 2020). Treatment was performed more than 3 days in a pilot concentration on COVID-19 using nitric oxide (Eastman et al., 2020). Furthermore, clinical studies assessing iNO for treatment or anticipation of SARS-CoV-2 are arranged or in progress. Furthermore, in March 2020, FDA conceded crisis extended admittance permitting its iNO conveyance framework (INOpulse) to be quickly utilized for the therapy of SARS-CoV-2. At last, extra investigations are expected to assess the likely job of iEPO and iNO in the therapy of SARS-CoV-2 patients.

20.5.2.5 Sirolimus

Sirolimus, named rapamycin, is an immunosuppressive drug that's employed to forestall organ relocate dismissal and to treat lymphangioliomyomatosis by inhibiting rapamycin (mTOR) enzyme (Cai et al., 2020) and industrially accessible as Rapamune (Pfizer). In an in vitro study, sirolimus has been exhibited to influence PI3K/AKT/mTOR pathway that hindered MERS coronavirus movement (Prakash et al., 2020). Another randomized twofold visually impaired faux treatment controlled clinical preliminary by the University of Metropolis was conducted to check the impact of sirolimus on the patients hospitalized with SARS-CoV-2. Investigations of patients hospitalized with grippe will in addition reveal insight into the antiviral impact of sirolimus. A study led by the Chinese University of City is also scheduled to commence in August of 2020 to study the impact of sirolimus and oseltamivir on disease standardization, biomarker variations (viral polymer concentration, 10 cytokines/chemokines for provocative arbitrators), and other clinically specific endpoints in patients living with flu. An in silico study distinguished sirolimus mutually of the 16 attainable competitors for treatment of SARS-CoV-2 patients addicted to info from alternative human COVID-19 diseases utilizing a network-based drug repurposing model.

20.5.2.6 Tocilizumab

Tocilizumab (Actemra) is a refined mAb created by Roche and Chugai Pharmaceutical for treating rheumatic arthritis and elementary adolescent joint inflammation patients. The ClinicalTrials.gov recorded 20 organized investigations that enclosed the tocilizumab treatment arm, each one of them at the enrolling stage or previous. An investigation in April 2020 on 21 basic SARS-CoV-2 patients in China was cared with the compound,

with 20 of them recuperated at the hour of distribution and heading to convalescence (yet at the constant time in ICU). Motivated by these outcomes, an even bigger multicenter clinical trial was conducted (ChiCTR2000029765) in which around 500 patients treated with tocilizumab.

20.5.2.7 Convalescent plasma

This procedure has been employed for quite a very long time. Individuals benefit from plasma since it provides antibodies and quick relief to infection. The plasma will be utilized as a preventative measure and for effectively contaminated individuals to reduce clinical severity. Part of the activity is through antibodies present against the microorganism. Beforehand, healing plasma was employed for SARS and MERS. Clinical benefits were shown in extreme cases of SARS and MERS disease, according to restricted data from Taiwan and South Korea. Elaborated measuring fluctuated generally so much because of the life of plasma and counter-acting agent concentration. The pilot study on COVID-19 infection disclosed clinical improvement in symptoms followed by convalescent plasma therapy.

20.5.2.8 Anticoagulation

SARS-COV-2 patients obtaining anticoagulants had diminished death (Te et al., 2007). Polysaccharide has calming properties and will likewise repress microorganism affiliation by means of conformational variation to the SARS-CoV-2 surface receptor (spike) S1 (Prakash et al., 2020). Low sub-atomic weight polysaccharide administered in SARS-COV-2 patients was connected with IL-6 level, recommending that there can be a further instrument aside from counteraction/treatment of attack (Dienstag & McHutchison, 2006). The blood vessel occlusion prevention with an unfractionated polysaccharide in hospitalized sufferers is a must to reduce mortality.

20.5.3 Traditional herbal medicines

Generally, customary natural medications are used within the past to manage and treat infections (Gunn et al., 2018) such as SARS and H1N1 influenza. In China, 85th of COVID-19 patients had given various ancient Chinese herbal medicines. SARS-CoV-2, like SARS-CoV, requires the ACE2 receptor for cell entry; evidently, certain standard prescriptions have the flexibility to inhibit ACE2, and they show numerous pledges to prevent COVID-19 infection. Because of the similarity in genetics, and pathologic symptoms between SARS-CoV-2 and SARS-CoV, several home-grown restorative items were employed for the treatment of SARS-CoV-2-infected patients in China and Korea (Cai et al., 2020; Prakash et al., 2020). Also, home full-grown herbs, like Shen Fu and Re Du Ning Injection, showed a decline in the level of TNF- α , IL-1 β , IL-6, IL-8, IL-10, and other different cytokines, preventing cytokine mediated respiratory organ injury. The house full-grown Qingfei Paidu boiling was urged by each China and Korea rules. As per a replacement distribution, this natural formula builds insusceptibility and lessens irritation thereby prevents the respiratory organ and spleen in COVID-19 patients. It was found that Lianhuaqingwen, a TCM formula, effectively inhibited SARS-CoV-2 replication in Vero E6 cells and greatly reduced inflammation. Sangju rule and Yinqiao San have

employed “lung heat,” taking away secretion, which eases headache, direct the patient’s lungs, and alter standard respiratory organ work (Cai et al., 2020). Similarly, Yinqiao San used antiviral and medicinal properties of TCM in many clinical studies (Cai et al., 2020; Dienstag & McHutchison, 2006; Ergönül et al., 2018; Prakash et al., 2020). All in all, apparently TCM things were typically used in COVID-19 patients with light indications to extreme facet effects and will forestall or hinder the movement of the infection. Albeit the exact mechanism of inhibition is still unknown, the possible role of calming/antioxidative pressure, antiviral workouts, might be additional causes. Further subsequent investigations are likely to reveal the mechanism of action.

20.6 Approaches for vaccine against SARS-COV-2

The whole world’s lab is racing for fostering a victorious immunization against COVID-19 illness, which decreases grimness and mortality. As of now, there is far more than 64 vaccine candidates reported and many are under the pipeline. The strategies for preparing a successful candidate vaccine involves various approaches such as messenger RNA antibodies, replication-blemished microorganism vector antibodies, inactivated organism, etc. So far, various approaches are made for immunization which is being created against SARS-CoV-2 by analysis teams in organizations and faculties across the planet (Gautret et al., 2020).

20.6.1 Viral-vector antibody

Viral vectors–based immunizations, for example, measles or adenovirus, are hereditarily designed with the goal that it can create an antibody against COVID-19 p in the body. These viral infections are debilitated so they can’t cause serious illness (Gautret et al., 2020). There are two types: those that can, in any case, imitate inside cells and those that can’t because key qualities have been impaired.

20.6.2 Inactivated virus immunizations

The debilitated or inactivated virus can elicit a strong antibody response. Several existing immunizations are tested using this approach, like those against rubeola and polio, however, they need broad security testing (Chen, Zhang, Huang et al., 2020; Chen, Zhang, Wang et al., 2020; Chen, Zhou et al., 2020). Sinovac Biotech in Beijing has begun to check an inactivated adaptation of SARS-CoV-2 in folks.

20.6.3 Nucleic acid immunizations

Several teams utilize hereditary directions (such as deoxyribonucleic acid or ribonucleic acid) for making COVID-19 vaccine that enhances an entrenched response. The nucleic acid–based vaccine candidate can be embedded into human cells, which then, at that time turn out duplicates of the infectious agent protein (Hung et al., 2020); such as spike protein thereby eliciting the immune response.

20.6.4 Protein-based antibodies

Numerous analysts infused SARS-CoV-2 proteins straightforwardly into the body. Pieces of proteins or protein shells that impersonate the SARS-CoV-2 external coat can likewise be utilized (Gautret et al., 2020). The essential SARS-CoV-2 natural qualities that are important for the vaccination plan are well explained by Chen, Zhang, Huang et al. (2020), Chen, Zhang, Wang et al. (2020), and Chen, Zhou et al. (2020). Additionally, they discussed significant findings from previous SARS-CoV-2 and MERS-CoV-2 inoculation studies, including the benefits and drawbacks of each vaccine technique (Hung et al., 2020).

20.6.5 Mechanism of activity of different vaccine candidate

Long-term antigen-dependent immune responses produced by plasma cells are induced by the best-authorized vaccinations. In the instance of COVID-19 disease, both humoral and cell-mediated immune reactions are pivotal for the protection against the virus (Hung et al., 2020). Recombinant viral vectors once introduced into the cytoplasm of the host cell, much like an indigenous pathogen elicit an immune reaction. The primary antigenic determinants of subunit peptide vaccine candidates, particularly RBD of S protein of SARS-CoV-2, can induce virus-neutralizing antibodies. The SARS-CoV-2, S protein can likewise instigate CD8 + T-cell reactions (Hung et al., 2020). The RBD of S protein contains various epitopes, which can elicit neutralizing antibody and T-cell reactions against SARS-CoV-2 infection making it important for vaccine design (Wu et al., 2020). Likewise, Adenoviral vectors can incite powerful immune reactions which include humoral and T-cell reactions with varieties in the other responses relying upon the serotype utilized. Replication-inadequate Ad5, quite possibly the most generally utilized adenoviral vectors, can initiate extraordinarily intense CD8 + T-cell just as virus neutralizer. Besides deoxyribonucleic acid vaccines are likewise ready to stimulate both humoral and cell-mediated response, through the enactment of CD8 + cytotoxic and CD4 + partner T-cells (Hung et al., 2020). Deoxyribonucleic acid antibodies are detected in the cell by a variety of natural invulnerable receptors, such as the AIM2 inflammasome, and a variety of other components are involved with DNA vaccine candidates, but the specific mechanism has yet to be determined. Nonetheless, in a mouse model, vaccination with S protein-encoding deoxyribonucleic acid immunization induced protective immunity against COVID-19 illness by stimulating T-cells and humoral response (Wu et al., 2020).

20.7 Currently available/under clinical trial vaccines

20.7.1 Vaccines available

20.7.1.1 Principles of vaccine

A general method to control the spread of the virus is to artificially expose the immune system to the viral threat. It is achieved by inserting a very small amount of dead or semi-dead virus inside our body, this process is called vaccination. Fig. 20.4 shows the process of vaccines development in normal and in pandemic situations from preclinical and

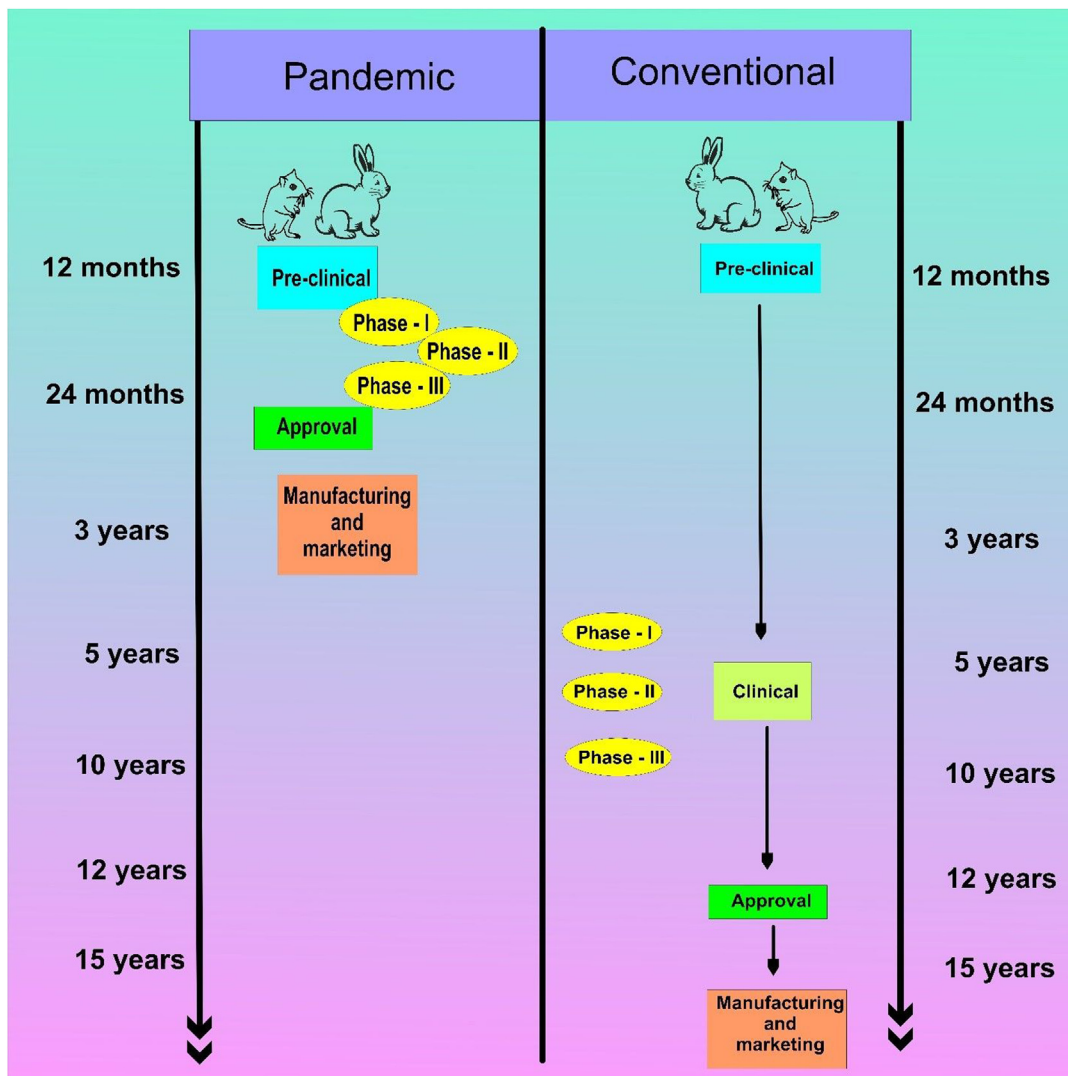


FIGURE 20.4 Process of vaccines development in normal and pandemic situations from preclinical and exploratory phase till the manufacturing and post-marketing monitoring.

exploratory phase to the manufacturing and post-marketing monitoring. SARS-CoV-2 basic structure consists of a single positive-strand nucleic acid, an S protein, an envelope, and a nucleocapsid protein. The S protein, for example, is accountable for detecting and binding to receptors on the exterior of host cells and is vital in the earliest stages of viral illness. The viral cell section is worked with by the combination of viral and host cells after the RBD of S protein ties to cell ACE2 receptors. Reports have shown that the mechanical soundness of RBD (250 pN) assumes a fundamental part in expanding the spread of

SARS-CoV-2 because of more grounded intermolecular collaborations when contrasted with RBD of SARS-CoV (200 pN) (Walls et al., 2020). The fiery investigations of RBD have given extra data concerning the adjustment of S protein during the change from near open conformity before ACE2 acknowledgment (Yan et al., 2020). Furthermore, the M and E proteins are liable for infection, and the N protein assumes a significant part in the RNA blend (Trezza et al., 2020).

20.7.1.2 Live attenuated virus Vaccines and inactivated vaccines

Live attenuated vaccines is induced antibodies against infection however there are feeble chances of virus emergence; while inactivated immunizations induce immune responses and could not multiply in vivo. (Chen et al., 2006; Imai et al., 2008).

20.7.1.3 Subunit vaccines

Subunit vaccines are mostly produced from nonhereditary viral proteins or peptide components (Chen et al., 2006). Investigations have shown that a large portion of the SARS-CoV-2 subunit vaccine from targets proteins, especially the spike protein, in explicit regions; while some other subunit vaccines center around N proteins. (Chen et al., 2006). MigVax is currently fostering SARS-CoV-2 subunit immunization (Bestle et al., 2020; Imai et al., 2008; Yamamoto et al., 2020).

20.7.1.4 Vector vaccines

Depending on the ability to imitate, vector antibodies are divided into two categories: replicating and nonreproducing vectors. Large numbers of these viral vectors proved unable or can just make restricted multiplication in human body cells, and accordingly, have the least security worries upon application. Viral vectors for the most part can perform a speedy blend of recombinants, confirm protein articulation, and speed up the improvement of the insusceptible framework. Further, if the antibody has been recently presented against the designated viral infection, the viability of the immunization could be diminished because of the all-around existing resistance over the vector. At present, Hamilton, MIT Institute, is helping out Oxford to foster a chimpanzee adenovirus vector-based vaccine. The University of Oxford and AstraZeneca collaborated to develop AZD1222, against spike protein and it is presently in phase 2/3 clinical trial (Idris et al., 2020).

20.7.1.5 Nucleic acid vaccines (mRNA vaccines and DNA vaccines)

Without utilizing live pathogens, nucleic acid vaccinations may be bulk produced at a low cost. Because they have usually little or no risk of damage or sickness when they're used (M et al., 2021). Notwithstanding, at the momentum phase of exploration, the conveyance of DNA antibodies is somewhat difficult as the necessary measurement is generally huge. Then again, RNA immunizations face difficulties within in vivo transfection productivity (M et al., 2021). Up to March 21, the INO-4800 antibody is leading phase 2 clinical trial, and the essential engineer has likewise wanted to test the immunization against the recently arisen variations (Liu, Liu et al., 2020; Liu, Luo et al., 2020; Liu, Zhou et al., 2020). While phase 3 trials are being directed, the Moderna has granted approval for immunization in Switzerland. Pfizer and BioNTech are working together to develop four m-ribonucleic acid-based vaccine strategies, as well as two nucleoside adjusted m-ribonucleic acids including uridine and

self-intensifying ribonucleic acid–based vaccine (Tripathi et al., 2018; Weston et al., 2020). Royal College London has likewise investigated a “self-intensifying” ribonucleic acid–based vaccine however the venture was ended on January 27, 2021 because of fast infection transformation (Weisberg et al., 2020; Xia et al., 2019).

20.7.2 Vaccines under trial

In the current scenario of the pandemic, scientists and researchers have rushed to control the spread of this deadly virus. An effective way to control is to vaccinate all humans so that the severity of disease due to SARS-CoV-2 can be avoided. Fig. 20.5 shows the schematic depicting SARS-CoV-2 and possible vaccine targets. In addition to the spike S protein, the virus also contains membrane and envelope proteins. SARS-CoV-2 is a single-stranded RNA virus. From the viral sequence, DNA- and RNA-based vaccinations can be produced. For example, adenovirus vector vaccines integrate genetic material from SARS-CoV-2 into the viral genome. Some vaccine candidates contain SARS-CoV-2 that has been inactivated by physical or chemical agents.

A huge advancement in the field of vaccine development and innovation has occurred recently which include ribonucleic acid and deoxyribonucleic acid–based vaccine,

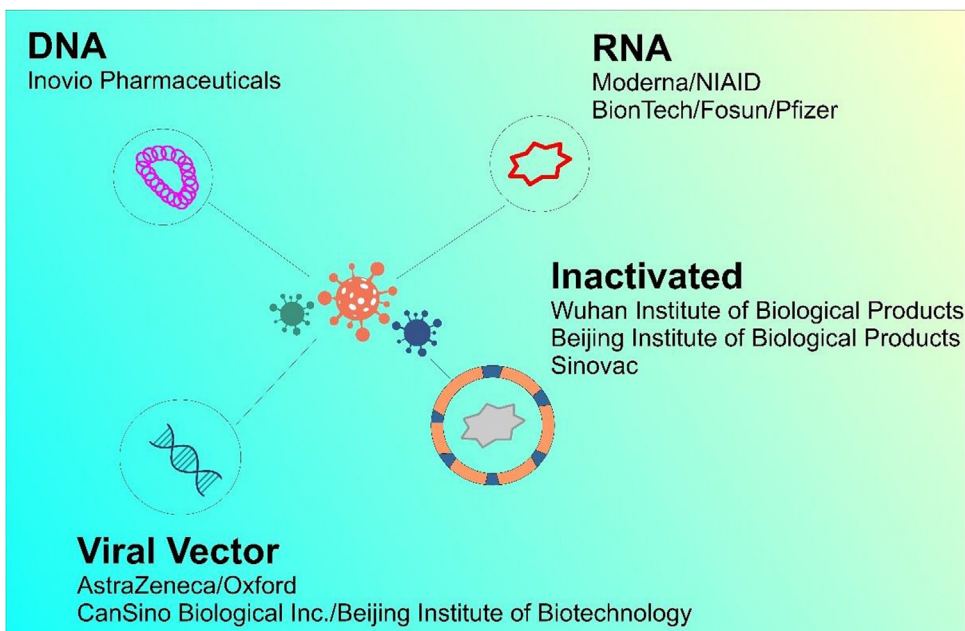


FIGURE 20.5 Schematic depicting severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) and possible vaccine targets. In addition to the spike S protein, the virus also contains membrane and envelope proteins. SARS-CoV-2 is a single-stranded RNA virus. From the viral sequence, DNA- and RNA-based vaccinations can be produced.

vectored immunizations, recombinant supermolecule, and cell-culture-based immunizations (Weston et al., 2020). As of currently 7, 28, 5, 25, and 20 teams are working on the development of vaccine candidates and many of them are under clinical trial (Callaway, in the year 2020) (Xia, Liu et al., 2020; Xia, Zhu et al., 2020). Normally, vaccine development which involves follows Research and development, clinical trials, and endorsement from government body organizations, require at least 12 years to come to market, but COVID-19 vaccine trials took a much shorter period and the vaccine come to the market in approximately 18 months. Vaccine approaches available against COVID-19 include ribonucleic acid—deoxyribonucleic acid, recombinant supermolecule, microorganism vector-based mostly, live constricted, and inactivated vaccine (Carroll et al., 2020; Jin et al., 2020; Müller et al., 1984; Zhu et al., 2020). Moderna medical specialty (Cambridge, US) with alternative two associations area unit reciprocally operating for its flip of events and clinical preliminary. (Holshue et al., 2020). it's expected that, once infusion, have cells can take up informational RNA and manufacture supermolecule within the safe framework to make reactions toward SARS-CoV-2 spikes protein. m-Ribonucleic acid-1273 protein has passed stages 1 and 2 through 10,000 and 600 volunteers (matured 18–54), and therefore the recommended portion is 50-50, nevertheless, this immunization is at this time inaccessible in business sectors (Cohen, 2020). As of late, vaccination of m-Ribonucleic acid-1273 (NCT04283461) among 45-sound grown-ups separated in three portion gatherings (25, 100, and 250 µg). Moreover, no trial limiting upbeat worries was distinguished among those members, that support more advancement of the protein. In another study, SCB-2019 a piece ongoing by herbaeous plant Biopharmaceuticals (Changxing from China), which is in stage I clinical trial (NCT04405908) of a 150 folks. A trimeric CoV-2 S supermolecule is delivered by class cell culture, once infusion could foster neutralizer antibody against this infection limiting with having cells to forestall contamination. Initially, immunogenic nanoparticles were created using Sf9 creepy-crawly cells contaminated with baculovirus vectors to spike SARS-CoV-2 S supermolecule at the cell surface. Antigen-introducing cells were able to access the surrounding bodily fluid hubs after contractile organ infusion of those nanoparticles. Likewise, right away mRNA-based immunizations from vital drug organizations such as CureVac (Tubingen from Germany), Pfizer (New royal family from US), and BioNTech (Mainz from Germany) clinical trials are also going on (Tang et al., 2020) Fig. 20.6 shows the available vaccine (A) AstraZeneca, (B) Pfizer, (C) Moderna, and (D) Sputnik V. Table 20.3 shows a comparison of available COVID-19 vaccines for emergency use against SARS-CoV-2 along with their dosage and relevant information.

The inactivated animal virus vaccine Ad5-nCoV is in stage II trial. Its stage 1 clinical trial enclosed 108 volunteers (matured 18–60 years) in urban center, China, and is relied upon to be finished in December 2022 (Yamamoto et al., 2020). Shenzhen Geno-resistant Medical Institute, China created COVID-19/fake antigen-introducing cells (aAPCs) and LVSMENP-DC immunizations by the lentivirus-mediated vaccine, for SARS-CoV-2 are also in a row (SMENP) (Naidoo et al., 2020; Kandeel et al., 2021; Quimque et al., 2021; Rut et al., 2021; Zhang, Du et al., 2020; Zhang, Lin et al., 2020; Zhang, Wu et al., 2020; Carroll et al., 2020; Feng et al., 2020). Another lot of affordable methodologies may be to style monumental scope, logical cooperative examinations



FIGURE 20.6 Available vaccines: (A) AstraZeneca, (B) Pfizer, (C) Moderna, and (D) Sputnik V.

(adaptive trials) with institutional supports, for instance, by the NHS within the UK which embraced the RECOVERY preliminary, WHO-supported commonness, the ACCORD stage likewise within the UK, or ACTIV within the US. the chance to urge speedy outcomes regarding the adequacy of another or notable drug/vaccine in a very altogether strange setting got to support the necessity to create travel medication analysis teams during which the mastery of various clinical consultants will deeply cross therewith of diagnosis scientists (e.g., pharmacologists, scholar, biotechnologist, organic chemistry and, physiologist). Within the worldwide systems administration amount, early reports on the potential viability of medicines, prescription, or different advances will beyond any doubt flow and establish a big profit for the advancement and also the structure of energizing “rapid” analysis results. Then again, we will not neglect to altogether explore by maintaining measures that make sure the well-being of medication answers.

TABLE 20.3 Available Coronavirus disease-2019 vaccines along with their dosage and relevant information.

Developer	Bharat Biotech Covaxin	Moderna	AstraZeneca	Novavax	Johnson & Johnson	Pfizer-BioNTech	Sputnik V
Vaccine type	Whole virion inactivated with adjuvant Alhydroxiqum-II	mRNA	Carrier	Protein adjuvant	Carrier	mRNA	Adenovirus viral vector
Recommended for	18 years and older	18 years and older	18 years and older	18 years and older	18 years and older	12 years and older	18 years and older
Dosage	2 doses with gap of 4 weeks	2 doses with gap of 4 weeks	2 doses with gap of 4 to 12 weeks	2 doses with gap of 3 weeks	1 dose	2 doses with gap of 3 weeks	2 doses with gap of 3 weeks
Overall efficacy	77.8%	94%	76%	90%	72%	95%	90%
Common side-effects	Injection-site pain, swelling, redness, itching, headache, fever, malaise/body ache, nausea, vomiting rashes.	Fever, muscle aches, headaches lasting a few days. Effects worse after second dose.	Injection-site pain, fever, muscle aches, headache.	Injection-site tenderness, fatigue, headache, muscle pain.	Injection-site pain, headache, fatigue, muscle pain.	Fatigue, headache, chills, muscle pain, especially after the second dose.	Flu-like illness, headache, fatigue, injection-site reactions.
Extremely rare side-effects	–	Chest pain, shortness of breath or feelings of having a fast-beating, fluttering or pounding heart within a week of getting the vaccine.	Extremely rare cases of transverse myelitis have been reported.	–	Severe symptoms include shortness of breath, persistent stomach pain, chest pain, leg swelling, easy bruising, and tiny red spots on the skin.	Heart problems after mRNA vaccination, particularly after the second dose of the vaccine and within several days of vaccination.	Deep vein thrombosis, hemorrhagic stroke, and hypertension.

20.8 Future prospects

An effective drug/vaccine would be definitive prevention to combat SARS-CoV-2 mediated pandemic, but the availability of immunization/drugs is a matter of concern among the folks. Also, early detection of SARS-CoV-2 infection among individuals plays a crucial role to curb down the spread of infection (Parihar et al., 2020). The New York Times assessed that a COVID-19 immunization to the whole world might be achieved in 2036, once the end of scholastic exploration, a progression of diagnosing and clinical trials, building plants, assembling, endorsement, and dispersion would be achieved. Aside from these, vaccines cannot be infused on people while not thorough eudaimonia checks, that is implausibly tedious, because it includes varied clinical stages with various volunteers of varied age gatherings, racism, and medical issues, but such trials are vital forerunners to the endorsement of another immunization/vaccine. Other than all the frustration and misery, some of the immunizations that area unit enrolling volunteers and specialists leading varied trials will presumably be amended in the pandemic circumstance shortly. Besides, remedial medications that are supported against varied infectious agent contaminations beforehand could facilitate in handling COVID-19. Aside from the impediments, emplacement of these medications and vaccines might facilitate the setup, creation, and dissemination through the market. As we tend to see quickly mutating strains of SARS-CoV-2, it's going to need a chase down viable drug which can also be the best option for the administration and therapy of SARS-CoV-2 indicative cases. Utilizing bioinformatics tools to an additional elevated level of exactitude can be exploited as a customary technique in this context for getting more suitable repurposed drugs.

20.9 Conclusion

The COVID-19 pandemic addresses the best worldwide general well-being emergency in the previous 100 years. Further examination and investigation might be justified later on to decide the advantages and ideal utilization of some of the accessible treatment choices through a repurposing strategy. Other than vaccines and medication, corresponding and substitute medicines utilizing plant-based phytochemicals could be extraordinarily encouraging for diminishing the seriousness of the disease. With all boundless conceivable outcomes soon, investigators are yet going through with a few promising methodologies with the last expectation, the fix from COVID-19, and along these lines controlling the pandemic around the world (Khan et al., 2021). The prospective therapeutic choices mentioned in this study are exclusively based on the most recent research findings for the treatment of COVID-19. The present state of repurposing medicines, such as remdesivir, favipiravir, lopinvar/retinavar, hydroxychloroquine, monoclonal antibodies, and vaccines against the SARS-CoV-2 illness, has been summarized in this chapter. New medication development is a lengthy and complicated process. As a result, repurposed medicines might be a viable option for combating COVID-19. Vaccines, on the other hand, are showing promising outcomes in clinical studies when compared to alternative treatment approaches. More than 100 vaccinations are being tested, but only four have been

authorized by the WHO for the prevention and treatment of COVID-19. In several countries, the WHO supports COVID-19 vaccine producers and assures its safety in vaccination. Even those with preexisting autoimmune diseases were shown to be safe after receiving the vaccinations. Many nations have granted emergency use authorization to several vaccines, although high-risk persons over the age of 60 must still be closely monitored. Given that a major percentage of the clinical preliminary studies recruited at various sites are expected to be completed by 2021 or mid-2022, it is expected that effective avoidance and treatment estimates will be available shortly. Overall, the newly discovered COVID-19 vaccinations offered hope for a future brighter than 2020, but they also presented obstacles. Several vaccinations have been licensed in a number of countries. Russia and China began vaccinations in the second half of 2020, while the rest of the world began in December 2020. By the year 2021, these vaccinations will have been widely distributed, and the desired aim of suppressing the COVID-19 pandemic will have been achieved. COVID-appropriate behavior and immunization remain the mainstays of disease management due to restricted therapeutic alternatives (Khan et al., 2021). The scientific community is still grappling with a few questions about the efficacy of vaccinations in terms of the form and duration of the protective immune response against SARS-CoV-2. The observed mutation in the spike glycoprotein and its probable impact on T-cell immunity is a serious concern for vaccination effectiveness. However, it is important to remember that widespread vaccination will result in fewer vulnerable individuals and less chance for SARS-CoV-2 to proliferate and evolve. Covishield and Covaxin are the vaccinations now being used in India. Based on published results, the COVID-19 Working Group amended and increased the time between the two doses of the Covishield vaccine from 6–8 weeks to 12–16 weeks. Because no such information is available for Covaxin, the interdose interval has been maintained at 28 days. Although we may not know for several years if vaccinations are successful in reducing COVID-19 symptoms, severe disease, or deaths, the urgent requirement is to increase large-scale immunization by addressing vaccine shortages and micromanagement of immunization programs on the ground. We all bear joint responsibility for an efficient vaccination program in India, because vaccination protects not only the vaccinated but also the people with a weakened immune system that cannot be vaccinated. However, in addition to this Sputnik V is also rolled out in some parts of the country. There are both free and paid vaccinations available in almost many countries and people are getting successful results with the application of all these drugs and vaccines in play. The booster shot is available and under trial for most of the vaccines which increases the efficacy of a particular vaccine with others.

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