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Review Article

COVID-19 Insights: Pathology, Mechanism, Diagnosis, Treatment Approaches & Novel Anti-Viral Agents

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ABSTRACT

In Wuhan, Hubei Province, China, in December 2019, a novel coronavirus that is now known as SARS-CoV-2 caused a number of acute atypical respiratory illnesses. This virus created a condition known as COVID-19. Human-to-human transmission of the virus has led to a global pandemic. There were no pandemic-causing targeted therapies or methods of diagnosis at the time. After then, standard antibiotics and antiviral treatments were utilised in the treatment. Vaccines for immunisation have been created. In order to respond to the present pandemic quickly, it is essential to evaluate and use the antiviral medications that are currently on the market. Here, we looked at the anti-SARS-CoV-2 drug groups—fusion inhibitors, protease inhibitors, neuraminidase inhibitors, and M2 ion channel protein blockers—that are currently on the market. Clinical trials for these vaccinations and antiviral medications have been running up until this point for total coronavirus immunity. We have complied with permitted and in-development coronavirus vaccines, antiviral drugs, and other drugs.

INTRODUCTION

In Wuhan, Hubei, China, on December 31, 2019, a number of acute unusual respiratory illnesses manifested. This quickly spread outside of Wuhan. It rapidly became apparent that a brand-new coronavirus (beta-coronavirus) from the Coronaviridae family was causing the problem. Due to its strong homogeneity to SARS-CoV, which caused acute respiratory distress syndrome (ARDS) and a respiratory pandemic with a high fatality rate in 2002–2003, the novel coronavirus was given the name severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCoV). 1,2 Using zoonotic transmission linked to seafood in a market in Wuhan, China, SARS-CoV-

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2 spread across the community. Later, it was shown that SARS-CoV-2 transfer from person to person is a major factor in the disease's global spread and the development of a pandemic crisis.3 After being a public health emergency and wide community spread throughout 200 countries WHO declared COVID-19 pandemic on March 11, 2020.4,5 A lot of people have been impacted by COVID-19, which has been documented in about 200 nations and territories worldwide. According to the Centre for Systems Science and Engineering (CSSE) at John Hopkins University, there have been over 1,400,000 cases reported globally as of April 7th, 2020, with approximately 536 893 documented deaths.6 Although other organ systems are also affected, the respiratory system is the one that is initially impacted by novel coronavirus. In the first case series from Wuhan, China, symptoms associated with lower respiratory tract infections such as fever, dry cough, and dyspnea as well as headache, generalised weakness, and vomiting were noted.6,7 The COVID-19 mortality rate is higher in elderly people with comorbidities such hypertension, diabetes mellitus, cardiac risks, and acute or severe renal and hepatic disorders, according to epidemiological studies. When infected with a virus, patients who are immunosuppressed, have cancer or are pregnant are also more likely to experience severe illness. Since there isn't a known specific treatment for SARS-CoV-2, the majority of medical attention provided nowadays is supportive.2,8 When compared to earlier respiratory pandemics of SARS-CoV-1 in 2003 and the Middle East Respiratory Syndrome coronavirus (MERS-CoV) in 2012, this virus is more dangerous to humans and spreads quickly throughout communities than other endemic viruses.1 Coronavirus has large (around 30 kb) single-stranded, positive-sense RNA genomes and shares about 80% of its nucleotides with other coronaviruses. RaTG13-2013, a virus found in bats, is very similar to SARS-CoV-2 (shares 90% of its nucleotide structure).2,9

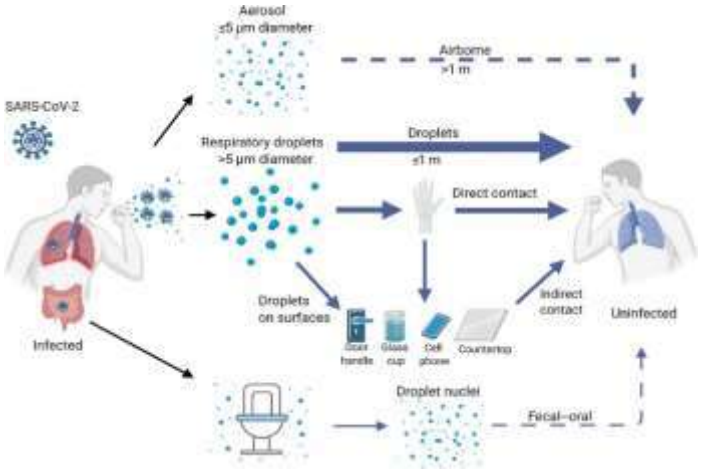


Figure 1 Proposed Route of Transmission of COVID-19 39

As a result of the ongoing COVID-19 epidemic, various human-to-human transmission routes have been reported. The most prominent and highly implicated route of transmission documented during the epidemic is droplet transmission (>5 µm). (Figure 1) Human-to-human transmission has also been linked to direct contact between an infected person and a naïve person, particularly in homes where family members interact closely. Although it occurs less frequently than droplet or contact-driven transmission, the contagiousness of SARS-CoV-2 after disposition on fomites (e.g., door handles) is still being investigated. 39

Although they have not yet been noted in the present crises, both airborne and fecal–oral human-to-human transmission events have been recorded in the preceding SARS-CoV epidemic. Solid arrows show confirmed viral transmission from one infected individual to anotherviral transmission from one infected individual to another is shown by solid arrows; a decreasing gradient in arrow width indicates the relative contributions of each transmission pathway. The probability of transmission types that are not yet confirmed is indicated by dashed lines. When an RNA or infectious virus is found, it is indicated by the SARS-CoV-2 symbol in the "infected patient" field. 39

PATHOLOGY

Coronaviruses are positive-sense, 30 kb enclosed viruses with a single-stranded RNA genome. They affect many different host species. 1 Based on their genetic structure, they are typically divided into four genera: α, β, γ, and δ. mammals are infected by only α and β coronaviruses.10 Human coronaviruses, including 229E and NL63, are known to be the source of the common cold and croup. MERS-CoV is the coronavirus responsible for the Middle East respiratory syndrome, but SARS-CoV, MERS-CoV, and SARS-CoV-2 are all coronaviruses. The five stages of the virus's life cycle within the host are attachment, penetration, biosynthesis, maturation, and release. 4 Pathogens, such as viruses, are those that adhere to host receptors and penetrate host cells by endocytosis or membrane fusion. (Figure 2)

Structure of virus:

The four principal structural protein-coding genes present in coronaviruses are spike protein (S), envelope protein (E), membrane protein (M), and nucleocapsid protein (N). 11 Angiotensin-converting enzyme (ACE2) serves as the SARS-spike CoV-2 protein's cell surface receptor, controlling the tropism of the virus.2 The most important component for viral attachment and host penetration, the S protein, is visible and protrudes from the viral surface. Two functional subunits (S1 and S2) make up this protein, with S1 being in charge of attaching to the host cell receptor and S2 being in charge of fusing the membranes of the host and viral cells. 1 While the viral M protein facilitates integration into the cellular endoplasmic reticulum, the viral N protein binds the new genomic RNA. 11 These recently produced Nucleocapsids are then encapsulated in the ER membrane and transported to the lumen, where they are then transported to the cell membrane via Golgi vesicles and, finally, to the extracellular environment by exocytosis.4

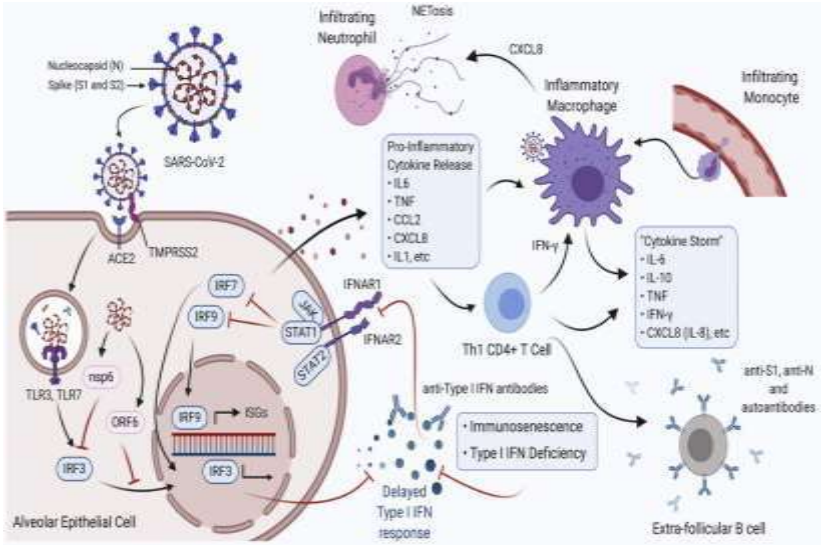


Figure 2 The Replication cycle of SARS- CoV-2 14

Physiological and Pathological host response

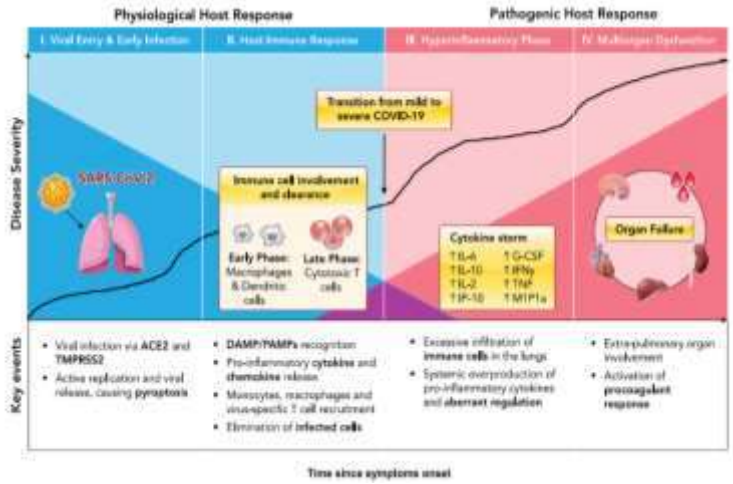


Figure 3 Pathophysiological changes in the host during COVID-19 infection 11

DIAGNOSIS

In patients with clinical evidence of COVID-19 infection, laboratory tests may reveal I lymphocytopenia, (ii) thrombocytopenia, (iii) elevated liver transaminases, (iv) elevated C-reactive protein and erythrocyte sedimentation rate, (v) elevated serum lactate dehydrogenase, and (vi) decreased or normal serum albumin.1,2

1. Viral testing

This test, known as RT-qPCR, is used to qualitatively identify the SARS-CoV-2 nucleic acid. Swabs are typically obtained from lower respiratory tract aspirates or washes, nasal, nasopharyngeal, oropharyngeal, sputum, or sputum. Positive test results show that SARS-CoV-2 RNA is present, which supports the diagnosis when combined with the clinical presentation. Negative test findings should be interpreted in the context of the clinical picture and available epidemiological data, as they do not rule out SARS-CoV-2 infection. 1,2

2. Serology

The test cannot be used to diagnose an infection that is currently present, but it can evaluate previous exposure to the virus. There could be cross-reactivity with different human coronaviruses. When the viral test is unavailable, the serology test is especially helpful (i). Making decisions can be guided by the serology test in conjunction with the clinical picture; (ii) Patients who present with late complications of the disease require prompt medical attention from physicians due to the longer turnaround time for viral testing results; (iii) In certain patients, viral shedding is reduced, leading to false negative results from RT-qPCR. IgM and IgG antibodies against SARS-CoV-2 can be found in serum, plasma, and whole blood using the serology test. 1,2

3. Rapid antigen testing

This assay uses a monoclonal antibody to detect the nucleocapsid (N) protein of SARS-CoV-2. Infected cells express this protein abnormally. SARS-CoV-2 can be detected utilising enzyme-linked immunosorbent test (ELISA) and monoclonal antibodies that are particularly directed towards N protein. The test's stated specificity is 98.5%, and its sensitivity is 84.1%. There were no known cross-reactions between the assay's human and animal coronaviruses. As of yet, there are no reports of using this test on SARS-CoV-2. 1,2

4. Ultrasonography

Complete body point of care Ultrasonography has been applied to COVID-19 patients. When treating patients with cardiorespiratory failure, ultrasound is seen to be a crucial tool in the

intensive care unit (ICU) and the wards. As of right now, using it for multisystem and whole-body sonography for thoracic, cardiac, abdominal, and deep vein thrombosis is advised. 1,2

5. **Computed tomography (CT) scan of the chest**

Prior research conducted during the Chinese outbreak revealed that pneumonia patients with and without SARS-CoV-2 could be distinguished using CT chest imaging in addition to clinical presentation. The authors suggest that clinical features and radiological imaging can make good COVID-19 diagnostic tools. A patient's age, the existence of comorbidities, a high viral load, an elevated neutrophil lymphocyte ratio (NLR), changes in the CT chest and the extent of the lesion, and CT chest changes are all potential indicators of severe disease. 1,2

Extrapulmonary changes in COVID-19

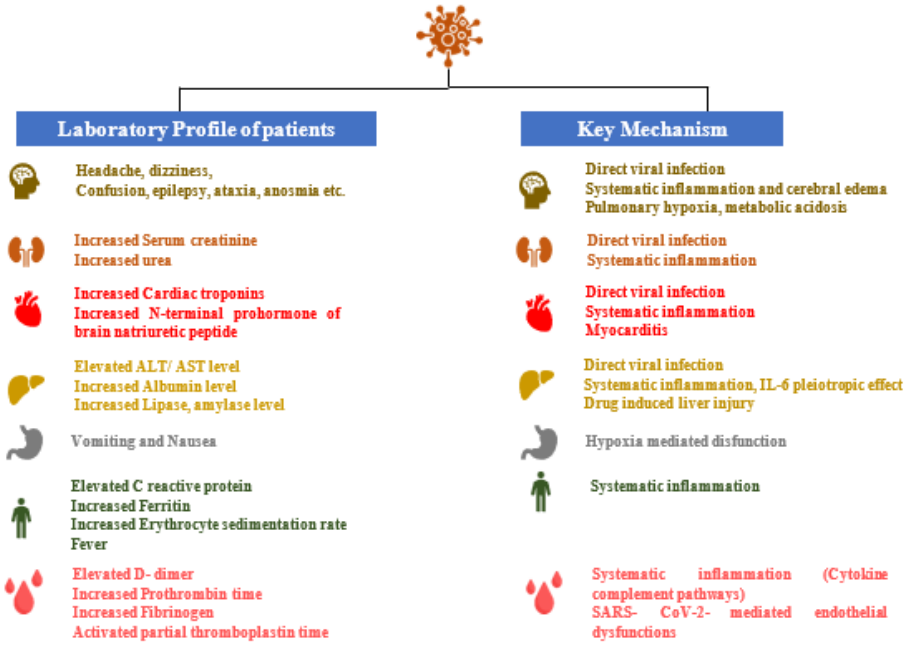


Figure 4 Extrapulmonary changes in COVID-19 [11]

Figure 4 Extrapulmonary changes in COVID-19 11

Vaccines for COVID-19

There is an international effort to develop a SARS-CoV-2 vaccine, and as of the end of August 2020, 30 vaccines were undergoing clinical trials, with more than 200 others in various stages of development. 12 A number of platforms are being taken into consideration for the development of COVID-19 vaccines. (Table 1) Among these are RNA, DNA, non-replicating viral vectors, and inactivated vaccines.13

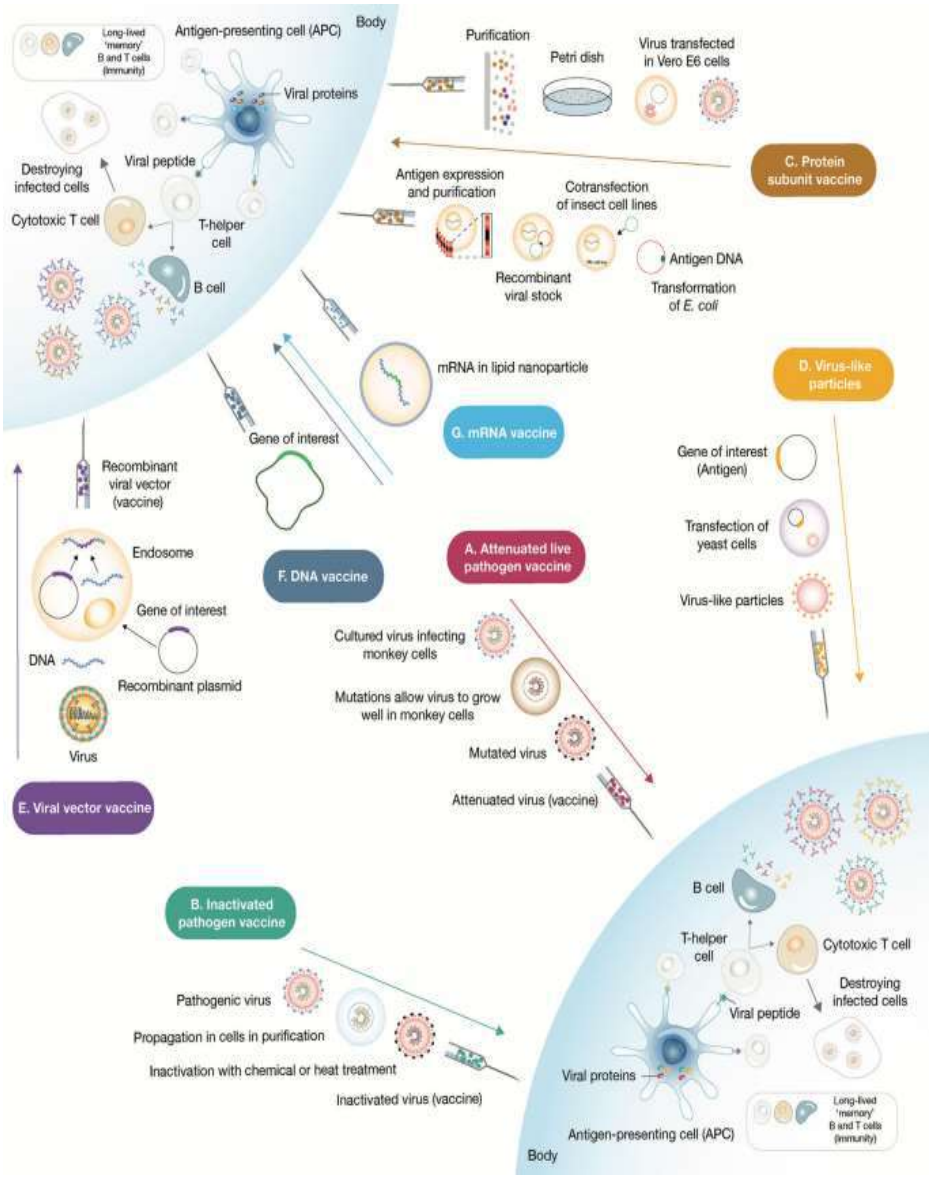


Figure 5 Candidates for vaccine 22

Table 1 Covid-19 vaccines12,13

Manufacturer	Target of antigen	Type of vaccine	Immune response	Advantages	Disadvantages
Inovio Pharmaceuticals	Spick protein	INO-4800 DNA plasmid vaccine with electroporation	Both humoral and cellular	An active immunological response results from electroporation.	It can be challenging and problematic to conduct electroporation. DNA vaccines need a unique delivery system.
Moderna	Spick protein	M-RNA 1273	Both humoral	Scalability. rapid development and	m-RNA vaccines

		Lipid nanoparticle [LNP]-encapsulated mRNA	and cellular	design. Highly safe. Handling infectious agents is not necessary.	exhibit instability and require storage at < −20°c. LNP is temperature sensitive
Biontech/Fosun Pharma/Pfizer -	Spick protein	LNP-mRNAs	Both humoral and cellular		
AstraZeneca/ University of Oxford	Spick protein	AZD1222 Replicated defective viral vector	Both humoral and cellular		
Cansino Biological Inc./Beijing Institute of Biotechnology	Spick protein	Adenovirus type 5 vector Replicated defective viral vector	Both humoral and cellular		
Gamaleya Research Institute/Health Ministry of the Russian Federation/Acellena Contract Drug Research and Development	Spick protein	Gam-COVID-Vac/Sputnik V Replicated defective viral vector	Both humoral and cellular	Safe and effective immunologically	Immunity from the past may limit clinical use and weaken immune response.
Janssen and Beth Israel Deaconess Medical Center	Spick protein	JNJ-78436735/Ad26.COV2.S Replicated defective viral vector	Both humoral and cellular		
Wuhan Institute of Biological Products/Sinopharm	Whole virus	Inactivated pathogen vaccine	Mostly humoral	due to the pathogen's death, safety. Storage and transportation.	The pathogen must be processed in large quantities. Antigen immunogenicity may be affected by the inactivation process.
Sinovac Research and Development Co.	Whole virus	Coronavac Inactivated pathogen vaccine with aluminum adjuvant	Mostly humoral		

Beijing Institute of Biotechnology/ China National Biotech Group-Sinopharm	Whole virus	BBIBP-corv Inactivated pathogen vaccine	Mostly humoral		
Bharat Biotech/ Indian Council of Medical Research/ National Institute of Virology	Whole virus	Covaxin/BB V152 Inactivated pathogen vaccine	Bharat Biotech/ Indian Council of Medical Research/ National Institute of Virology		
Novavax	Spike protein	NVX-cov2373 Protein subunit vaccine	Both humoral and cellular	safety during production. can be given to immunocompromised patients without risk. Handling infectious agents is not necessary.	Antigen uptake by APCs is reduced by their modest size. minimal immunogenicity. Adjuvants and multiple booster doses are required. Do not cause cellular reactions. Confirmation of antigen integrity is required. Scalability of antigen production places a cap on output.
Anhui Zhifei Longcom Biopharmaceutical/Chinese Academy of Medical Sciences	Spike protein	ZF2001 Protein subunit vaccine	Both humoral and cellular		
Medicago	Attenuated pathogen	Covlp	Not reported		

Antiviral treatment for covid

The majority of COVID-19 medications are authorized antiviral agents or antibodies that are used to treat diseases other than COVID-19.14 Theoretically, in the early stages of COVID-19, treatment with effective antiviral agents could provide greater benefits. In addition to antiviral therapy, anti-inflammatory agents may aid crucial COVID-19 patients with cytokine release syndrome. (Table 2)15

Table 2 Antiviral agents

Class of drug	Name of drug	Mechanism of drug	Dose	Adverse effects
Nucleotide reverse-transcriptase inhibitors	Remdesivir **Error! Reference source not found.–Error! Reference source not found.**	RNA viruses like Coronaviridae and Flaviviridae are susceptible to the effects of this monophosphate prodrug, which metabolises to an active C-adenosine nucleoside triphosphate analogue. Remdesivir, in its triphosphate form, inhibits the production of viral RNA by acting as a substrate for RNA-dependent RNA polymerase complexes in coronaviruses.	Remdesivir under investigation is a single 200 mg loading dose, followed by a 100 mg daily infusion.	Elevated liver Enzymes, diarrhea, Hypotension, acute Kidney injury, atrial Fibrillation, deep Venous thrombosis.
Fusion inhibitors	Baricitinib**Error! Reference source not found.**	A Janus kinase (JAK) inhibitor with a strong affinity for AAK1 (AP2-associated protein kinase 1) and the ability to bind to and inhibit it.	1mg/2mg/4 mg tablet once daily	Acute tonsillitis Nausea Cold sores. Shingles.
Fusion inhibitors	Umifenovir**Error! Reference source not found.**	Targeting the fusion mechanism of the influenza virus's hemagglutinin envelope glycoprotein (HA).	200mg three times a day	Nausea and vomiting
Fusion inhibitors	Camostat mesylate **Error! Reference source not found.**	Inhibitor of serine proteases. Mesylate has TMPRSS2 inhibitory effects. It prevents surface fusion by downregulating the expression of the SARS-cov-2 spike (S) protein, which in turn prevents the virus from entering cells.	600mg three times a day	Edema and urticaria
Protease inhibitors	Lopinavir/ritonavir**Error! Reference source not found.,Error! Reference source not found.,Error! Reference source not found.**	Inhibitor of the human immunodeficiency virus's aspartate protease. Unlike coronavirus, which has a C2-symmetric pocket, lopinavir suppresses the activity of protease 3CL-pro in HIV by interacting with this protein.	Lopinavir 400 mg and ritonavir 100 mg every 12 hr	Anorexia, nausea, Abdominal Discomfort, diarrhea, Acute gastritis, liver Dysfunction, Thrombocytopenia And skin eruptions.
Protease inhibitor	Darunavir[14]	Against SARS-COV-2, it exerts a replication-inhibiting action. Another medication used to treat COVID-19 is PREZCOBIX®, a fixed-dose mixture of cobicistat and darunavir.	800mg	Headache Diarrhea Vomiting Stomach pain Constipation
Protease inhibitors	Atazanavir**Error! Reference source not found.**	Atazanavir decreased SARS-COV-2 replication by binding more firmly to the SARS-COV-2 M-pro active site.	300 mg once daily with 100 mg of lopinavir	Nausea Vomiting Stomach pain Diarrhea Headache Depression

Reverse transcription inhibitors	Favipiravir Error! Reference source not found.,Error! Reference source not found.,Error! Reference source not found.	A purine nucleotide that inhibits viral replication is the prodrug known as RNA polymerase inhibitor. It integrates with viral RNA to compete with guanine nucleosides during RNA viral replication, which results in selectively blocking the RDRP to halt the production of viral RNA.	2,400–3,000 mg every 12 h	Nausea, vomiting, Liver dysfunction
Reverse transcription inhibitors	Ribavirin Error! Reference source not found.	A guanine derivative analogue called ribavirin has antiviral action against the HCV virus. Its antiviral mechanism interferes with the functioning of polymerases, prevents RNA capping from destabilising viral RNA, and ultimately prevents replication. Furthermore, ribavirin accelerates the breakdown of viral RNA by inhibiting the activity of the enzyme inosine monophosphate dehydrogenase, which prevents the synthesis of guanosine.	400mg every 12 hr	Vomiting. Diarrhea. Constipation. Heartburn. Loss of appetite.
Reverse transcription inhibitors	Sofosbuvir Error! Reference source not found.	Nucleotide analogues that inhibit NS5B polymerase function as a chain terminator to stop the spread of viruses.	400 mg once daily	Diarrhea. Headache. Muscle pain. Difficulty falling asleep or staying asleep.

Other than antiviral agents for the treatment of COVID-19 2,14,

Table 3 Agents other than anti-viral

Class of drug	Drug name	Mechanism of action	Dose	Adverse effects
Antimalarials and amebicides	Hydroxychloroquine phosphate	Inhibits lysosomal acidification and autophagy. Inhibits viruses from entering in vitro. Suppress the production of sialic acid receptors to stop sars-cov-2 from adhering to host cells.	500 mg on day 1, 250 mg per day for the next 4 days)	QT prolongation Headache, nausea, loss of appetite, vomiting, diarrhea, and rash.
Antimalarials	Chloroquine Error! Reference source not found.	Chloroquine has a higher affinity for binding to host cell receptors than the S protein of SARS-CoV-2, and as a result, it inhibits glycogen synthase kinase-3 and prevents the virus from attaching to and entering the target cell by	500 mg once daily	QT prolongation Headache, nausea, vomiting

		competitively binding to sialic acid and gangliosides on the surface of the target cell.		
Antibiotic	Azithromycin	Azithromycin works by attaching to the 50S ribosomal subunit of bacteria that are susceptible to it.	500 mg once daily	QT prolongation Headache, dizziness, cholestasis, hepatitis, diarrhea
Antiprotozoal agent	Nitazoxanide	Disrupts anaerobic bacteria's metabolism and blocks the viral transcription factor	500 mg every 12hr	Nausea, vomiting, abdominal pain, headache, dizziness, skin rash.
Immunomodulator tor (monoclonal antibody)	Tocilizumab **Error! Reference source not found.**	A monoclonal antibody that inhibits the interleukin-6 (IL-6) pathway and blocks the IL-6 receptor.	Intravenous dose 8mg/kg every 2 weeks	Nasopharyngitis, headache, hypertension, elevated ALT, Rash, dizziness, leukopenia, liver injury.
Immunomodula tor (monoclonal antibody)	Sarilumab	An interleukin-6 (IL-6) receptor blocker that also inhibits the IL-6 pathway is a monoclonal antibody.	200 mg once every 2 weeks administered as a subcutaneous injection	Allergy Thrombocytopenia Neutropenia Elevated liver transaminases
Immunomodulator tor (monoclonal antibody)	Siltuximab	A monoclonal chimeric antibody that binds to and inhibits the effects of IL-6.	Intravenous 11 mg/kg once every 3 weeks	Elevation of liver transaminases Thrombocytopenia Skin rash, itching. Sweating
Plasma, neutralizing antibodies	Convalescent plasma **Error! Reference source not found.**	IgG and IgM anti-SARSCOV-19 antibodies that are specific to convalescent plasma are present and can neutralise the virus.	1 unit of convalescent plasma (approximately 200 mL)	Anaphylaxis

Novel Anti-Viral agents used in COVID-19:

Molnupiravir:

Merck Sharp & Dohme and Ridgeback are collaborating to create the experimental pharmaceutical drug molnupiravir (Table 4), also known as MK-4482, EIDD-2801, and MOV; Lagevrio is a possible brand name for the drug.32

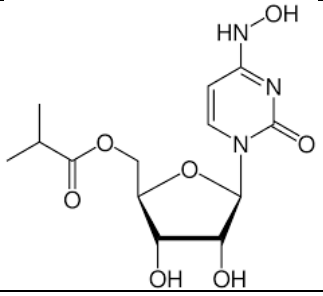
The ribonucleoside analogue prodrug Molnupiravir (EIDD-2801) is ingested and is available as a tablet. In addition to coronaviruses like SARS-CoV-2, MERS-CoV, and SARS-CoV, molnupiravir exhibits broad-spectrum antiviral efficacy against influenza. Research on COVID-19, as well as seasonal and pandemic influenza, has the potential to use molnupiravir.33

In clinical trials, molnupiravir is offered as a 200 mg hard capsule for oral dosages. The suggested dosage is 800 mg of molnupiravir (given as four 200 mg capsules) taken orally every 12 hours with or without food for five days.34

The antiviral ribonucleoside analogue N-hydroxycytidine (NHC) has a 5'-isobutyrate prodrug called molnupiravir. The pharmacologically active ribonucleoside triphosphate (NHC-TP), which operates through a viral error catastrophe mechanism, is created when the prodrug molnupiravir is metabolised to NHC. NHC-TP is incorporated into viral RNA by the viral polymerase, which leads to an accumulation of errors in the viral genome and replication inhibition.33

Physicochemical properties:33,34

Table 4 Molnupiravir

Sr.no	Properties	Inference
1	Physical appearance	White to off-white powder
2	Structure	
3	Solubility	Water-39.7 mg/l Ethyl acetate-3.9 mg/l Acetonitrile- 9 mg/l Methyl tert-butyl ether-0.8 mg/l 2-propanol- 10.0 mg/l Methanol- >100 mg/l(freely soluble) N-heptane-<0.0005 mg/l
4	pKa	pKa1, pKa2, pKa3 values are 2.2, 10.2, and 12.0.
5	Partition coefficient	Log D (pH 7) = 0.46
6	Hygroscopicity	Molnupiravir is non-hygroscopic with a moisture gain of 0.1% at 95% RH and 25°C
7	Photosensitivity	Not sensitive to light exposure
8	Physical state	Crystalline material with two known anhydrous forms, form 1 and form 2
9	BCS class	Molnupiravir and its active metabolite n-hydroxycytidine (NHC) are highly soluble (NLT 41 mg/ml and 21 mg/ml respectively) and have been demonstrated to be highly permeable, i.e. Biopharmaceutical Classification System (BCS) class I compounds.
Pharmacology		
10	Class of drug	Anti-viral agent
11	Mechanism of action	Molnupiravir acts by inhibiting RNA- dependent RNA polymerase (RDRP) of sars-cov-2 to induce RNA mutagenesis in two steps. Molnupiravir is converted to eidd-1931 in the body, which phosphorylation by host kinases provides the eidd-1931-triphosphate. In the body, on phosphorylation by host kinases provides the EIDD-1931-triphosphate.
12	Absorption	Molnupiravir is a 5´-isobutyrate ester prodrug cleaved by esterases present in the intestine and liver during absorption/hepatic first pass, delivering the nucleoside metabolite NHC into the systemic circulation, as a result

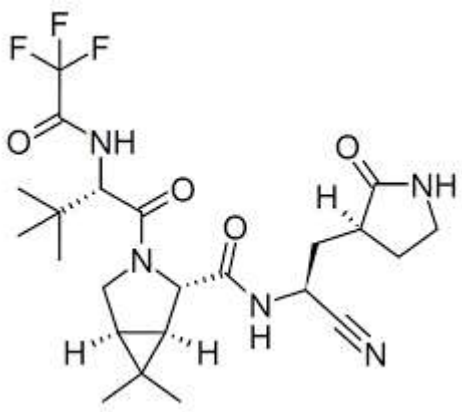
		only very low levels of molnupiravir were detected in plasma.
13	Distribution	Molnupiravir, NHC, and NHC-TP were quantified in some tissues (lung, spleen, kidney, liver, heart, and brain) from mice, rats, dogs, monkeys and ferrets following single or multiple oral doses of molnupiravir. NHC and NHC-TP were observed in all tissues and their exposures were generally dose-dependent. In most species, NHC-TP typically had the highest exposures in the lung and spleen and the lowest levels in the brain.
14	Metabolism	In vitro metabolism observed, the majority of the dose was ultimately metabolized to pyrimidine metabolites (uridine, cytidine, etc.), which then enter the endogenous pyrimidine pool.
15	Excretion	Excretion from the bile ducts urine and fesses, majority of the dose was retained in the body
16	Biological half-life	7 hours
17	Dose	200 mg

Nirmatrelvir:

Nirmatrelvir (Table 5), also known as 3CLpro or NSP5 protease, is a peptidomimetic inhibitor of the SARS-CoV-2 3C-like protease main protease (Mpro).37 The Pfizer-developed SARS-CoV-2 3CL protease inhibitor prevents viral replication by inhibiting the digestion of polyprotein precursors. Lufotrelvir, an earlier clinical candidate, was modified to become nirmatrelvir.36 A SARS-CoV-2 major protease inhibitor with wide coronavirus antiviral effectiveness, strong off-target selectivity, and consequently fewer adverse medication reactions is nirmatrelvir (or PF-07321332)/ritonavir, produced by Pfizer, Inc.37

Physicochemical properties:36–38

Table 5 Nirmatrelvir

Sr. No	Properties	Inference
1	Physical appearance	Pink color powder
2	Structure	
3	Solubility	Water: 2mg/ml DMSO; 100 mg/ml Ethanol: 100 mg/ml
4	pKa	7.1

5	Partition coefficient	2.12
6	Hygroscopicity	Nirmatrelvi non-hygroscopic with a moisture gain of 0.1% at 95% RH and 25°C
7	Photosensitivity	Not sensitive to light exposure
8	Physical state	crystalline Powder
9	BCS class	Low solubility in aqueous media under physiologically relevant pH
PHARMACOLOGY		
10	Class of drug	Anti-viral agent
11	Mechanism of action	Nirmatrelvir is a peptidomimetic inhibitor of the SARS-CoV-2 3C-like protease main protease (Mpro), also referred to as 3CLpro or NSP5 protease. Inhibition of the SARS-CoV-2 3CL protease renders it incapable of processing polyprotein precursors, preventing viral replication
12	Absorption	Nirmatrelvir oral dosing, the bioavailability was low (<10%) requires potential techniques to enhance absorption. Dosing with a high fat meal modestly increased the exposure of nirmatrelvir
13	Distribution	The protein binding of nirmatrelvir in human plasma is approximately 69%.
14	Metabolism	In vitro, studies assessing nirmatrelvir without concomitant ritonavir suggest that nirmatrelvir is primarily metabolized by CYP3A4. Administration of nirmatrelvir with ritonavir inhibits the metabolism of nirmatrelvir. In plasma, the only drug-related entity observed was unchanged nirmatrelvir. Minor oxidative metabolites were observed in the feces and urine.
15	Excretion	Approximately 49.6% and 35.3% of the administered dose of nirmatrelvir 300 mg was recovered in urine and feces, respectively. Nirmatrelvir was the predominant drug-related entity with small amounts of metabolites arising from hydrolysis reactions in excretion.
16	Biological half-life	Along with ritonavir 7 hours
17	Dose	150 mg

CONCLUSION

People all across the world are currently being affected by the COVID-19 pandemic. Current management focuses on stopping the spread of the virus and giving sick patients supportive care without fundamental therapeutic procedures. Although the FDA has not yet licenced any specific antiviral medications for COVID-19, using some currently existing antiviral medications that target particular phases of the

SARS-CoV-2 life cycle may be an alternative therapeutic approach to combating this pandemic. Some of the effective classes of antivirals to be taken into consideration for the same are transcription inhibitors, protease inhibitors, and fusion inhibitors. In addition to antiviral medications, there are currently numerous vaccinations and convalescent plasma, the use of which has demonstrated a decrease in viral load and patient morbidity.

Declaration of interests

- The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
- The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

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Authors' contributions

Krupal Shanishchara: Paper writing and data collection

Bhargavi Mistry: Evaluation of Manuscript data

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