Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 11 [4] March 2022 : 218-233

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Cell Biology of SARS-COV-2 and Current Preventive Strategies for Covid-19: A Systematic Review

Namrata Gundettiwar, Vijayshri Rokde*, Kishor Danao
Department of Pharmaceutical Chemistry, Dadasaheb Balpande College of Pharmacy, Nagpur, Maharashtra 440037, India
Correspondence Email: vijayshritekade@gmail.com

ABSTRACT
SARS-CoV-2, is a global pandemic that impacts societal and economical across the countries. SARS-CoV-2 is widely spread and infected to mammals that lead to death. Hence, to avoid the consequences of covid-19, there has been a need to know the cell biology of SARS-CoV-2. This review aims to highlight molecular developments in the cell biology of SARS-CoV-2 and contemporary preventive measures for covid-19. Methods: To analyse current evidence of SARS-CoV-2 related cell biology and existing preventive measures for covid-19, we combed through literature in a variety of pharmaceutical and medical databases including as Google Scholar, PubMed, and Science Direct. Results: We discussed every possible aspect of SARS-CoV-2 including its basic biology, replication, genome characterization, structural-based functional information of proteins, as well as current approaches to preventing its spread and severity were all discussed. Conclusion: This paper methodically details the most recent advancements on SARS-CoV-2 basic cell biology and preventative techniques used around the world to combat COVID-19. This current knowledge could be extremely useful in the development and design of anti-SARS-CoV-2 drugs.
Keywords: *SARS-CoV-2, Covid-19, Cell biology, Protein, Genome, Vaccine*

Received 12.12.2021 Revised 25.01.2022 Accepted 26.02.2022

INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a crown-shaped coronavirus that causes severe sickness and death around the world. It is classified as a virus that affects mammals and birds. SARS-CoV-2 infection caused by coronavirus was declared by WHO in 2019. Middle East Respiratory Syndrome (MERS) in 2012 and severe acute respiratory syndrome (SARS) in 2003 preceded the coronavirus as the third-generation virus in the coronaviridae family. Coronavirus [1] follows rhinoviruses in providing cold symptoms without causing illness. SARS-CoV-2 began spreading over the world in the Wuhan city of China [2]. Approximately 96,000 instances of covid 19 infection have been documented, with 3300 deaths reported as of March 5, 2020. A large number of linear single-stranded positive-RNA viruses identified in fish, birds, and mammals belong to the coronaviridae family of viruses. Coronaviruses are categorized into four categories: alpha coronavirus (α-CoV), beta coronavirus (β-CoV), gamma coronavirus (γ-CoV), and delta coronavirus (δ-CoV) [5-6]. The first coronavirus, avian infectious bronchitis virus [7], was found in 1930, and the first human coronaviruses, HCoV-229E and HCoV-OC43, were discovered in 1960 [8, 9]. SARS-CoV also affects ciliated bronchial epithelial cells and type-II pneumocytes via the angiotensin-converting enzyme 2 receptor (ACE2). The processes behind SARS-CoV-2 infection and spread ability are yet unknown, although structural research suggests that the human cell is infected via the ACE2 receptor. SARS-CoV-2 is a recently discovered virus that resembles SARS-Cov more than MERS-CoV. As a result, both SARS-CoV and SARS-CoV-2 may infect through similar mechanisms [11]. Nonetheless, the sequence of SARS-structure CoV-2's is like to that of SARS-CoV [13].

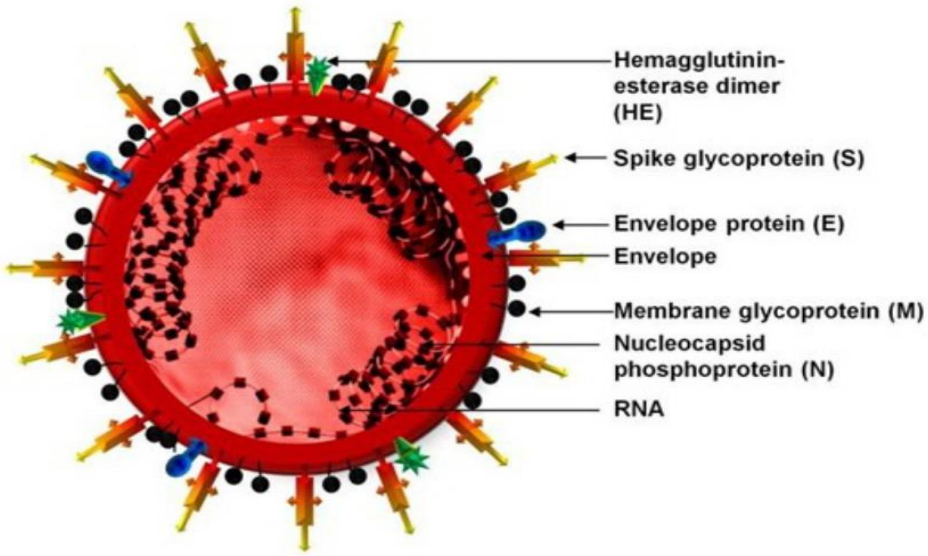


Figure 1. SARS CoV-2 structure[12]

SARS-viral CoV-2's structure is made up of lipid bilayers with viral RNA, protein spikes in the outer region, and membranes (Fig. 1) [14]. As a result, the structure of protein spikes [15] and protease enzymes [16-18] has been targeted for the creation and evaluation of new pharmacological therapies.

Brief overview of the SARS-CoV-2 genome

Genome arrangement

SARS-CoV-2 is a virus with a genomic size of 26 to 32 kb. Specifically, structural and pharmacological investigations of α-CoV and β-CoV revealed two distinct features: binding towards the human receptor ACE2, and a breakage location at the S1-S2 boundary through the attachment of 12 nucleotides. It is made up of 29903 nucleotides that encode 9680 amino acid polyproteins [19, 20], and it is ssRNA linear with 13 open reading frames (ORF) that were interpreted using SARS-CoV homology. The S, E, M, and N genes code for the coronavirus structural protein. The hemagglutinin esterase gene is missing.

Receptors

The three main domains identical, N-terminal with two units S1 and S2, cytoplasmic C-terminal, and a trans-membrane, are mediated by the virus's entry into the host. S1 and S2 are glycosylated and substantially maintained. S 1-protein is primed by a cellular protease for breakdown at a definite point, and S2-protein then joins the viral in addition to host membranes. The presence of the receptor-binding domain (RBD) in the spike protein is critical for ACE2 binding to the host membrane. Furthermore, RBD has a crystal structure coupled to ACE2 with a resolution of 2.45 A, indicating that it is identical to SARS-CoV RBD. [21-24]

Genome expression

Due to the presence of S-protein, the host's cytoplasm has been involved in genome expression. The translation product of this encoded version of S-gene is 1273 amino acids long. It did, however, make the envelope's union by means of the host cell membrane easier. Furthermore, SARS-CoV-2 protein sequence information is based on SARS-CoV equivalency.

Genome replication and transcription

When compared to additional RNA viruses, Coronavirus has a large RNA genome that is translated into structural and non-structural proteins (NSPS). SARS-CoV-2 polyprotein is formed by means of generated RNA sequences and a variety of enzymatic activities. NSPS has also experienced post-translational modifications, which have helped to balance the overall activity of replicative proteins.

2.5 Viral access and host immunereactions

SARS-CoV-2 go into the host through a procedure that resembles that of a typical virus life cycle (Fig. 2). Furthermore, the presence of spike protein bound to the host ACE2 receptors, cellular Human Airway-Trypsin-Like Protease (HAT) cathepsins, and trans membrane protease serine 2 (TMPRSS2) break the S-protein, allowing for the easier fusion of the cellular and virus-related membranes via the endosome pathway and release of SARS-CoV-2 RNA into the host cell. The RBD of SARS-CoV-2 enters the cell and aids the hACE2 receptor. Furthermore, non-pathogenic secondary responses have been observed (Fig.3).Due to the presence of plasmin and proteases that can degrade S- protein at the fine site, the result may be seen in individuals with lung disease, heart disease, diabetes, and kidney infections. Nonetheless, this enzyme is being investigated as a potential beneficial target in the future [25]. According to a

literature review, the spike protein of SARS-CoV-2 has a 10-20 times greater affinity than that of SARS-CoV [26].

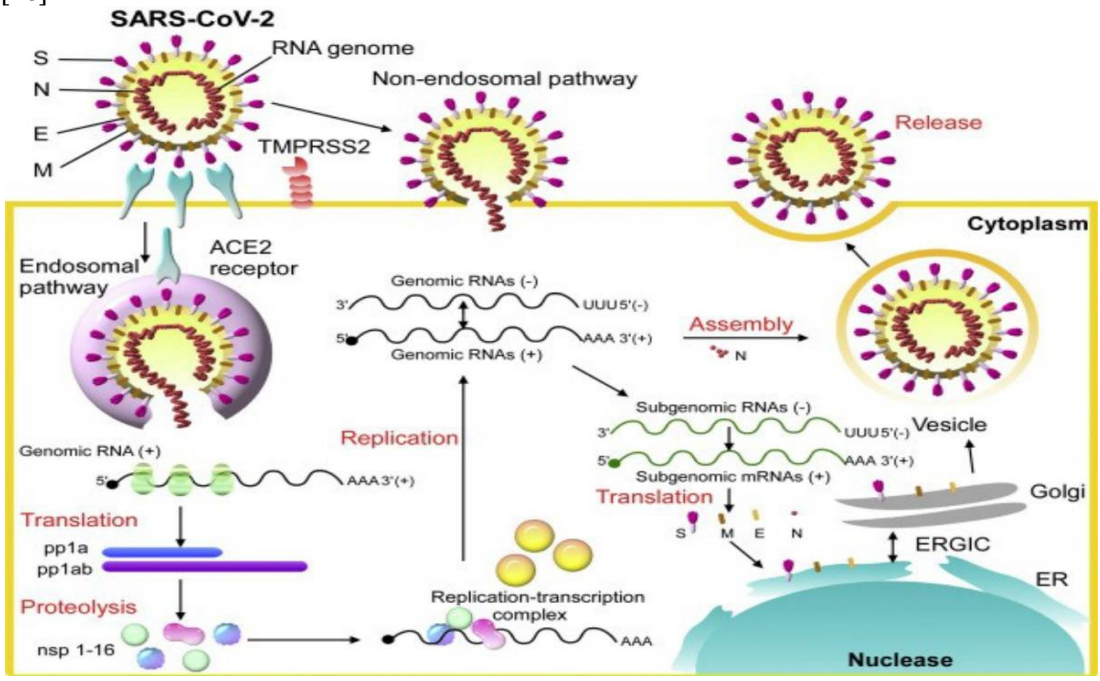


Figure 2. The lifecycle of SARS CoV-2 [27]

Proinflammatory cytokines such as IL-1, TNF-, and IL-6 in extreme conditions causes acute respiratory distress syndrome, which damages tissues and eventually leads to failure of multiple organs and Covid 19 patient's death. As a result, for the reduction of mortality rates, repurposed medicinal therapy to target proinflammatory cytokines and regulate the cytokines storm (Fig. 3) [28-29].

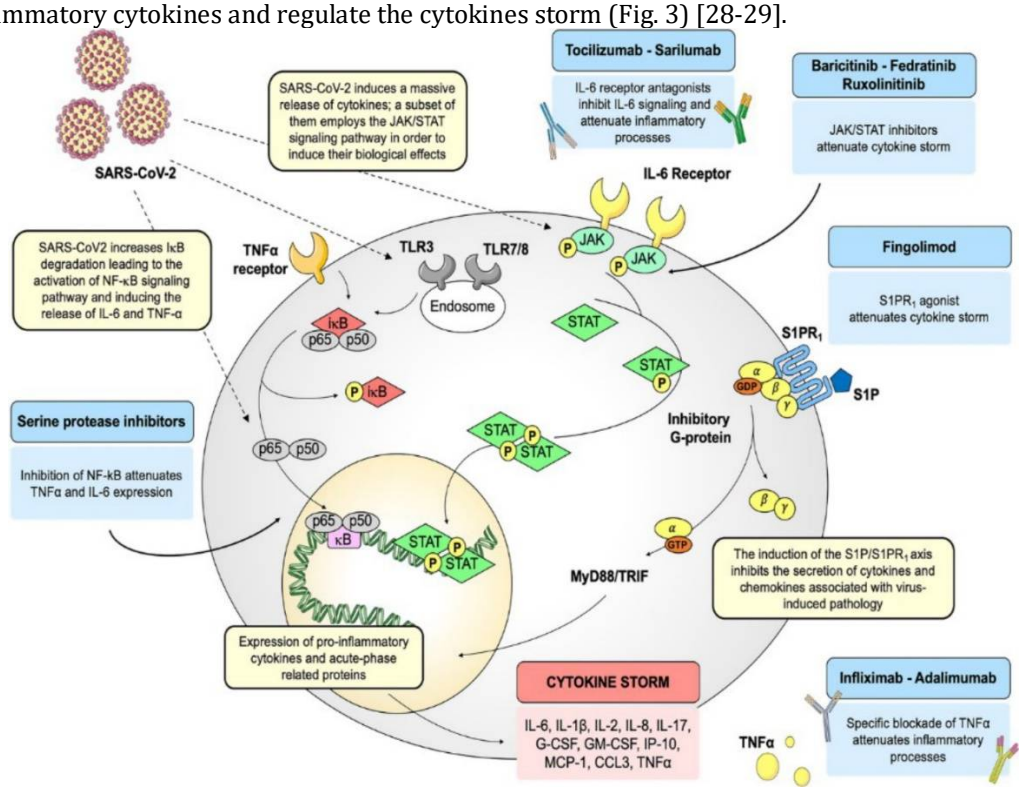


Figure 3. Cytokine storm and multiple tissue damage [30]

SARS CoV-2 transmission

By observing cases in Wuhan, the WHO was able to determine the mode of transmission of coronavirus, concluding that initial transmission was due to direct connection with local seafood wholesale markets, followed by transmission from locals [31]. However, tracheal intubation, non-invasive ventilation,

bronchoscopy, and tracheotomy have all been used to spread infection via disease-driven droplets produced by coughing, breathing out, and sneezing, as well as medical processes like tracheal intubation, non-invasive ventilation, bronchoscopy, and tracheotomy. Excreta has also disseminated illness by toilet flushing. Human actions such as walking, dusting an area, and unlocking the doors can re-aerosolize materials that have been put on surfaces. The spread of infection from biological specimens is also caused by improper laboratory procedures. In all of these circumstances, aerosolized illness poses a risk of infection to individuals, which is influenced by numerous environmental parameters such as the survival, transportation, and fate of aerosolized virus [32]. SARS-CoV-2 has spread via two modes of transmission: direct and indirect. The indirect method spreads infection through contaminated objects and airborne contagion, while the direct mode involves disease-driven droplets and human-to-human contact (Fig 4). As a result, the precautionary majors of airborne isolation, room ventilation, and adequate disinfectant application must be taken [34].

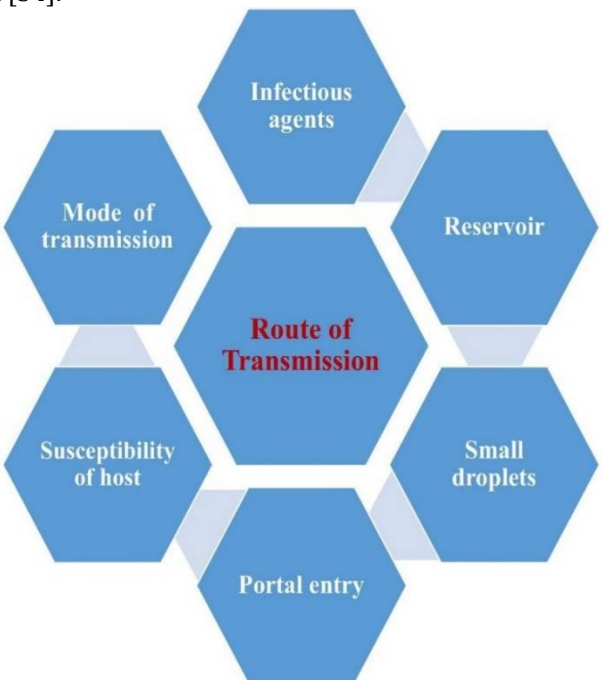


Figure 4. Way of spread of SARS CoV-2 infection [33]

As the link between the fish and wild animal markets, asymptomatic carriers [35] were identified for the spread of the virus from animals to individuals in the study. Furthermore, unlike SARS-CoV, SARS-CoV-2 infection can be spread by respirational droplets over a 2-meter distance or by infected surfaces, resulting in infection [36].

2.7 Symptoms of SARS CoV-2 infection

SARS and COVID-19 symptoms are split into two categories: systemic and respiratory diseases. Cough, fever, and weariness are common symptoms of SARS and COVID-19. Rhinorrhoea, sneezing, sore throat, and pneumonia are the greatest common respiratory indications of COVID-19 and SARS, however COVID-19 patients have greater respiratory symptoms. Lymphopenia, leukopenia, and a low platelet count, comparable to those reported in SARS patients, may be seen in hematology [37]. After 2–14 days, with an average of 5 days, COVID-19 infection signs were seen. COVID-19 signs containtiredness, fever, dry cough, and muscle pain (Fig 5), although other symptoms such as lymphopenia, headache, and drowsiness can also occur. Patients may experience breathing issues five days after ward the infection begins, and acute respiratory distress syndrome (ARDS) on day eight. From the time of infection to death, the period varies since 6 to 41 days, by way of an average of 14 days. This time depends upon various elements, including age and well-being, in addition to shorter for chronically ill patients and those over 70 years old [38].

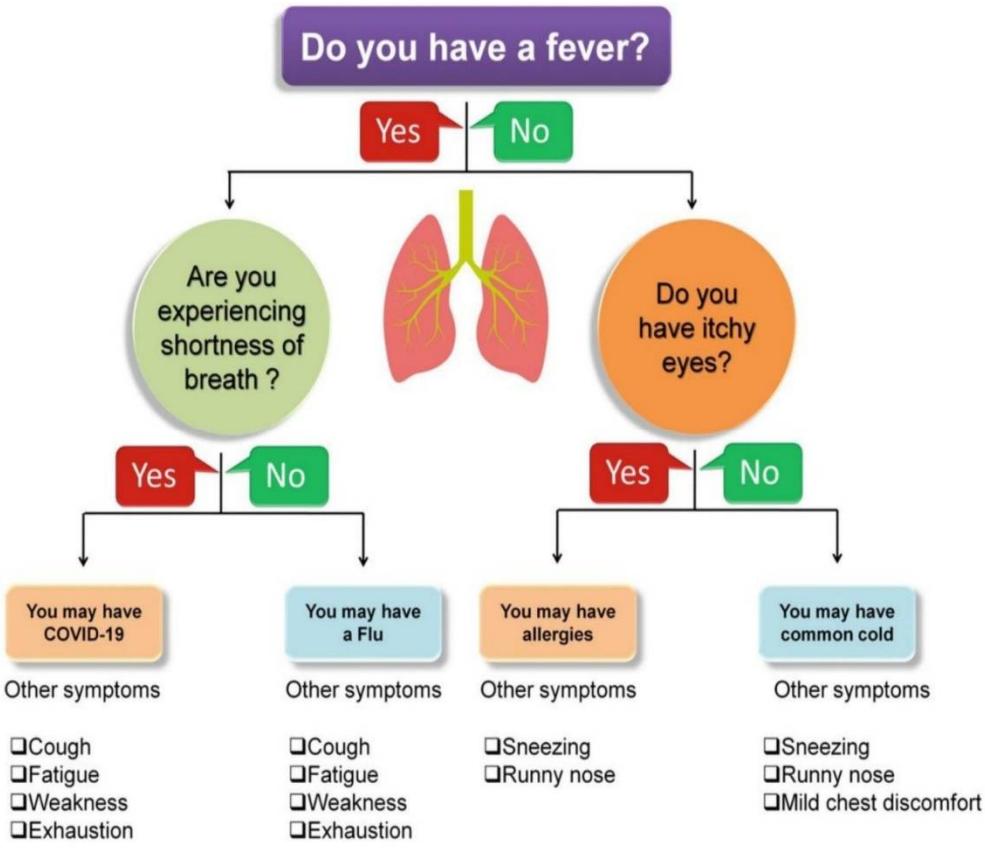


Figure 5. Flow diagram showing indications of covid-19 [39]

Family groups of asymptomatic cases of SARS-CoV-2 infection

Pneumonia outbreak driven via the novel SARSCoV-2 coronavirus has caused significant epidemics in China and other countries since December 2019, drawing international attention. Infected patients' family reunions have been observed, if not tightly supervised. However, several phenomena have had a significant impact on public health. Importantly, asymptomatic patients may be ignorant of their illness and hence will not be isolated or treated, or they may be overlooked by healthcare providers and thus unwittingly spread the virus to others. Family members infected with SARSCoV2 must be continuously examined and monitored for infection to avoid and control this highly infectious disease as soon as possible, even if there are no symptoms [40].

Diagnosis of SARS-CoV-2 infection

Covid-19 infection's spreadability and harshness early diagnosis and prediction of SARS-CoV-2 infection was difficult task meant for medical experts. As a result, medical professionals and the pharmaceutical industry concentrated on test kits for coronavirus infection diagnosis (Table 1). The best test for determining SARS and Coronavirus is RTPCR. The symptomatic aid is a processed Tomography examination (CT Output). When individuals are infected with SARS or Coronavirus, CT images may show pneumonic parenchymal ground-glass and solidify aspiratory opacities with an adjusted shape and a fringe lung dispersion. SARS RT-PCR is a method that associations an RNA inversion record by means of cDNA polymerase chain intensification (PCR). It is a quick as well as accurate SARS diagnostic test that follows World Health Organization's (WHO) guidelines was widely used during the SARS outburst. While respirational samples were collected during the SARS outburst, respirational samples, faecal samples, also pee samples could be performed on RT-PCR analysis. The most well-known and powerful nucleic corrosive detection approach for SARS-CoV-2 is *Reverse Transcription* Polymerase Chain Reaction (RT-PCR). For the time being, high-throughput sequencing technology has been used to make a decision. It has limited use because it is expensive. The reason behind care, for example, is an insusceptible recognizable proof technique. Other possible Coronavirus analytic methodologies include IgM/IgG testing (POCT) and protein-linked immunosorbent assay (ELISA), both of which are also being researched [41]. For discovery, polymerase chain reaction tests are commonly used. Because explicit approaches and accessibility vary, general health professionals may be able to assist with the implementation of demonstrative testing in certain locations [42].

Table 1 COVID-19 test kits with its characteristics [43]

Date of Release	Name of Vaccine Kit	Target Antigen	Duration of Test
March 2020	COVID-19 IgG/IgM Point of Care Rapid test	IgG/IgM	2-10 min.
March 2020	Wantai SARS-CoV-2 Ab Rapid Test	IgG/IgM	15 min.
March 2020	Biologics 2019-nCoV IgG/IgM Detection Ki	IgG/IgM	< 10 min.
March 2020	MAGLUMI IgG de 2019-nCoV	IgG	600 tests per hour
April 2020	m2000 SARS-CoV-2 assay	IgG	100–200 tests for every hour
April 2020	Antigen detection test for SARS CoV 2	S1 subunit	-
April 2020	COVID-19 Ag Respi-Strip	N protein	<15 min.
April 2020	SGTi-flex COVID-19 IgM/IgG	IgG/IgM	10-15 min.
April 2020	INNOVITA 2019-nCoV Ab Test (Colloidal Gold)	IgG/IgM	<15 min.
April 2020	Shanghai LiangRunLionRun Antibody IgM-IgG Diagnostic Kit for Novel Coronavirus COVID-19	IgG/IgM	<10 min.
April 2020	DiagnoSure COVID-19 IgG/IgM Rapid Test Cassette	IgG/IgM	<10 min.
May 2020	Anti-SARSCoV-2 Total Reagent Pack from VITROS Immunodiagnostic Products	IgG/IgM/IgA	150 tests per hour
May 2020	ASSURE® SARS-CoV-2 IgG/IgM Rapid Test from MP Diagnostics	IgG/IgM	<25 min.
May 2020	Anti-SARS-CoV-2 Roche Elecsys	N protein/IgG	18 min

Prevention of SARS CoV-2 infection

Training, disengagement, avoidance, transmission regulator, in addition management of tainted people are the basic stages in preventing contagious illnesses like Coronavirus, according to the WHO. Implementing the following measures can help to reduce the blow-out of pollution. Staying at home (home isolate) also away from any immediate interaction by way of some solid (possibly asymptomatic patients) or tainted individual, also known as safeguarding; avoiding insignificant travel; seeing societal separating guidelines such as avoiding congested public spaces and keeping a two-meter separation between all individuals, particularly at hacking or sniffling; refraining

Individuals by greeting with shake hands, after that washed hands in between 20 s through

Cleanser and hand sanitizer or water with roughly 60% alcohol [44].

5 Management for SARS-CoV-2 Infection

The purpose of the medicament is to guarantied sufficient oxygenated and complimentary help at the critical stage of sickness [45]. Antimicrobials and antibiotics such as Remdesivir (fig. 6) help with a variety of drug treatments (GS-5734).

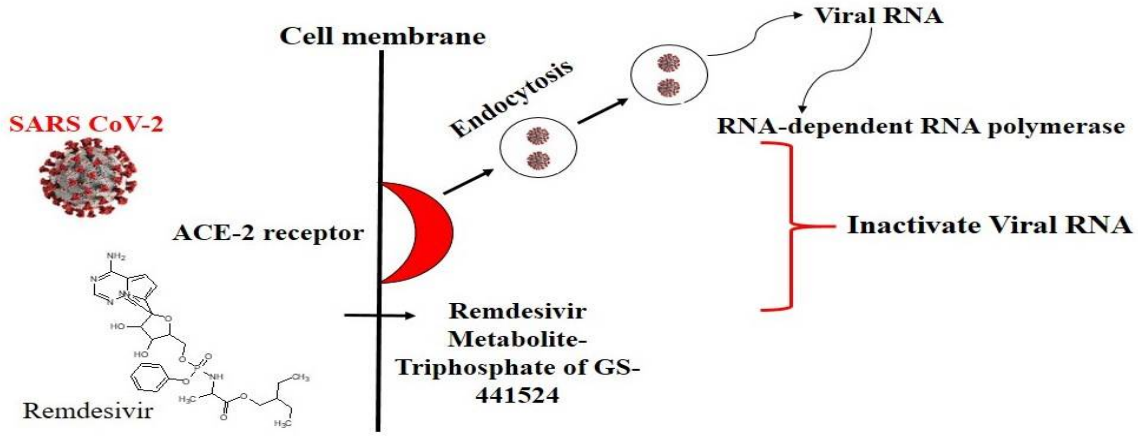


Figure 6. (GS-5734) Remdesivir's and (GS-441524) mechanism of action [46-47]

Table 2 Antiviral drugs against SARS CoV-2 infections [48-52]

Target	Antiviral Drugs	Emergency use for Covid-19
Inhibitor of Protease	Lopinavir	USA, Japan, Singapore, Italy, China, IPC (Lopinavir- Ritonavir fix dose)
	Darunavir	Italy
	Atazanavir	Singapore
	Saquinavir	Singapore
Nucleoside reverse transcriptase inhibitor	Emtricitabine	Singapore
Nucleotide reverse transcriptase inhibitor	Remdesivir	WHO, IPC, USA, Singapore, Italy
	Favipiravir (Avigan)	Singapore, Japan, Indonesia
	Ribavirin	Singapore, IPC
	Sofosbuvir	Singapore
Inhibitor of neuraminidase (Virus discharge inhibitor)	Oseltamivir (Tamiflu)	IPC, Singapore, Indonesia
Drug for Influenza	Umifenovir (Arbidol)	China

Table 3 SARS Cov-2 infection and non-antiviral medicines [53-56]

Class of Non-Antiviral / Repurposed Drugs	Non-Antiviral / Repurposed Drugs
Broad-spectrum antiparasitic drug	Ivermectin, Niclosamide
Anti-malarial drug	Chloroquine Hydroxychloroquine
Antibiotics	Amoxicillin, amoxicillin-clavulanic acid, ampicillin, gentamicin, Erythromycin, benzylpenicillin, piperacillin/tazobactam, ciprofloxacin, Ceftazidime, cefepime, Vancomycin, meropenem Moxifloxacin, cefuroxime
Immunosuppressant	Bevacizumab
Corticosteroids	Methylprednisolone Dexamethasone
Anti-inflammatory	Baricitinib Melatonin
ACE 2 blockers	Promazine
Antifungal agents These agents used to treat mucormycosis infection due to covid - 19	Amphotericin B, Posaconazole, Isavuconazole, Voriconazole, Mucafungin

5.1 Bronchodilators

The majority of Coronavirus patients do not require a breathed-in bronchodilator. Breathed-in bronchodilators have no place in Coronavirus treatment unless the individuals suffered from severe exhausted breath or chronic obstructive pulmonary disease (COPD). MDIs are popular because they have the potential to usher in a new era of vapour sprayers, which could increase the risk of viral transmission with nebulized treatment.

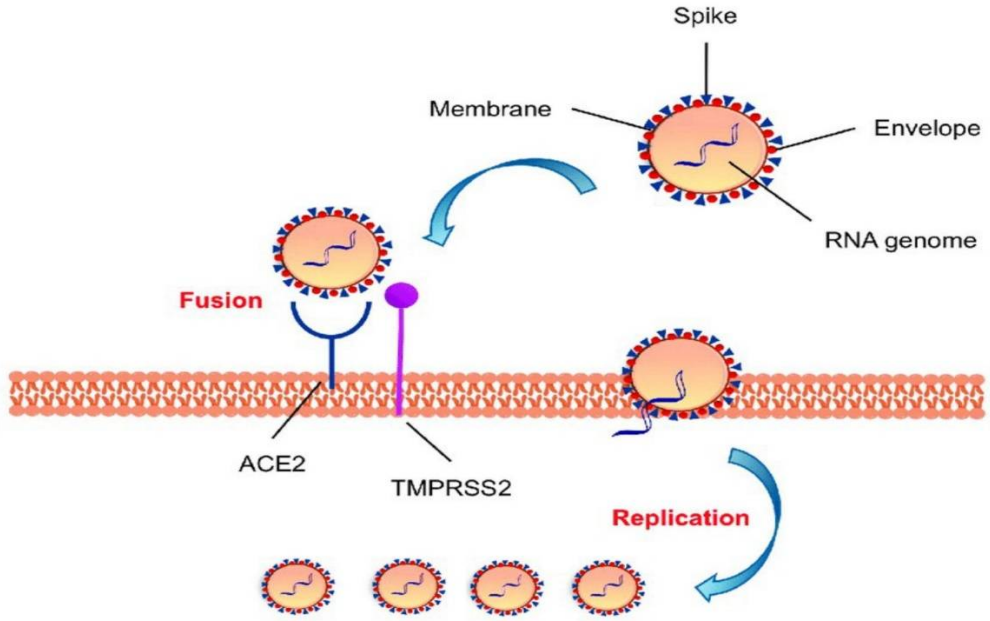


Figure 7. Schematic represents virus-induced host immune system response [57].
ACE2: Angiotensin-converting enzyme 2;
TMPRSS2: Type-2 Transmembrane Serine Protease

5.2 Interleukin-1 (IL-1)

In Coronavirus patients, cytokine release may be a sign of significant illness. Interleukin-1 antagonists such as anakinra and canakinumab prevent IL-1 (a pro-inflammatory cytokine that mediates a variety of metabolic and immunological reactions, including IL-6) from binding to interleukin-1 receptors. Anakinra works similarly to the interleukin blocker and prevent binding to receptor of interleukin IL1.Canakinumab is a monoclonal antibody that specifically targets and kills IL-1 beta, preventing it from communicating with IL-1 receptors [58].

5.3 Vaccines

Coronavirus pandemic has required to stop it from spreading, and finally prevent it from happening again, it's vital to develop safe and effective antibodies. The fatality of covid infection cause due to high sequencing homologus of SARS-CoV-2. Avoiding this fatality required only vaccination. [59].

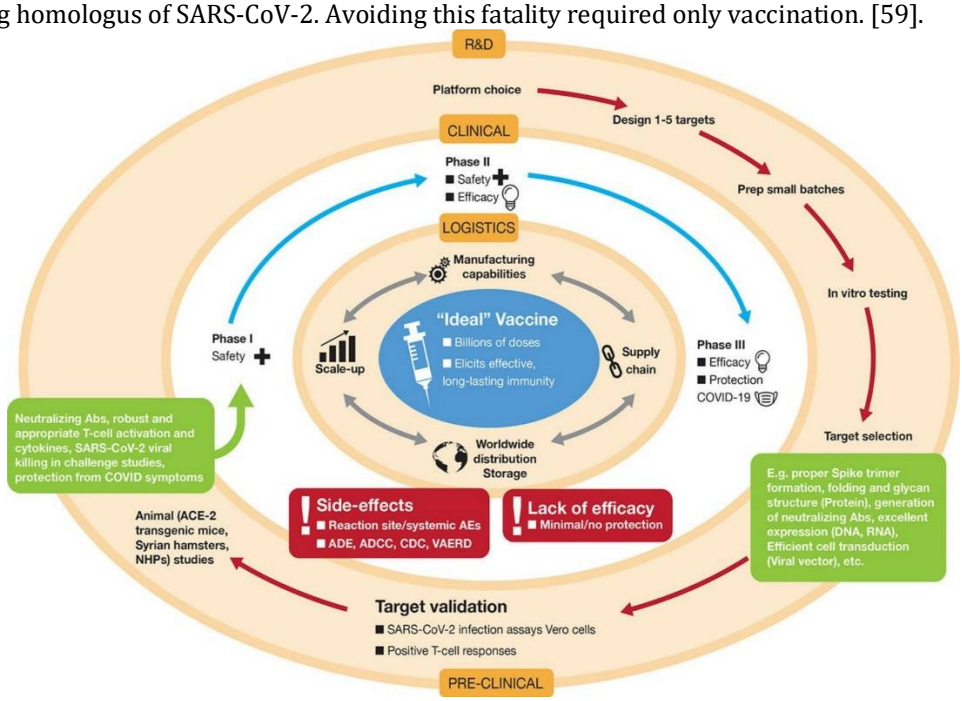
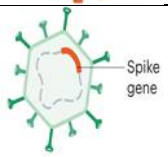
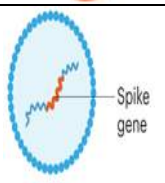
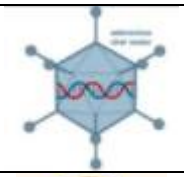
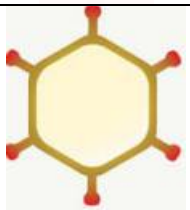
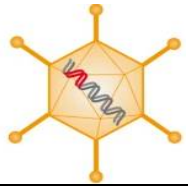


Figure 8. Covid-19 vaccine development phases [60]

Table 4 Vaccines for SARS CoV 2 [61-67]

Enlist of vaccine	Structure
Inactivated vaccine In this vaccine present inactivate cell culture of SARS CoV 2, for exampleCoronaVac or PiCoVacc under Sinovac Biotech in China. Aluminum hydroxide with other adjuvants found in this vaccine and preferably given by intramuscular route.	
Live attenuated vaccine Prepared by the version of the virus which is genetically weakened, it is given by the intranasal route which is the main advantage of this vaccine. It is developed by Codagenix/Serum Institute of India Meissa Vaccines, Ins	
Spike-protein-based vaccines It's a vaccination made from recombinant proteins.	
Recombinant RBD-based vaccines It is also a recombinant protein vaccine	
Vaccines based on virus-like particles (VLPs) It's a vaccination made from recombinant proteins. It doesn't have a genome, but it does have a spike protein on its surface.	
Replication-incompetent vectors vaccine It is ensemble of vaccine that transferred several extended cell of vaccinated person and inculcate spike protein within individuals. Store at 2-8 degrees C. Its Phase III trial started on 7 Sept 2020. Its types are AZD1222 and Ad5-nCoV	
Inactivated virus vector vaccine It depends upon viral vectors that have the spike protein on their surface but are inactivated before being used. It is developed by BioNTech/Fosun, Pharma/Pfizer (BNT162b2) Moderna (mRNA-1273)	
Inactivated pathogen vaccine It contains coronavac, Undisclosed, BBIBP-CoV, and Covaxin which are manufactured by Sinovac research and Development co., Wuhan institute of biological products, Beijing Institute of biotechnology, also Bharat Biotech respectively. Its storage condition is 2-8 degrees C.	
DNA vaccines It relies on plasmid DNA encrypting the spinegenetic material, which is promoted by a mammalian supporter. Zydus CadilaInovio Pharmaceuticals + International Vaccine Institute + Advaccine (Suzhou) Biopharmaceutical Anges + Takara Bio + Osaka University have collaborated on the project.	
RNA vaccine It contains RNA encoding the spike protein. It is divided into two categories. mRNA and RNA replicons of the conventional or non-amplifying kind derived from viruses using positive-stranded RNA	

Sputnik V or Gam-COVID-Vaccine It is a type of replication-defective viral vector vaccine. It is a Russian vaccine which is a vaccination based on adenovirus. In additionthis one is a vector-based vaccine. Specially used for the development of immunity. Its phase III clinical trial started on 7 Sept 2020.	
mRNA vaccine Vaccine name is mRNA-1273 and BNT162b2 developed by BioNTech/Fosun, Pharma/Pfizer (BNT162b2), Moderna (mRNA-1273). mRNA-1273 remains stable at -20degree up to 6 months and 30 days at 2-8 degrees C for 12 hours at room temperature	
Protein subunit vaccine It contains NVX-CoV2373 and ZF2001 Vaccine manufactured by Novavax Chinese Academy of Medicine respectively having 2-8 degree C storage condition	
Virus-like particle It contains a CoVLP vaccine manufactured by Medicago/ GSK. Its Phase III trial on Nov 2020.	
Adenovirus-vector vaccines CanSino Biological Inc./Beijing Institute of Biotechnology, Janssen-Johnson & Johnson, Oxford-AstraZeneca, and The Gamaleya Institute Moscow are among the vaccines utilised. One of the early adenoviral genes (E1) is replaced with the full-length SARS-Cov-2 S gene in the adenoviral DNA, which is a significant trait.	

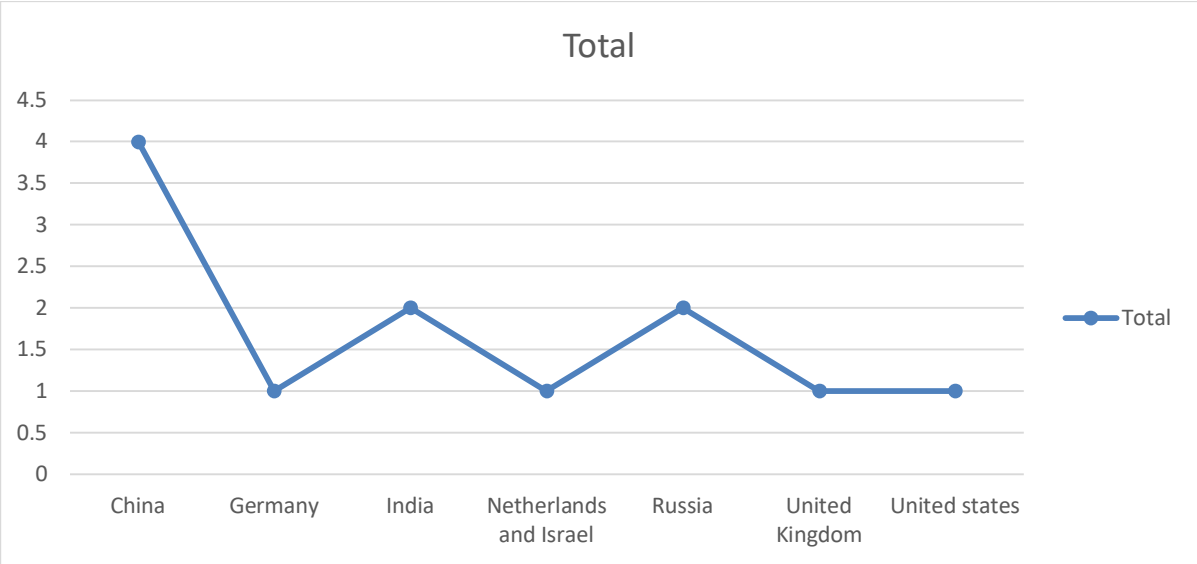


Figure 9. Approved vaccine status among countries

Russia designed two formulations of heterologous rAd26 and rAd5 vector-based COVID-19 vaccination using two techniques like frozen plus lyophilized technique, with a satisfactory safety profile [69].

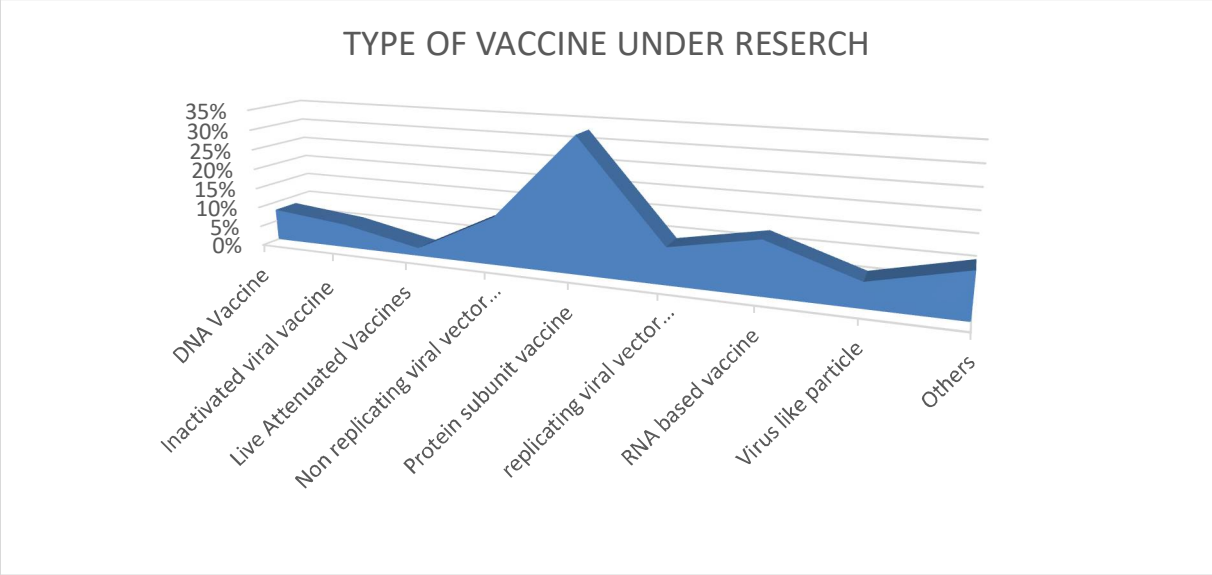


Figure 10. Vaccine status under research [68]

WHO emergency use listing

During public health emergencies, the Emergency Use Listing (EUL) process evaluates the appropriateness of innovative healthiness items. The goal is to get medicines, vaccinations, and diagnostics into the hands of people as soon as feasible to respond to an alternative however following strict safety, effectiveness, and quality criteria. EUL evaluates data from phase II and III clinical trials, as well as a wealth of other information on safety, effectiveness, superiority, and a danger managing strategy that were revised by a higher authority, such as WHO teams and independent experts, who reflect on the evidence of the vaccine under attention, as well as strategies for monitoring its use and future research. A vaccine manufacturer must promise to continuing to create records to obtain a complete license as part of the EUL procedure and WHO prequalification. WHO checks further clinical data obtained from vaccination studies and placement on a systematic base in the prequalification process to verify the vaccine satisfies the essential quality, protection, and efficiency standards meant for wider obtainability. The Pfizer/BioNTech vaccine will be available on December 31, 2020; two AstraZeneca/Oxford COVID-19 vaccines, made by AstraZeneca-SKBio (Republic of Korea) and the Serum Institute of India, will be available on February 15, 2021; and COVID-19 vaccine Ad26 will be available on February 15, 2021.On March 12, 2021, Janssen (Johnson & Johnson) developed COV2.S. Pfizer/BioNTech, Astrazeneca-SK Bio, Serum Institute of India, Janssen, and Moderna are among the vaccine companies listed by the WHO for emergency use [70].

Brazilian essential oils are being investigated as a potential cause for the development of a novel anti-COVID-19 medication.

Despite their diversity and widespread use, few species are approved for use as medication fixes. This is due to the lack of widely disseminated logical and ethnopharmacological information, as well as norms for confirming the quality and well-being of local plants. Clinical preliminaries utilizing indigenous Brazilian herbs, isolated, fundamental oils, or their dynamic fixes are significantly less common, notwithstanding widespread use by the local populace. The strict Brazilian principles for admittance to biodiversity, as well as the non-existence of appropriate documents meant for the exploitation plus guideline of these types, are one reason for a few studies using indigenous plant species [71]. The coronavirus disease 2019 (COVID-19) pandemic has caused a widespread respiratory illness outbreak. This review purposes to estimate the efficacy in addition side effects of natural medicines for the treatment of COVID-19. However, Up till the 12th of May 2020, twelve databases had been searched. The results of natural COVID-19 medicines are used to treat the virus were evaluated in randomized controlled trials (RCTs) and quasi-RCTs. The observation choice and statistics extraction had been done via way of means, unbiased reviewers. The Cochrane threat of bias device was used to evaluate the risk of bias in all randomized controlled trials [72]. Nepal stated that the use of medical flowers has improved throughout COVID-19, as well as the belief that information about medicinal flowers has expanded, and that to avoid COVID-19, the bulk of them propose medicinal flowers. Scientists propose that medicinal plant-based therapies must be effective in treating and preventing COVID-19. It was mentioned that herbal classes by tradition used as diet can support to strengthen the body's immune system and prevent

the emergence of COVID-19. Medicinal flowers have already been joint with western medications to treat a related condition, excessive acute respiratory syndrome (SARS) [73].

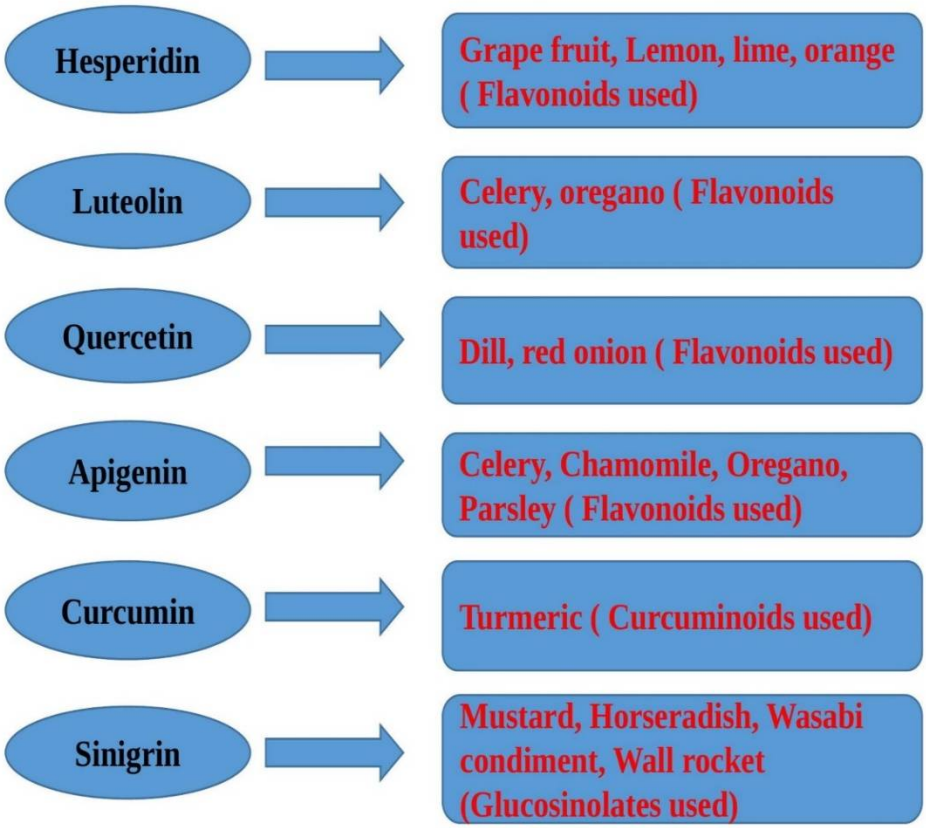


Figure11.SARS CoV2 infection suppression with phytoconstituents [74-77]

Flavonoids, tannins, and phlorotannins, terpenoids, fatty acids, glucosides, lectins, phenolic acids, and tanshinones are some of the phytoconstituents found in plants that can help to treat SARS CoV 2 infection. Flavonoids likes cyanidin, genistein, quercetin, catechin, mangiferin, elsamitrucin, isoquercetin, kaempferol, fisetin, apigenin, chrysin, bavachinin, psoralidin, and others have an inhibitory effect against SARS CoV2. Gallic acid, caffeic acid, and chlorogenic acid are examples of phenolic acids. Chalcones like xanthoangelol, isobavachalcone,etc., and phlorotannins examples are triphloretol A, dieckol, eckol, etcare used for suppression of SARS CoV2 infection [78- 79].

Abbreviations

SARS CoV: Severe Acute Respiratory Syndrome Coronavirus.
WHO: World Health Organization
MERS CoV: Middle East Respiratory Syndrome Coronavirus
TMPRSS: Tran's Membrane Protease Serine 2
RBD: Receptor-Binding Domain
ACE2: Angiotensin-Converting Enzyme 2
NSPS: Non-structural proteins
HAT: Human Airway-Trypsin
CRS: Cytokine Release Syndrome
ARDS: Acute Respiratory Distress Syndrome
RT-PCR: ***Reverse Transcription*** Polymerase Chain Reaction.
CT: Computed Tomography
ELISA: Enzyme-Linked Immunoassay.
COPD: Chronic Obstructive Pulmonary Disease.

CONCLUSION

SARS-CoV-2 is a worldwide epidemic with societal and financial ramifications in many nations. SARS-CoV-2 is a virus that is widely spreader in addition infects mammals, producing mortality. As a result, understanding the cell biology of SARS-CoV-2 is necessary to avoid the repercussions of covid-19. For detecting and capturing SARS-CoV-2 infection, improved new technology-based transcriptomics,

proteomics, RNA-single cell sequencing, global patient history and samples, cell culture in 3D form, and reversing genetic modifications of the coronavirus have all proven crucial. The SARS-CoV-2 vaccine, conversely, requires fundamental understanding of cell biology, and prophylactic measures are used to keep the virus from dispersal as well as infecting people. This paper methodically details the most recent advancements on SARS-CoV-2 basic cell biology and preventative techniques used around the world to combat COVID-19. This current knowledge could be extremely useful in the progress and design of anti-SARS-CoV-2 drugs.

Conflict of Interest
For the publication of this review article in the Journal, the authors declared that there was no conflict of interest.

Funding Information
None

Declaration of competing interest
The authors confirm that the conclusions of this review paper are not influenced by personal or financial interests.

Authors' Contribution

NG: The entire manuscript was physically authored, and a comprehensive literature review was conducted.

VR: Figures were created, a structured abstract was written, and references were established.

KD: Provided suggestions, corrected a few errors, final reviewing of this manuscript

REFERENCES

1. Rajendran, D. K., Rajagopal, V., Alagumanian, S., Santhosh Kumar, T., Sathiya Prabhakaran, S. P., & Kasilingam, D. (2020). Systematic literature review on novel corona virus SARS-CoV-2: a threat to human era. *Virusdisease*, *31*, 161-173.
2. Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., ... & Tan, W. (2020). China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*, *382*(8), 727-733.
3. Singhal, T. (2020). A review of coronavirus disease-2019 (COVID-19). *The indian journal of pediatrics*, *87*(4), 281-286.
4. V'kovski, P., Kratzel, A., Steiner, S., Stalder, H., & Thiel, V. (2021). Coronavirus biology and replication: implications for SARS-CoV-2. *Nature Reviews Microbiology*, *19*(3), 155-170.
5. Asghari, A., Naseri, M., Safari, H., Saboory, E., & Parsamanesh, N. (2020). The novel insight of SARS-CoV-2 molecular biology and pathogenesis and therapeutic options. *DNA and Cell Biology*, *39*(10), 1741-1753.
6. Kuri, T., & Weber, F. (2010). Interferon interplay helps tissue cells to cope with SARS-coronavirus infection. *Virulence*, *1*(4), 273-275.
7. Schalk, A. F. (1931). An apparently new respiratory disease of baby chicks. *J. Am. Vet. Med. Assoc.*, *78*, 413-423.
8. Hamre, D., & Procknow, J. J. (1966). A new virus isolated from the human respiratory tract. *Proceedings of the society for experimental biology and medicine*, *121*(1), 190-193.
9. McIntosh, K., Dees, J. H., Becker, W. B., Kapikian, A. Z., & Chanock, R. M. (1967). Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease. *Proceedings of the National Academy of Sciences*, *57*(4), 933-940.
10. Mason, R. J. (2020). Pathogenesis of COVID-19 from a cell biology perspective. *European Respiratory Journal*, *55*(4).
11. Khan, S., Siddique, R., Shereen, M. A., Ali, A., Liu, J., Bai, Q., ... & Xue, M. (2020). Emergence of a novel coronavirus, severe acute respiratory syndrome coronavirus 2: biology and therapeutic options. *Journal of clinical microbiology*, *58*(5), e00187-20.
12. Das, A., Ahmed, R., Akhtar, S., Begum, K., & Banu, S. (2021). An overview of basic molecular biology of SARS-CoV-2 and current COVID-19 prevention strategies. *Gene reports*, *23*, 101122.

13. Kumar, S., Maurya, V. K., Prasad, A. K., Bhatt, M. L., & Saxena, S. K. (2020). Structural, glycosylation and antigenic variation between 2019 novel coronavirus (2019-nCoV) and SARS coronavirus (SARS-CoV). *Virusdisease*, *31*, 13-21.
14. Finlay, B. B., See, R. H., & Brunham, R. C. (2004). Rapid response research to emerging infectious diseases: lessons from SARS. *Nature Reviews Microbiology*, *2*(7), 602-607.
15. Yan, R., Zhang, Y., Li, Y., Xia, L., Guo, Y., & Zhou, Q. (2020). Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. *Science*, *367*(6485), 1444-1448.
16. Ke, Z., Oton, J., Qu, K., Cortese, M., Zila, V., McKeane, L., ... & Briggs, J. A. (2020). Structures and distributions of SARS-CoV-2 spike proteins on intact virions. *Nature*, *588*(7838), 498-502.
17. Zhang, L., Lin, D., Sun, X., Curth, U., Drosten, C., Sauerhering, L., ... & Hilgenfeld, R. (2020). Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α-ketoamide inhibitors. *Science*, *368*(6489), 409-412.
18. Ziebuhr, J., Snijder, E. J., & Gorbalenya, A. E. (2000). Virus-encoded proteinases and proteolytic processing in the Nidovirales. *Journal of General Virology*, *81*(4), 853-879.
19. Guo, Y. R., Cao, Q. D., Hong, Z. S., Tan, Y. Y., Chen, S. D., Jin, H. J., ... & Yan, Y. (2020). The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak–an update on the status. *Military medical research*, *7*, 1-10.
20. Naqvi, A. A. T., Fatima, K., Mohammad, T., Fatima, U., Singh, I. K., Singh, A., ... & Hassan, M. I. (2020). Insights into SARS-CoV-2 genome, structure, evolution, pathogenesis and therapies: Structural genomics approach. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, *1866*(10), 165878.
21. Lan, J., Ge, J., Yu, J., Shan, S., Zhou, H., Fan, S., ... & Wang, X. (2020). Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. *nature*, *581*(7807), 215-220.
22. Thakur, S., Sarkar, B., Ansari, A. J., Khandelwal, A., Arya, A., Poduri, R., & Joshi, G. (2021). Exploring the magic bullets to identify Achilles' heel in SARS-CoV-2: Delving deeper into the sea of possible therapeutic options in Covid-19 disease: An update. *Food and Chemical Toxicology*, *147*, 111887.
23. Zhou, P., Yang, X. L., Wang, X. G., Hu, B., Zhang, L., Zhang, W., ... & Shi, Z. L. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. *nature*, *579*(7798), 270-273.
24. Letko, M., Marzi, A., & Munster, V. (2020). Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. *Nature microbiology*, *5*(4), 562-569.
25. Tian, X., Li, C., Huang, A., Xia, S., Lu, S., Shi, Z., ... & Ying, T. (2020). Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody. *Emerging microbes & infections*, *9*(1), 382-385.
26. Wrapp, D., Wang, N., Corbett, K. S., Goldsmith, J. A., Hsieh, C. L., Abiona, O., ... & McLellan, J. S. (2020). Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science*, *367*(6483), 1260-1263.
27. Liu, Y. C., Kuo, R. L., & Shih, S. R. (2020). COVID-19: The first documented coronavirus pandemic in history. *Biomedical journal*, *43*(4), 328-333.
28. Poduri, R., Joshi, G., & Jagadeesh, G. (2020). Drugs targeting various stages of the SARS-CoV-2 life cycle: Exploring promising drugs for the treatment of Covid-19. *Cellular signalling*, *74*, 109721.
29. Shah, V. K., Firmal, P., Alam, A., Ganguly, D., & Chattopadhyay, S. (2020). Overview of immune response during SARS-CoV-2 infection: lessons from the past. *Frontiers in immunology*, *11*, 1949.
30. Catanzaro, M., Fagiani, F., Racchi, M., Corsini, E., Govoni, S., & Lanni, C. (2020). Immune response in COVID-19: addressing a pharmacological challenge by targeting pathways triggered by SARS-CoV-2. *Signal transduction and targeted therapy*, *5*(1), 84.
31. Tang, S., Mao, Y., Jones, R. M., Tan, Q., Ji, J. S., Li, N., ... & Shi, X. (2020). Aerosol transmission of SARS-CoV-2? Evidence, prevention and control. *Environment international*, *144*, 106039.
32. WHO (2020b) Coronavirus disease 2019 (COVID-19) situation report—36. February 25, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200225-sitrep-36-covid-19.pdf? sfvrsn¼2791b4e0_2. Accessed 26 Feb 2020.
33. Patel, K. P., Vunnam, S. R., Patel, P. A., Krill, K. L., Korbitz, P. M., Gallagher, J. P., ... & Vunnam, R. R. (2020). Transmission of SARS-CoV-2: an update of current literature. *European Journal of Clinical Microbiology & Infectious Diseases*, *39*, 2005-2011.
34. Lotfi, M., Hamblin, M. R., & Rezaei, N. (2020). COVID-19: Transmission, prevention, and potential therapeutic opportunities. *Clinica chimica acta*, *508*, 254-266.
35. Jin, Y. H., Cai, L., Cheng, Z. S., Cheng, H., Deng, T., Fan, Y. P., ... & Wang, X. H. (2020). A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Military medical research*, *7*(1), 1-23.

36. Ghinai, I., McPherson, T. D., Hunter, J. C., Kirking, H. L., Christiansen, D., Joshi, K., ... & Uyeki, T. M. (2020). First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA. *The Lancet*, *395*(10230), 1137-1144.
37. Law, S., Leung, A. W., & Xu, C. (2020). Severe acute respiratory syndrome (SARS) and coronavirus disease-2019 (COVID-19): From causes to preventions in Hong Kong. *International Journal of Infectious Diseases*, *94*, 156-163.
38. Sharma, A., Tiwari, S., Deb, M. K., & Marty, J. L. (2020). Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): a global pandemic and treatment strategies. *International journal of antimicrobial agents*, *56*(2), 106054.
39. Gupta, A., Karki, R., Dandu, H. R., Dhama, K., Bhatt, M. L., & Saxena, S. K. (2020). COVID-19: benefits and risks of passive immunotherapeutics. *Human Vaccines & Immunotherapeutics*, *16*(12), 2963-2972.
40. Pan, X., Chen, D., Xia, Y., Wu, X., Li, T., Ou, X., ... & Liu, J. (2020). Asymptomatic cases in a family cluster with SARS-CoV-2 infection. *The Lancet Infectious Diseases*, *20*(4), 410-411.
41. Chakraborty, C., Sharma, A. R., Sharma, G., Bhattacharya, M., & Lee, S. S. (2020). SARS-CoV-2 causing pneumonia-associated respiratory disorder (COVID-19): diagnostic and proposed therapeutic options. *Eur Rev Med Pharmacol Sci*, *24*(7), 4016-4026.
42. Ali, S. A., Baloch, M., Ahmed, N., Ali, A. A., & Iqbal, A. (2020). The outbreak of Coronavirus Disease 2019 (COVID-19)—An emerging global health threat. *Journal of infection and public health*, *13*(4), 644-646.
43. Sharma, A., Ahmad Farouk, I., & Lal, S. K. (2021). COVID-19: a review on the novel coronavirus disease evolution, transmission, detection, control and prevention. *Viruses*, *13*(2), 202.
44. Manigandan, S., Wu, M. T., Ponnusamy, V. K., Raghavendra, V. B., Pugazhendhi, A., & Brindhadevi, K. (2020). A systematic review on recent trends in transmission, diagnosis, prevention and imaging features of COVID-19. *Process Biochemistry*, *98*, 233-240.
45. Phan, T. (2020). Novel coronavirus: From discovery to clinical diagnostics. *Infection, Genetics and Evolution*, *79*, 104211.
46. Wang, M., Cao, R., Zhang, L., Yang, X., Liu, J., Xu, M., ... & Xiao, G. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell research*, *30*(3), 269-271.
47. Frediansyah, A., Nainu, F., Dhama, K., Mudatsir, M., & Harapan, H. (2021). Remdesivir and its antiviral activity against COVID-19: A systematic review. *Clinical epidemiology and global health*, *9*, 123-127.
48. Frediansyah, A., Tiwari, R., Sharun, K., Dhama, K., & Harapan, H. (2021). Antivirals for COVID-19: a critical review. *Clinical Epidemiology and global health*, *9*, 90-98.
49. Liu, X., & Wang, X. J. (2020). Potential inhibitors against 2019-nCoV coronavirus M protease from clinically approved medicines. *Journal of Genetics and Genomics*, *47*(2), 119.
50. Vankadari, N. (2020). Arbidol: A potential antiviral drug for the treatment of SARS-CoV-2 by blocking trimerization of the spike glycoprotein. *International Journal of Antimicrobial Agents*, *56*(2), 105998.
51. Nojomi, M., Yassin, Z., Keyvani, H., Makiani, M. J., Roham, M., Laali, A., ... & Ranjbar, M. (2020). Effect of Arbidol (Umifenovir) on COVID-19: a randomized controlled trial. *BMC infectious diseases*, *20*(1), 1-10.
52. Joshi, S., Parkar, J., Ansari, A., Vora, A., Talwar, D., Tiwaskar, M., ... & Barkate, H. (2021). Role of favipiravir in the treatment of COVID-19. *International Journal of Infectious Diseases*, *102*, 501-508.
53. Caly, L., Wagstaff, K. M., & Jans, D. A. (2012). Nuclear trafficking of proteins from RNA viruses: potential target for antivirals?. *Antiviral research*, *95*(3), 202-206.
54. Saghir, S. A., AlGabri, N. A., Alagawany, M. M., Attia, Y. A., Alyileili, S. R., Elnesr, S. S., ... & Abd El-Hack, M. E. (2021). Chloroquine and hydroxychloroquine for the prevention and treatment of COVID-19: A fiction, hope or hype? An updated review. *Therapeutics and clinical risk management*, 371-387.
55. Patrì, A., & Fabbrocini, G. (2020). Hydroxychloroquine and ivermectin: A synergistic combination for COVID-19 chemoprophylaxis and treatment?. *Journal of the American Academy of Dermatology*, *82*(6), e221.
56. Cai, Q., Yang, M., Liu, D., Chen, J., Shu, D., Xia, J., ... & Liu, L. (2020). Experimental treatment with favipiravir for COVID-19: an open-label control study. *Engineering*, *6*(10), 1192-1198.
57. Cannalire, R., Stefanelli, I., Cerchia, C., Beccari, A. R., Pelliccia, S., & Summa, V. (2020). SARS-CoV-2 entry inhibitors: Small molecules and peptides targeting virus or host cells. *International journal of molecular sciences*, *21*(16), 5707.
58. Provenzani, A., & Polidori, P. (2020). Covid-19 and drug therapy, what we learned. *International Journal of Clinical Pharmacy*, *42*, 833-836.

59. Liu, C., Zhou, Q., Li, Y., Garner, L. V., Watkins, S. P., Carter, L. J., ... & Albaiu, D. (2020). Research and development on therapeutic agents and vaccines for COVID-19 and related human coronavirus diseases, *6*(3), 315–331.
60. Funk, C. D., Laferrière, C., & Ardakani, A. (2020). A snapshot of the global race for vaccines targeting SARS-CoV-2 and the COVID-19 pandemic. *Frontiers in pharmacology*, *11*, 937.
61. Gao, Q., Bao, L., Mao, H., Wang, L., Xu, K., Yang, M., ... & Qin, C. (2020). Development of an inactivated vaccine candidate for SARS-CoV-2. *Science*, *369*(6499), 77-81.
62. Wibawa, T. (2021). COVID-19 vaccine research and development: ethical issues. *Tropical Medicine & International Health*, *26*(1), 14-19.
63. Niebel, D., Novak, N., Wilhelmi, J., Ziob, J., Wilsmann-Theis, D., Bieber, T., ... & Braegelmann, C. (2021). Cutaneous adverse reactions to COVID-19 vaccines: insights from an immuno-dermatological perspective. *Vaccines*, *9*(9), 944.
64. Pascual-Iglesias, A., Canton, J., Ortega-Prieto, A. M., Jimenez-Guardeño, J. M., & Regla-Nava, J. A. (2021). An overview of vaccines against SARS-CoV-2 in the COVID-19 pandemic era. *Pathogens*, *10*(8), 1030.
65. Covaxin Vs Covishield Vs Sputnik V: Which Is Better, Efficiency Rate, Price, Side Effect https://crida.in/covaxin-vs-covishield-vs-sputnik-v/, 2020.
66. Kaur, S. P., & Gupta, V. (2020). COVID-19 Vaccine: A comprehensive status report. *Virus research*, *288*, 198114.
67. Heinz, F. X., & Stiasny, K. (2021). Distinguishing features of current COVID-19 vaccines: knowns and unknowns of antigen presentation and modes of action. *npj Vaccines*, *6*(1), 104.
68. Kyriakidis, N. C., López-Cortés, A., González, E. V., Grimaldos, A. B., & Prado, E. O. (2021). SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates. *npj Vaccines*, *6*(1), 28.
69. Logunov, D. Y., Dolzhikova, I. V., Shcheblyakov, D. V., Tukhvatulin, A. I., Zubkova, O. V., Dzharullaeva, A. S., ... & Gintsburg, A. L. (2021). Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. *The Lancet*, *397*(10275), 671-681.
70. WHO lists additional COVID-19 vaccine for emergency use and issues interim policy recommendations, 2020; https://www.who.int/.
71. Amparo, T. R., Seibert, J. B., Silveira, B. M., Costa, F. S. F., Almeida, T. C., Braga, S. F. P., ... & de Souza, G. H. B. (2021). Brazilian essential oils as source for the discovery of new anti-COVID-19 drug: a review guided by in silico study. *Phytochemistry Reviews*, *20*(5), 1013-1032.
72. Ang, L., Song, E., Lee, H. W., & Lee, M. S. (2020). Herbal medicine for the treatment of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis of randomized controlled trials. *Journal of Clinical Medicine*, *9*(5), 1583.
73. Khadka, D., Dhamala, M. K., Li, F., Aryal, P. C., Magar, P. R., Bhatta, S., ... & Shi, S. (2021). The use of medicinal plants to prevent COVID-19 in Nepal. *Journal of ethnobiology and ethnomedicine*, *17*(1), 1-17.
74. Guijarro-Real, C., Plazas, M., Rodríguez-Burruezo, A., Prohens, J., & Fita, A. (2021). Potential in vitro inhibition of selected plant extracts against SARS-CoV-2 chymotripsin-like protease (3CLPro) activity. *Foods*, *10*(7), 1503.
75. Bellavite, P., & Donzelli, A. (2020). Hesperidin and SARS-CoV-2: New light on the healthy function of citrus fruits. *Antioxidants*, *9*(8), 742.
76. Shawan, M. M. A. K., Halder, S. K., & Hasan, M. (2021). Luteolin and abyssinone II as potential inhibitors of SARS-CoV-2: An in silico molecular modeling approach in battling the COVID-19 outbreak. *Bulletin of the National Research Centre*, *45*(1), 1-21.
77. Colunga Biancatelli, R. M. L., Berrill, M., Catravas, J. D., & Marik, P. E. (2020). Quercetin and vitamin C: an experimental, synergistic therapy for the prevention and treatment of SARS-CoV-2 related disease (COVID-19). *Frontiers in immunology*, 1451.
78. Alzaabi, M. M., Hamdy, R., Ashmawy, N. S., Hamoda, A. M., Alkhayat, F., Khademi, N. N., ... & Soliman, S. S. (2021). Flavonoids are promising safe therapy against COVID-19. *Phytochemistry Reviews*, 1-22.
79. Das, A., Pandita, D., Jain, G. K., Agarwal, P., Grewal, A. S., Khar, R. K., & Lather, V. (2021). Role of phytoconstituents in the management of COVID-19. *Chemico-biological interactions*, *341*, 109449.

CITATION OF THIS ARTICLE

Namrata Gundettiwar, Vijayshri Rokde, Kishor Danao.Cell Biology of Sars-Cov-2 and Current Preventive Strategies for Covid-19: A Systematic Review. Bull. Env. Pharmacol. Life Sci., Vol 11[4] March 2022 : 218-233.