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Review article

Effectiveness of Traditional Remedies, Antivirals, and Vaccines against COVID-19

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ABSTRACT

There are no specific or licensed antivirals for the treatment of COVID-19 and the approved vaccines for emergency use are not 100% effective to provide protection. This study aims to summarize and highlighted the effectiveness of traditional remedies, antiviral drugs, and vaccines for treating COVID-19 patients all over the world. Trials for treating COVID-19 patients, various therapies were used including antivirals, antibiotics, anti-inflammatory drugs etc. during the pandemic situation worldwide. Patients with moderate COVID-19 symptoms can be treated with plant-based traditional treatments to reduce morbidity and mortality. Further, a very low dose of remdesivir achieved effective inhibitory action against COVID-19. Favipiravir, hydroxychloroquine and chloroquine are also found more efficacious to treat SARS-CoV-2. Additionally, the efficacy of the Moderna vaccine was found to be higher after the initial dosage compared to other vaccination types. Knowledge of this summarizing will help to find more effective treatment for COVID-19.

Introduction

The coronavirus disease (COVID-19) firstly met in Wuhan province of China during late-December 2019 and outbreak all over the world. It was declared by the WHO (World Health Organization) as a pandemic on 12th March 2020 (Gautret et al. 2020). It is an alarming public issue now (Elmezayen et al. 2021; Rahman et al. 2021; Haque et al. 2022). A total number of 775,481,326 cases were confirmed worldwide of which 7,049,376 were died till 28 May 2024 (WHO 2024). A novel corona virus (single stranded RNA virus) named SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) is the causative agent responsible for the COVID-19 infection (Rizzo 2020). They are called coronavirus as they have crown like surface spikes. They are divided into four main sub classes, α, β, γ and δ. The SARS-CoV-2 belongs to the beta sub groups (Wu et al. 2020). The highly transmissible and contagious nature of the coronavirus makes the outbreak harder to control (Fan et al. 2020). ACE2 (Angiotensin-converting enzyme 2) is the receptor of SARS-CoV-2 at which coronavirus can bind to initiate the invasion process includes severe symptoms and mortality by endocytosis. ACE2 receptor is an S protein receptor which is found on the surface of the host cell. Mainly over activation of T cells and high cytotoxic effects of CD_8 T cells are responsible for severe immune injury (Yang and Wang 2020). Innate immune response of COVID-19 patient may be uncontrolled and engaged harmful injuries of respiratory tissue. The severity increas-

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ses due to the elevation of interleukin (IL)-2, 6, 8, 17 and 1β, IP (Interferon gamma-induced protein)-10, G-CSF (granulocyte colony stimulating factor) and TNF (tumor necrosis factor) etc. on the patient's serum which are cytokines that causes cytokine storm. Failure of multiple organs like respiratory failure, heart and liver damage may occur due to the elevated levels of pro-inflammatory cytokines which may also lead to death (Cao 2020). Clinical symptoms of COVID-19 are comparable with MERS (Middle East respiratory syndrome) and SARS (severe acute respiratory syndrome). Though, it poses lower fatality that might be increased with time (Cao et al. 2020). Although a number of drugs have been evaluated for COVID-19 but there are no approved drugs (Kapoor and Kapoor 2020).

Numerous studies have been carried out with a focus on different aspects of the COVID-19 pandemic. To the best of the author's knowledge, no study has thoroughly assessed the effectiveness of traditional remedies, antiviral drugs, and vaccinations in the fight against COVID-19. Thus, the key objective of the article is to provide a comprehensive overview on the effectiveness of traditional remedies, antiviral medications, and vaccines against COVID-19.

Traditional remedies for COVID-19

Traditional remedies primarily consist of plant-based medicines. Since the ancient era, individuals worldwide, particularly those from Asian regions such as India, China, and Japan, as well as certain African countries, have employed plants as medicinal agents (Hoareau and DaSilva 1999). In many developing countries, the therapeutic choices still rely heavily on traditional medicine, even the developed nations have lately demonstrated a growing interest in plant-based herbal formulations for safe therapeutic use (Garcia 2020). The primary reason for the folkloric use of these plants among tribal people is their pervasive availability and relatively low cost (Jahan and Onay 2020). Plants remain highly prospective therapeutic sources for the treatment of a variety of complications, including cancer, diarrhea, depression, fever, thrombosis, and oxidative stress, as well as infectious diseases, even in the modern era. Given the lack of targeted evidence-based treatment for SARS-CoV-2, certain researchers have turned to plant-based medicines, as a significant number of medications are derived from plant components (Silveira et al. 2020). This provides us with optimism that therapeutics can be created to exert anti-COVID-19 efficacy from phyto-wellsprings through a variety of mechanisms of action. This approach was highly efficient in managing symptoms (Hong-Zhi et al. 2020). Available evidence (Chowdhury and Barooah 2020; Rahman et al. 2020; Rouf et al. 2020) supports the perspective that herbal therapy has the ability to enhance resistance against COVID-19. Schematic representation of traditional remedies against COVID-19 presented in Fig. 1.

The National Health Commission of China has granted approval for the utilization of herbal medicine as a supplementary treatment for COVID-19. At the onset of the COVID-19 outbreak, Chinese traditional medicine was extensively utilized either alone or in conjunction with western medicine in the majority of hospitals in China. Additionally, the regulator has issued multiple guidelines on herbal therapy (Ang et al. 2020). The field of traditional Chinese medicines (TCM) has a long and extensive history in the management and control of infectious diseases. They exert their effects by enhancing the body's ability to defend against harmful substances, maintaining a balanced immune response, decreasing excessive inflammation, and promoting the body's ability to heal. Historically, TCM treatments have shown the ability to impede the advancement of diseases into dangerous and severe states, so effectively decreasing the deaths rate. Emerging clinical evidence suggests that TCM can have a significant impact on the treatment and prevention of COVID-19, therefore offering new possibilities for its therapy (Ren et al. 2020). Another classical medicinal philosophy, Ayurveda, has its origins in India. It places increased emphasis on developing physical strength and cognitive prowess. Ayurveda employs several treatment modalities, including steam inhalation, immunomodulators, herbal infusions, and gargling hot water, to address respiratory problems. These therapeutic approaches provide valuable hope for the current pandemic scenario (Golechha 2020). These remedies could serve as a viable option to combat the virus and potentially decrease the overall dangers associated with it, including the number of cases and deaths.

The majority of the participants studied by Islam et al. (2021) depended on plants and traditional home medicines derived from plants for managing COVID-19. Within this study, 44.72% of participants obtained home remedies directly from plants and plant-derived

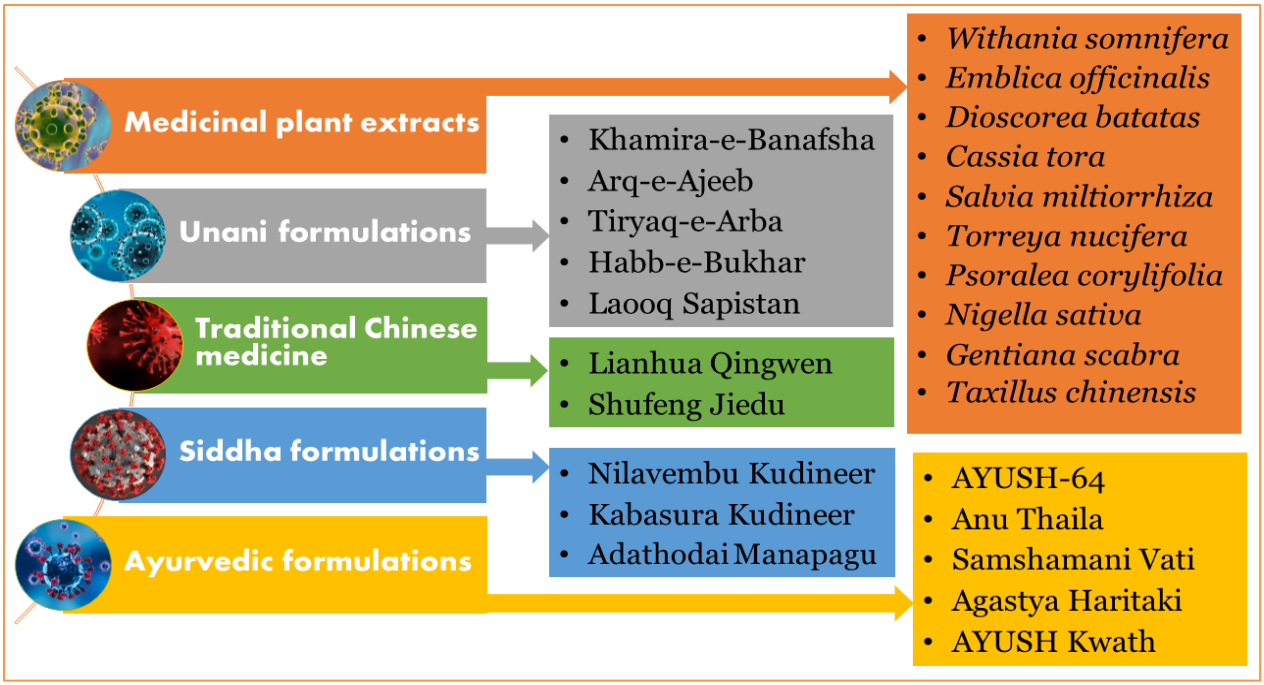

Fig. 1. Schematic representation of traditional remedies (medicinal plants extracts and their herbal formulations) against COVID-19 (modified from Sruthi et al. 2023).

products, known as herbal medicines based home remedies. Additionally, 49.54% of participants received both herbal and allopathic synthetic medications. In this instance, the individual has ingested fever and pain relievers that are classified as synthetic medications, such as Paracetamol recommended by a physician during a telephone consultation. In contrast, a mere 5.73% of the respondents who were questioned underwent allopathic treatment that relied on synthetic medications. Islam et al. (2021) found that fruit (dried and fresh), flower bud, seed, leaf, bulb, rhizome, and bark were eaten alone or with heated rice, honey, milk, tea, water, and vinegar. At 39%, fruit was the most used plant part. The next most used plant part was leaves at 29%. Other plant parts used were seed (14%), bulb (7%), bark (4%), flower bud (4%), and rhizome (3%). Before use, plant components were prepared using several methods, including boiling, fresh, mashing, decoction, juice, raw, and powdering. The most common preparation methods were boiling and fresh form, accounting for 20% overall. Also popular are mashing and juice (16%), raw and decoction (13%), and powdering (2%). These herbal medicines made from various plant components were either given orally (74%), or breathed (26%).

According to Islam et al. (2021), 26 species of medicinal plants from 23 genera and 17 botanical families were traditionally utilized by Bangladeshis to prevent and manage COVID-19 symptoms at residence. A study from Nepal (Khadka et al. 2021) discovered that applied 60 herbs from 36 groups to avoid COVID-19. Chaachouay et al. (2021) reported Moroccan herbal practitioners used 20 plant species from 14 families for COVID-19 prophylaxis and therapy. Most herbalists use the Lamiaceae medicinal plants to prevent and treat COVID-19 (Islam et al. 2021). Furthermore, computational studies have verified that selected plants such as *Withania somnifera*, *Emblica officinalis*, *Andrographis paniculata*, *Glycyrrhiza glabra*, and *Ocimum sanctum* have a strong attraction to the major protease of SARS-CoV-2. This indicates that these plants have the potential antiviral effects against the virus (Ren et al. 2021; Zhao et al. 2021; Xu et al. 2022; Shahriar et al. 2022; Sao et al. 2024). Plant-based traditional treatments are readily available to underprivileged individuals. The side effects of this product are deemed to be minimal and insignificant, and their usage and application are acknowledged to be safe. Patients with moderate symptoms of COVID-19 are advised to consider utilizing plant-based traditional remedies as they have the potential to decrease the overall risk of COVID-19, including morbidity and death (Islam et al. 2021).

Mechanism of traditional remedies

SARS-CoV-2 is a strain of the β-coronavirus genus, characterized by a spherical envelope and single-stranded positive-sense RNA. It has ultra-structural spike proteins on the surface with a crown-like structure. The genome of this virus contains structural, accessory, and non-structural proteins. The primary structural proteins are nucleocapsid (N), spike protein (S), membrane protein (M), and envelope protein (E). This virus's proliferation comprises various phases mediated by several functional molecules, which might be interesting targets for therapeutic treatment research (Haake et al. 2020; V'kovski et al. 2021). Bioactive metabolites obtained from medicinal plants prevalent in Bangladesh can inhibit or interfere with coronavirus's cellular and molecular targets (Fig. 2).

The viral multiplication process begins with attachment to the host cell surface, which is then followed by endocytosis via viral S protein binding and contact with the host cell's ACE2 receptor. Inhibitors of S protein, ACE2 receptor blockers, or interferers with S protein-ACE2 receptor interaction may all impede viral entrance into the host cell. A number of in silico studies revealed several metabolites derived from Bangladeshi medicinal plants including (a) hesperidin, seselin, 6-gingerol, and humulene epoxide interacted with and inhibited S protein of SARS-CoV-2; (b) hesperidin, kaempferol, apigenin, luteolin, quercetin, and curcumin inhibited ACE2 receptor; and (c) hesperidin, seselin, EGCG (epigallocatechin-3-gallate), curcumin, 6-gingerol, and humulene epoxide interfered with the interaction of S protein-receptor (Bellavite and Donzelli 2020; Goyal

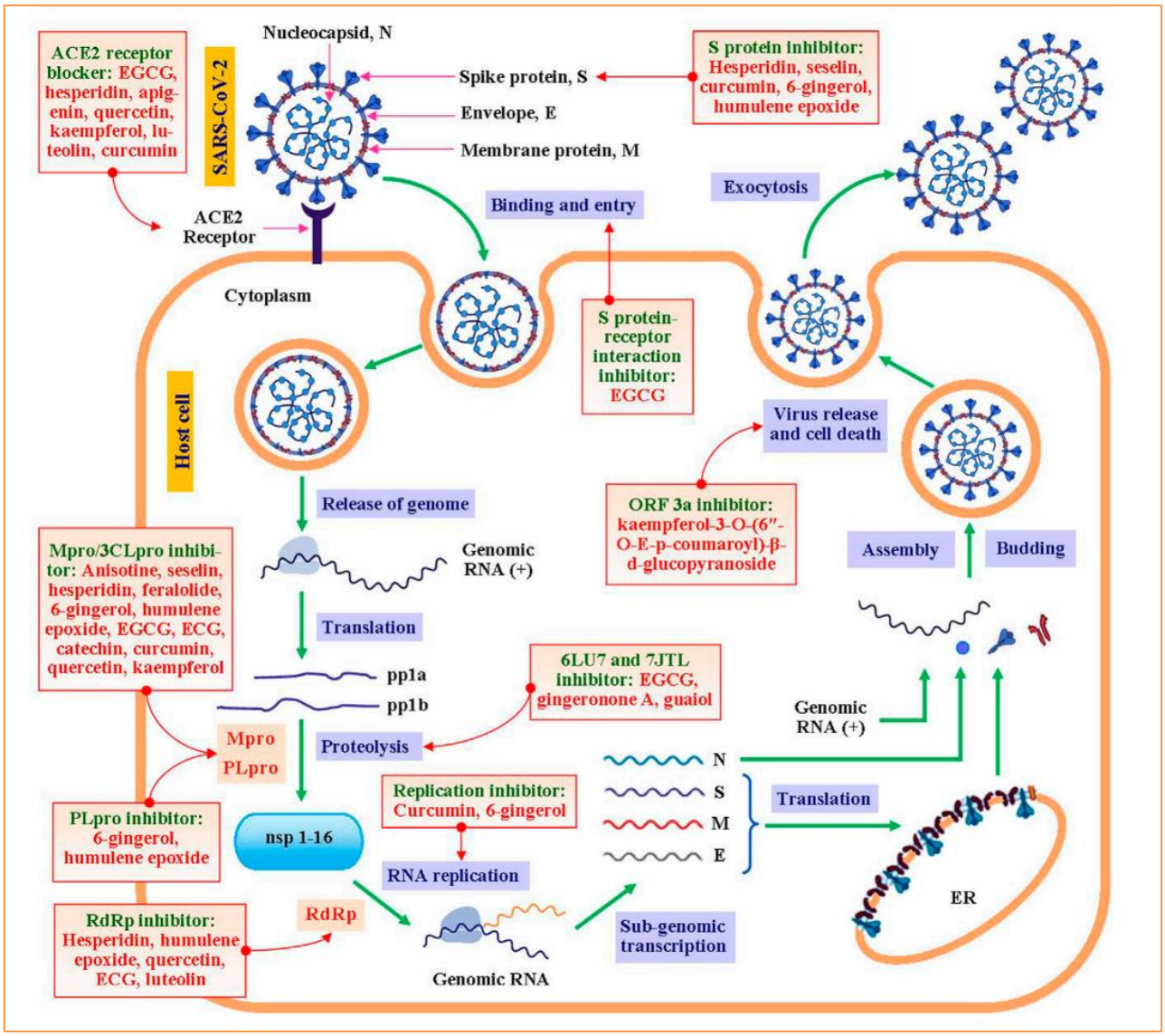

Fig. 2. Impact of bioactive metabolites derived from medicinal plants on molecular targets of various steps of multiplication process of SARS-CoV-2 (Bachar et al. 2021).

et al. 2020; Manoharan et al. 2020; Amparo et al. 2021; Bachar et al. 2021; Henss et al. 2021). These metabolites may be used to produce potential SARS-CoV-2 entry inhibitors. Following endocytosis, genomic RNA is translated into nonfunctional polypeptides, which are subsequently cleaved into functional proteins by the proteolytic activity of M^{pro} (main protease)/$3CL^{pro}$ (3-chymotrypsin-like protease) and PL^{pro} (papain-like protease) enzymes. Anisotine, hesperidin, seselin, feralolide, 6-gingerol, humulene epoxide, catechin, ECG (epicatechin gallate), EGCG, curcumin, quercetin, and kaempferol have been shown to inhibit the main protease, M^{pro}/$3CL^{pro}$ enzyme; however, 6-gingerol and humulene epoxide inhibited the PL^{pro} enzyme, producing proteolysis inhibition and non-infective, nonfunctional proteins. Aside from these, gingeronone A and guaiol inhibited 6LU7 and 7JTL, which are required for the proteolysis process (Bachar et al. 2021). The replication of genomic RNA from 16 kinds of nonstructural proteins (nsp 1-16) is controlled by RdRp (RNA dependent RNA polymerase), which is suppressed by hesperidin, luteolin, quercetin, ECG, and humulene epoxide (Goyal et al. 2020; Amparo et al. 2021). According to the newest study on therapeutic development against the SARS-CoV-2 virus, ACE2 receptor blockers and RdRp enzyme inhibitors are the most promising possibilities. Hesperidin is now in phase II clinical studies for the treatment of COVID-19 owing to its potential activity against these two primary targets (Bachar et al. 2021).

Besides, curcumin and 6-gingerol have been reported for inhibiting this replication process (Khaerunnisa et al. 2020; Bachar et al. 2021). After translation and posttranslational maturation, the genomic RNA and proteins get assembled, and initiated exocytosis mechanism resulting apoptosis of host cell. Kaempferol – 3 – O - (6 ″ - O – E – p – coumaroyl) – β – d - glucopyranoside, a plant-derived bioactive compound inhibited ORF (open reading frame) 3a, a viral protein of coronavirus involves in release mechanism (SARS-CoV-1) as well as induction of apoptosis (SARS-CoV-2) (Schwarz et al. 2014; Bachar et al. 2021).

Antiviral medications for COVID-19 treatment

Treatments of patients are done through repurposing of the existing therapeutics including different antiviral therapy, antibiotics, anti-inflammatory remedies and general corticosteroids (Cao et al. 2020; Wu et al. 2020). There are many ongoing clinical trials in which a small number of patients are involved but the studies have also some limitations (Trivedi et al. 2020). Antivirals are the molecules which can inhibit the replication cycle of viruses. They have some possible mode of actions like extracellular inactivation of viruses, inhibition of viral entry or attachment, prevention of viral protein synthesis, destruction of the assembly of virions etc. (Smith et al. 1980). Mostly used antivirals are remdesivir, hydroxychloroquine, chloroquine, favipiravir, umifenovir, lopinavir and ritonavir, azithromycin, ivermectin, recombinant interferons, darunavir, camostat mesilate, ribavirin and Tamiflu (Trivedi et al. 2020). More clear-sightedness about the role of antivirals can be obtained from clinical trials in COVID-19 infection.

Remdesivir

Remdesivir is the best nucleoside analogue drug. On 18th September 2015, it was considered as an orphan drug for the treatment of Ebola virus disease (Eynde 2020). It has strong antiviral activity against SARS-CoV-2 (Meyer et al. 2020). Both in vivo and in vitro study confirmed that remdesivir with a very low dose has inhibitory effect against MERS-CoV (Middle East respiratory syndrome coronavirus) and SARS-CoV (Yang and Wang 2020). It inhibits the replication of coronavirus in the respiratory epithelial cells by inhibiting the RdRp of the virus (Cao et al. 2020). It causes pre-mature termination by incorporating into viral RNA chains (Wang et al. 2020). GS-441524 is the active form of remdesivir which decreases viral RNA production by shading viral RNA polymerase and eludes viral exonuclease (Wu et al. 2020). It is excreted from the human body by renal excretion. Remdesivir was first approved in Japan on 7 May 2020, which is now available in the USA under an emergency use of authorization (Trivedi et al. 2020). In the USA, first SARS-CoV-2 infected patient was detected on January 19 who was hospitalized and treated with remdesivir. The clinical conditions of the patient were improved and all the symptoms have resolved (Eynde 2020). Animal study has shown that remdesivir can effectively decrease viral load (MERS virus) in the lung tissue as a result lung function is improved and damage is reduced in MERS virus infected mice (Provenzani and Polidori 2020). An in vitro study showed that remdesivir is the strongest among other six antivirals against COVID-19 infection (Fan et al. 2020).

Favipiravir (Avigan)

An endogenous guanine named favipiravir was first developed in 2002 in Japan. It is an inhibitor of RNA polymerase enzyme which structurally resembles remdesivir (Trivedi et al. 2020). Though it is normally approved for the treatment of influenza, it has also inhibitory activity against many RNA viruses like Ebola virus and West Nile virus (Fan et al. 2020; Tu et al. 2020). It is a pro drug which is first metabolized into its active form favipiravir ribofuranosyl phosphate thus inhibits viral replication by inhibiting the RdRp of the virus. Favipiravir is very much effective with low adverse effects for the treatment of COVID-19 patients (Fan et al. 2020). According to clinical studies, treatment of COVID-19 patients with favipiravir can provide more clinical benefits than umifenovir. In case of favipiravir the recovery rate was 71.43% compared to umifenovir (55.86%). Favipiravir groups have alleviated more rapidly from fever and cough than umifenovir group (Wu et al. 2020).

Chloroquine

Chloroquine is a 4-aminoquinoline compound which is widely used for the treatment of malaria and auto immune disease also has broad spectrum antiviral effects (Wu et al 2020; Wang et al. 2020). It acts by targeting lysosome where it alters cellular pH. It increases endosomal and lysosomal pH that inhibits replication of the virus (Touret and de Lamballeri 2020). A small pilot study conducted by Huang and colleagues in COVID-19 patients into two groups. Group one were treated with chloroquine 500mg orally, twice daily doses and group two were treated with combination therapy of lopinavir 400mg and ritonavir 100mg by oral route twice daily for 10 days. They were monitored for 14 days. In 13th day, all the patients treated by chloroquine were virologically 100% cured (Becker 2020).

Hydroxychloroquine (HCQ)

Hydroxychloroquine has been approved for use in the treatment of malaria and autoimmune diseases. It has an antiviral effect by reducing the interaction of the virus's genome with the host's cellular membrane, preventing viral DNA ejection, and affecting the immune system (Negrut et al. 2021). An analogue of chloroquine called hydroxychloroquine shows anti SARS-CoV activity in vitro study (Gautret et al. 2020). It is also used for the treatment of lupus erythematosus and rheumatoid arthritis (Meyer et al. 2020). It is clinically safe and more effective than chloroquine as it contains a hydroxyl group. There are fewer concerns about drug interactions so higher daily dose could be given in case of treatment with hydroxychloroquine (Gautret et al. 2020). It is also therapeutically effective against various viruses like dengue, Ebola which is confirmed by in vitro studies (Fan et al. 2020). The antiviral effect is believed to be from hydroxychloroquine's ability to increase endosomal and lysosomal pH thereby attenuating glycosylation and release of antigenic proteins by the virus. It increases cellular pH from 4 to 6 thus interferes with lysosomal acidification, phagocytosis of neutrophils, cytokine production and superoxide production (Becker et al. 2020). Study showed that, treatment of COVID-19 patients with combination therapy of HCQ + Azithromycin and HCQ (single drug) was successful and all the patients were virologically cured with lower mortality (Brouqui et al. 2023). In case of single drug, the success rate was 57.1% compared to combination therapy 100% after 6 day post treatment (Kapoor and Kapoor 2020).

Lopinavir and Ritonavir (Kaletra)

The combination of two antiviral drugs (lopinavir and ritonavir) officially named as Kaletra is a HIV protease inhibitor (Mahase 2020). Protease is the enzyme that is responsible for the replication of many viruses like HIV and Coronaviruses (Trivedi et al. 2020). It also inhibits the coronaviral proteinase (3CL^{pro}). In HIV, inhibition of HIV protease prevents fission of the gag-pol polyprotein thus noninfectious, immature virus is produced. Although it has anti-SARS-CoV activity in vitro, it can't significantly improve the clinical condition (Fan et al. 2020; Tu et al. 2020). A nucleoside analogue called Ribavirin has broad spectrum antiviral effects. A study showed that ribavirin+ lopinavir/ritonavir combination can reduce the risk of ARDs (acute respiratory distress syndrome) and death in patients with SARS (Dong et al. 2020). However, Negrut et al. (2021) recommended lopinavir/ritonavir treatment for COVID-19 infection.

Arbidol Hydrochloride (Umifenovir)

Arbidol is a broad spectrum non-nucleoside antiviral agent. It acts against SARS-CoV, arbo viruses, influenza viruses and many DNA and RNA viruses (Fragkou et al. 2020; Tu et al. 2020). It acts by inhibiting viral replication by interfering with lipid membrane fusion of the virus. It can also stimulate

humoral immunity and activity of interferons (Fan et al. 2020; Fragkou et al. 2020). According to an in vitro study, 10–30 μmol concentration of arbidol can inhibit the proliferation of SARS-CoV-2 thus the disease pathology of the virus is inhibited (Fan et al. 2020). Another study showed that, arbidol + lopinavir and ritonavir combination can increase the rate of negative conversion of coronavirus and also improve results of computed tomography scan of chest (Wu et al. 2020).

Azithromycin

Azithromycin is a broad spectrum antibiotic which belongs to macrolide groups. It has strong antibacterial activity against both gram positive and gram negative bacteria (Schögler et al. 2015). It acts by inhibiting bacterial protein synthesis thus able to relieve inflammation and can stimulate or suppress the immune system (Provenzani and Polidori 2020). It can inhibit translation of messenger RNA (Wu et al. 2020). It increases phagocytosis while decreases cytokine production which is responsible for inflammation. STDs (sexually transmitted diseases), asthma, COPD (chronic obstructive pulmonary disease), skin infections, respiratory infections, and cystic fibrosis can be treated effectively by azithromycin (Swartz 2020). According to clinical studies, treatment with azithromycin + hydroxychloroquine can be able to stop viral growth in COVID-19 patients after 6-day treatment (Wu et al. 2020).

Ivermectin

Ivermectin is a broad spectrum antiparasitic agent which can inhibit the replication of the SARS-CoV-2 in vitro. It is approved by FDA (Food and Drug Administration, USA) which has also antiviral, antibacterial and anticancer activity. It acts by inhibiting nuclear transport which is mediated by the α/β1 heterodimer thus affecting the translocation of SV40, HIV-1 which is viral specific proteins (Rizzo 2020). An in vitro study showed that, ivermectin treatment can destroy essentially all viral material after 48 hours treatment (Caly et al. 2020).

Recombinant Interferon

Interferons are a heterogenous group of naturally occurring proteins (cytokines). Interferon alpha (IFN-α) and IFN- β are type I while IFN-γ is a type II interferon. When a virus attacks human body, endogenous interferons are produced which exert immune responses to destroy the virus (Trivedi et al. 2020). They can prevent proliferation in cancer cells, stimulate or suppress the immune system and also prevent virus infection (Fan et al. 2020). Type I interferons are widely used for the treatment of RSV (respiratory syncytial virus), MERS-CoV, HCV (hepatitis C virus) and SARS-CoV. They are used alone or in combination with other drugs. Study showed that, IFN-α can reduce viral load and mitigate symptoms thus shorten the course of disease (2020). According to phase two trials result for asthma patients, IFN- β can improve lung function (Mahase 2020).

Darunavir

Darunavir is an FDA approved HIV protease inhibitor. It prevents HIV replication by inhibiting the cleavage of polyproteins called Gag-pol in virus infected cells. As a result, immature virus particles are produced (Pediatric oncall 2020). A study showed that, in 300 μmol/l concentration darunavir can inhibit viral replication (Fan et al. 2020). It is now being studied as a possible treatment for SARS-CoV-2, but no significant clinical benefit is observed. So, the use of darunavir is not supported by the study data against COVID-19 (Meyer et al. 2020).

Camostat mesilate

Camostat mesilate is a serine protease inhibitor which is first approved for the mitigation of the inflammation of pancreas in Japan. It's mechanism of action involves the deactivation of the spike protein by inhibiting the entry of SARS-CoV virus into lung cells. A combination therapy of camostat mesilate and imatinib is fully effective to inhibit the endosomal fusion of virions (Provenzani and Polidori 2020).

Ribavirin

Ribavirin is a wide spectrum antiviral agent which has inhibitory activity against both DNA and RNA viruses like SARS-CoV and MERS-CoV. The combination therapy of ribavirin and α-interferon/lopinavir is very much effective to improve the condition of patients. An in vitro study showed that ribavirin can be able to decrease viral infection. Further studies are needed to confirm the effectiveness of ribavirin for COVID-19 infection. It should be used with caution as the chances of adverse drug reactions are more (Fan et al. 2020).

Oseltamivir (Tamiflu)

Tamiflu is another antiviral drug which is used to treat influenza A and B. It inhibits the spread of the influenza virus by targeting neuraminidase enzyme found on the surface of the virus. No clinical benefits

were observed in COVID-19 patients treated with Tamiflu (Wu et al. 2020).

Mechanism of antiviral medications

Antiviral medications are being developed to target the major biochemical events and components in the replication cycle of coronavirus. These consist of the spike protein, proteolytic enzymes, and RdRp. SARS-CoV-2 is mostly spread between people through breathing droplets, but it can also be spread through the air (Ghosh et al. 2020). The virus can get into host cells in two ways: either through endosomes or by fusing with the plasma membrane. ACE2 acts as the entry receptor in both ways. The viral S protein helps the cell membrane bind to the virus. A recent investigation demonstrated that the interaction between S protein and ACE2 is triggered by a host protease known as transmembrane serine protease 2 (Hoffmann et al. 2020; Frediansyah et al. 2021). S protein neutralizes antibodies, helping the virus bind to host receptors. Fusion inhibitors can stop these fusion steps (Shang et al. 2020).

Upon the successful fusion, the envelope is detached, allowing the genome of SARS-CoV-2, together with its nucleocapsid, to enter the cytoplasm of the host cell (Fig. 3). Its genome includes ORF1a and ORF1b genes that encode two polyproteins, pp1a and pp1b, which facilitate the hijacking of host ribosomes for viral translation. These polyproteins are then hydrolyzed by M^{pro} and P^{pro} to generate several non-structural proteins. On the basis of a three-dimensional analytical model showing a 96% resemblance with SARS-CoV, it has been proposed that $3CL^{Pro}$ exists in SARS-CoV-2, in addition to M^{pro} and P^{pro}. Such proteases are crucial for the reproduction and transcription of viruses, and protease inhibitors that block these proteases have the potential to be antiviral agents for SARS-CoV-2 (Hoffmann et al. 2020; Lu et al. 2020).

Non-structural protein (nsp12) assembles a replication and transcription complex known as RdRp. In SARS-CoV, the protein complex formed by the association of nsp12 with its cofactors (nsp7 and nsp8) generates a complementary negative-sense RNA by utilizing the original positive RNA as a template. The negative-strand RNA is subsequently utilized by viral replicase to produce fresh positive RNA molecules for undergoing another translation and replication procedure, so constructing the genome of the latest viral particles (Nagy and Pogany 2012; Frediansyah et al. 2021). The mechanism in SARS-CoV is mediated by topoisomerase III-beta. These steps can be interrupted by the use of reverse transcription inhibitors. For the assembly and budding of the enveloped virus, post-translational modification is necessary. The sub-genomic RNA establishes a structural protein complex comprising of S, E, M, and N. Subsequently, S, E, and M proceed to the endoplasmic reticulum. Within the cytoplasm, the positive-strand RNA and N combine to create a nucleoprotein complex. Upon merging, these complexes finalize the replication of the virus within the endoplasmic reticulum-Golgi apparatus compartment. Once mature, the viruses are transported to the extracellular space via the Golgi apparatus and vesicles, and then released from the cells to infect additional cells (Klumperman et al. 1994; Nal et al. 2005; Chang et al. 2014).

Vaccines for COVID-19

While several substances and medications have been used to fight COVID-19, they have only served as supplementary therapy options. Vaccinations, on the other hand, continue to be the most efficient and successful technique for safeguarding persons against this lethal disease (Tavilani et al. 2021). A vaccination is a biological substance that induces active and adaptive immunity against a specific disease. In the production of vaccines, the disease-causing microorganisms are employed in either weakened or inactivated form, or their toxins or surface proteins are applied. Vaccines are provided through nasal, oral, or injectable routes (intramuscular, subcutaneous, or intradermal) to stimulate the immune system's response to foreign substances (Dai et al. 2019). In order to acquire immunity, the body generates antibodies (immunoglobulins) against germs, hence creating the body's defense system. The antibodies generated by the immune system upon re-exposure to the same microbe serve to hinder or reduce the severity of the disease (WHO 2020; Dai et al. 2019). Significant progress has been made in the development of vaccinations. In early December 2020, Europe initiated the first large-scale vaccination programme, prioritizing individuals who are at a high risk of severe COVID-19 infection, such as the elderly, as well as those who are at a high risk of viral exposure and transmission, such as front-line medical staff (Paules et

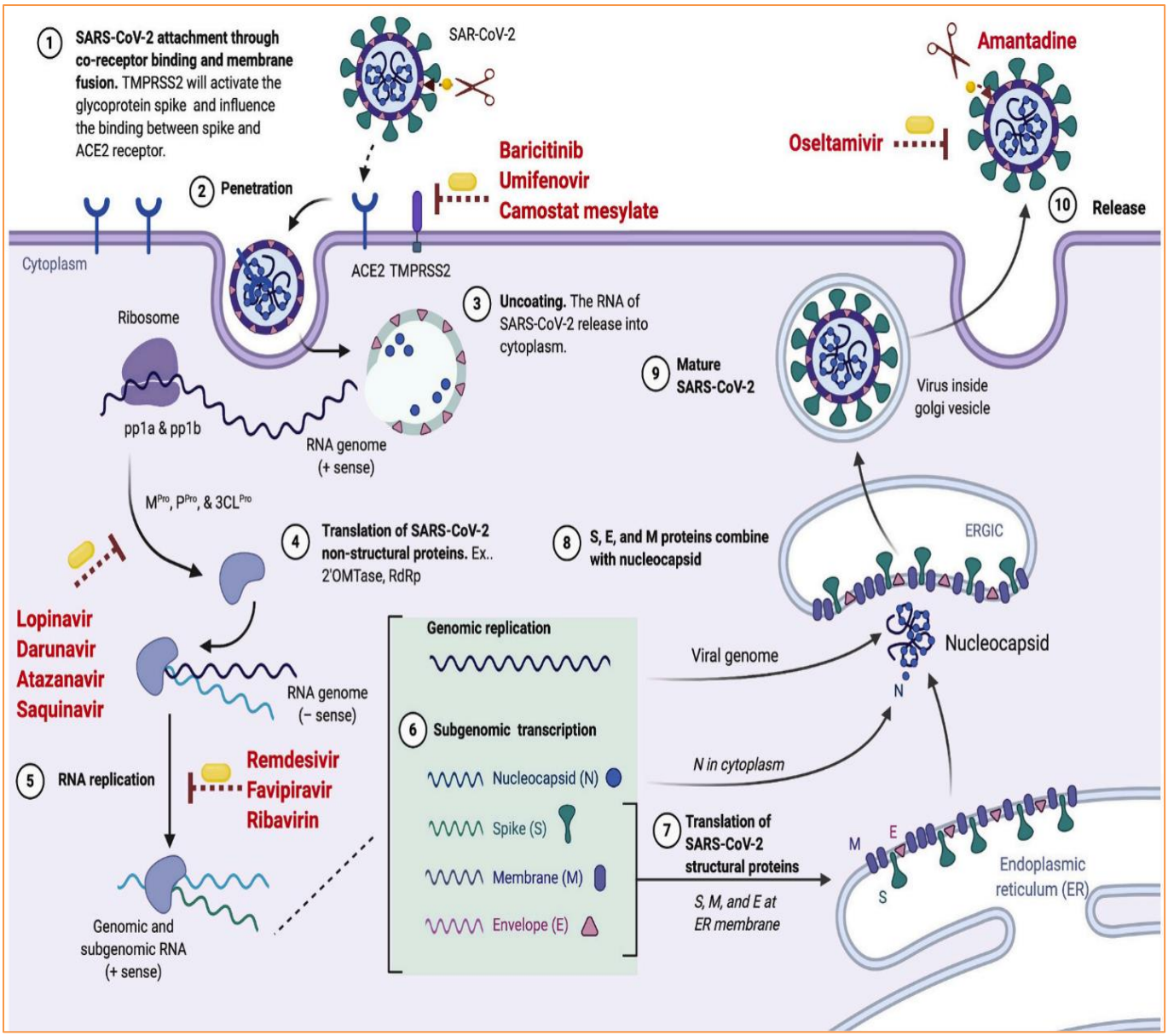

Fig. 3. The life cycle of SARS-CoV-2 and possible inhibition targets of antiviral drugs. Fusion inhibitors inhibit the fusion process of viral entry, while protease inhibitors target some proteases. Transcription inhibitors target reverse transcription step by blocking RNA-dependent RNA polymerase and therefore prevent viral replication. Some of the transcriptase inhibitors are nucleoside reverse-transcriptases (Source: Frediansyah et al. 2021).

2020). Numbers of vaccines were developed by serval countries to fight COVID-19 and authorized by competent organization (Table 1).

***Mechanism of messenger RNA vaccines*:** These vaccines rely on artificial messenger RNA (mRNA) to infect host cells and create a specific component of the spike protein. Once the body undergoes degradation, the protein stimulates the synthesis of antibodies. Immunoglobulins, often known as antibodies, prime the body to effectively combat future infections while minimizing the likelihood of adverse reactions. The Pfizer and Moderna vaccines employ this method (CDC 2021a). The BNT162b2 vaccine, created by Pfizer/BioNTech, induces an immune response by triggering the production of IgG, IgA, CD8+ cells, and CD4+ cells. On the other hand, the mRNA-1273 vaccine, developed by Moderna, specifically stimulates CD8 T cells (Goyal et al. 2021).

***Mechanism of Viral vector based vaccines*:** These are modified variants of a virus from a distinct genus that are used as a carrier. By engaging with immune cells, it facilitates their ability to identify and outsmart harmful pathogens. Upon injection into the body, the immune cells promptly detect the existence of foreign

Table 1. Overview of well-known COVID-19 vaccine brands

Features	**Moderna** (mRNA-1273)	**Pfizer-BioNTech** (BNT162b2, Comirnaty)	**AstraZeneca** (AZD1222 (ChAdOx1))	**Sinopharm** (BBIP-CorV)	**Bharat Biotech** (Covaxin (BBV152))
Manufacturer	Spain	Germany	Sweden	China	India
Vaccine type	mRNA	mRNA	Adenovirus viral vector	Inactivated virus	Inactivated virus
Approval	WHO, FDA, EMA	WHO, FDA, EMA	WHO, EMA	WHO, FDA, EMA	WHO
Age groups	Adults (FDA), ≥ 6 years (EMA)	≥ 5 years	≥18 years	≥ 18 years	≥ 18 years
Storage condition	2-8 °C for 30 days	6 months at 70°C. Undiluted vials at room temp. for ≤ 2 hrs.	2-8 °C	2-8 °C	2 8°C up to 6 hrs.
Doses required	2 shots, 28 days apart	2 shots, 21 days apart	2 shots, 28 days apart	2 shots, 21 days apart	2 shots, 28 days apart
Effectiveness	94.5%	95%	72%	79%	78%

mRNA, messenger ribonucleic acids; WHO, World Health Organization; FDA, Food and Drug Administration; EMA, European Medicines Agency

antigens and initiate an immune response by releasing B cells and T cells that produce antibodies. These cells then locate and eliminate contaminated cells. T cells operate by scrutinizing the repertoire of proteins that are presented on the cell's outer membrane. Upon encountering a foreign protein, the immune system initiates a response against the cell harboring it due to its ability to recognize the body's own proteins as "self" (WHO 2021a). The Janssen/Johnson & Johnson, Sputnik V, and AstraZeneca vaccines utilize this mechanism (CDC 2021b).

***Mechanism of Protein subunit vaccines*:** There are components (proteins) of the virus that causes COVID-19 that are contained within protein subunit vaccines. These fragments of the virus constitute the spike protein. In addition, the vaccination includes a component known as an adjuvant, which is a component that assists the immune system in responding to the spike protein in the future instances. After the immune system has gained the knowledge necessary to respond to the spike protein, it will be able to promptly react to the genuine virus spike protein and provide protection against COVID-19 (CDC 2021b).

Table 2. Effectiveness of COVID-19 vaccine type and variant (modified from Soheili et al. 2023)

Vaccine/variant	**Dose**	**Effectiveness % (95% CI)**
Vaccine		
Moderna	1st	74 (65 - 83)
	2nd	93 (89 - 97)
AstraZeneca	1st	69 (55 - 82)
	2nd	89 (80 - 97)
Pfizer	2nd	90 (83 - 96)
	1st	67 (51 - 83)
Variant		
Alpha	1st	74 (62 - 86)
	2nd	86 (73 -98)
Beta	1st	61 (61 - 62)
	2nd	96 (96 - 96)
Delta	1st	65 (40 - 89)
	2nd	87 (82 - 92)
Gamma	1st	74 (73 - 75)
	2nd	95 (95 - 96)
Other	1st	74 (55 - 93)
	2nd	95 (92 - 98)

***Mechanism of Inactivated or whole virus vaccines*:** There types of vaccines that have been used for a long time and are widely available: live attenuated vaccines or/and inactivated vaccines. Chemicals, heat, and radiation are employed to eradicate the genetic material of the virus in order to produce inactivated immunizations. These vaccines, being derived from weakened natural pathogens, elicit a broad array of

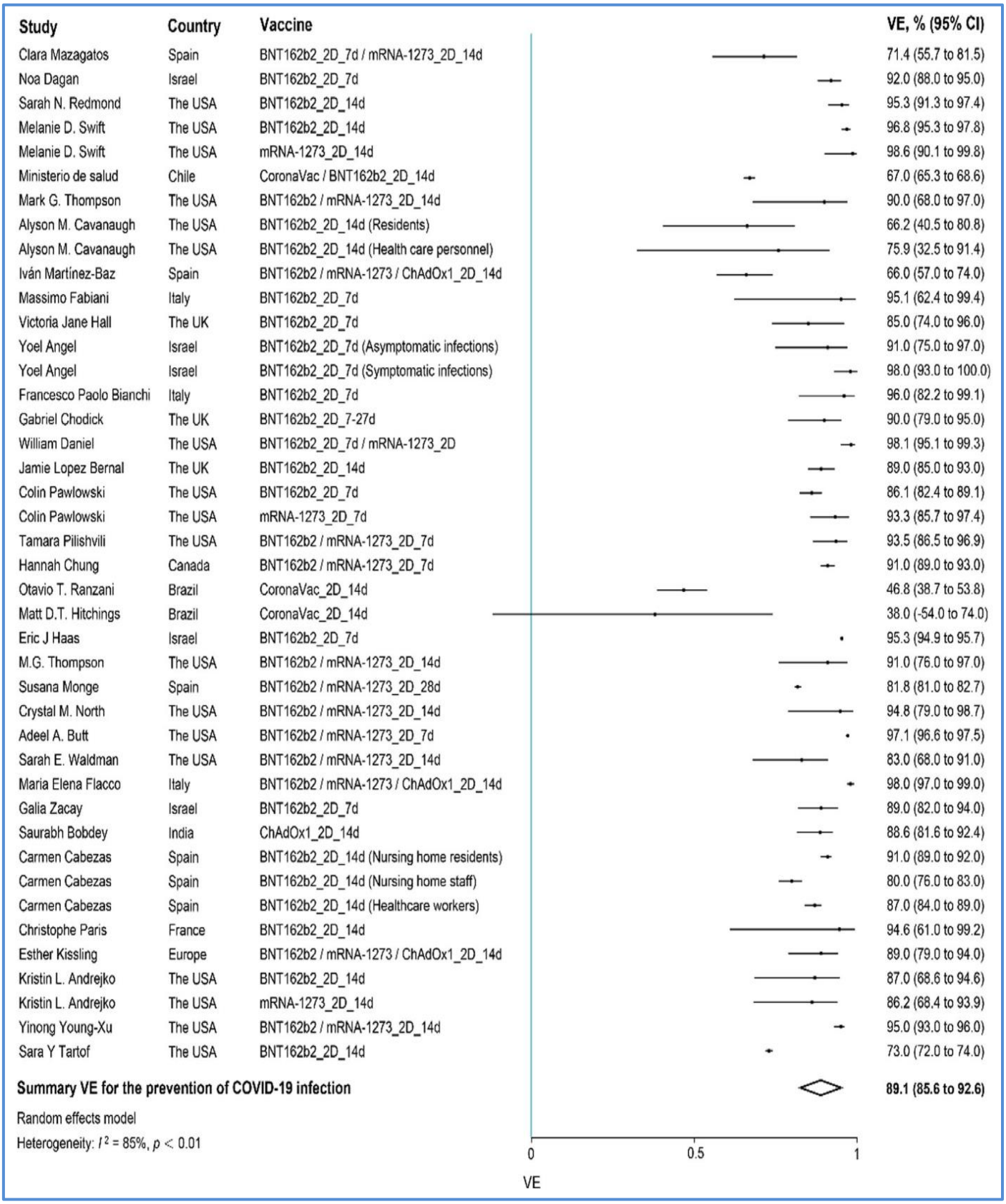

Fig. 4. Vaccine effectiveness (VE) for the prevention of SARS-CoV-2 infection with a fully vaccinated status. Forest plot showing effectiveness against COVID-19 infection for fully vaccinated populations (Zheng et al. 2022).

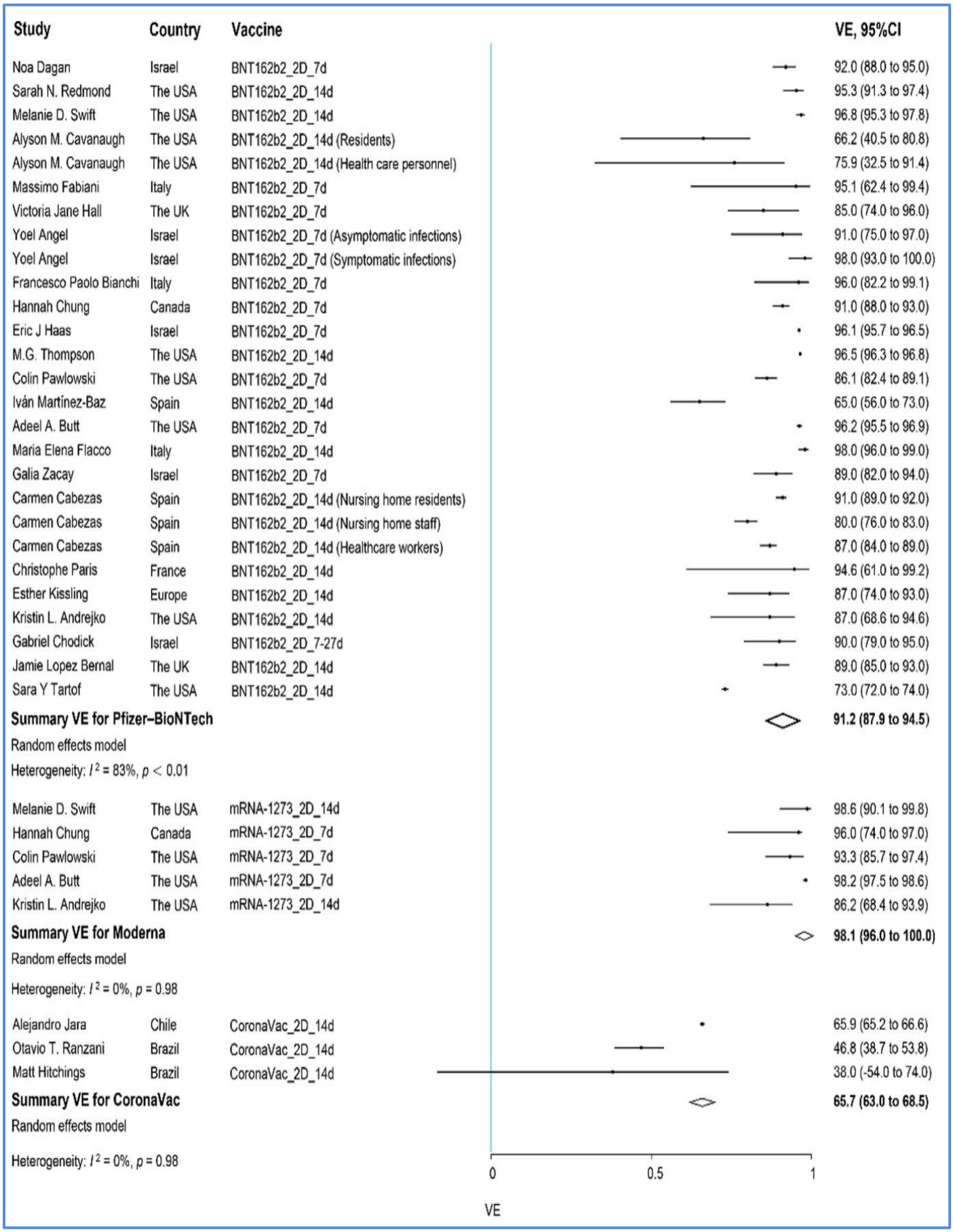

Fig. 5. Vaccine effectiveness (VE) against SARS-CoV-2 infection for the different brands with a full vaccination status. Forest plot showing effectiveness against COVID-19 infection for fully vaccinated populations with different vaccine brands (Zheng et al. 2022).

immune responses. This includes the activation of killer T cells, which eliminate infected cells, helper T cells, which aid in antibody production, and B cells, which generate antibodies to target pathogens (WHO 2021b). Upon introduction into the body, they elicit antibody-mediated reactions that are feeble and of relatively brief duration. Consequently, they are given in conjunction with an adjuvant, and additional dosages are often necessary. On the other hand, live attenuated vaccines employ a debilitated form of the virus within the body. Once within the body, these viruses have the ability to undergo growth and reproduction, however they do not result in symptomatic disease in the host (NIAID 2021). The Sinopharm, Covaxin, Sinovac, and Corovac vaccines utilize this deactivated mechanism. The Covivac vaccine (Shahzamani et al. 2021) utilizes the live attenuated method.

Effectiveness of COVID-19 vaccines

By studying several vaccines, Soheili et al. (2023) shown that the combined rate of effectiveness for Moderna, AstraZeneca, and Pfizer after the initial dose were 74% (95% CI 0.065, 0.83), 69% (95% CI 0.55, 0.82), and 67% (95% CI 0.51, 0.83) respectively. The efficacy of the Moderna vaccine was found to be higher after the initial dosage compared to other vaccination types. The combined efficacy rates after the second dosage of Moderna, AstraZeneca, and Pfizer vaccines were 93% (95% confidence interval [CI] 0.89, 0.97), 89% (0.80, 0.97), and 90% (95% CI 0.83, 0.96) correspondingly. Among the vaccines analyzed, Moderna exhibited the highest efficacy after the second dose, as shown in Table 2. Moreover, the efficacy of both the first and follow-up COVID-19 vaccinations against various variations is documented. The initial efficacy of vaccination against the Gamma variant was 74% (95% CI: 0.73-0.75), surpassing that of other variants. The total efficacy of the first dose was 82% with a 95% confidence interval of 0.81 to 0.82. The Beta version had the best efficacy of 96% after the administration of the second dose. The efficacy of the second vaccine dose was 96% (Table 2).

The authorized vaccines are highly protective against COVID-19 in real-world settings from the results of phase III clinical trials (Zheng et al. 2022). Based on the study of Zheng et al. (2022), the effectiveness of COVID-19 vaccine against SARS-CoV-2 infection among fully vaccinated people was 89.1% with 95% CL of 85.6–92.6% (Fig. 4). The effectiveness of the different vaccine brands was also estimated among the fully vaccinated people. The summary effectiveness was 91.2% (95% CI: 87.9–94.5%) for Pfizer-BioNTech, 98.1 % (95% CI: 96.0–100.0%) for Moderna, 65.7% (95% CI 63.0–68.5%) for CoronaVac against COVID-19 infection (Fig. 5). The actual effectiveness (or evaluation of population effectiveness) of different vaccines relies on a series of factors including vaccinated population, epidemic severity, study design, validity and completeness of data sources, potential methodological biases, etc. (Patel et al. 2021). It is important to remember that vaccination does not completely remove the possibility of infection (Brosh-Nissimov et al. 2021). Therefore, it is crucial to conduct preventative and control measures carefully, particularly for individuals in high-risk categories including maintaining social distance and personal hygiene, wearing face masks, taking adequate rest which are primary preventive measures against the pandemic.

Conclusion

COVID-19 pandemic has spread all over the world and people became detached from daily work. The results of both in vitro and in vivo studies using traditional remedies, antivirals, and vaccines for the treatment of COVID-19 infection are absolutely promising. Traditional remedies based on plants could serve as an option for patients suffering moderate COVID-19 symptoms. Antivirals with higher percentage of success should be treated before specific medicines targeting SARS CoV-2 are available. Clinical studies demonstrates that authorized vaccinations provide effective protection against COVID-19. However, proper cautions should be taken during treatment for compromised patients who have infected. Along with proper clinical and medical treatment, other necessary steps should be taken like early detection, early isolation, proper management and elimination of the source of infection to defend the pandemic.

Conflicts of interest

The author declare that no conflicts of interest exist.

References

Amparo TR, Seibert JB, Silveira BM, ... & de Souza GHB (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.

Ang L, Song E, Lee HW & Lee MS (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.

Bachar SC, Mazumder K, Bachar R, Aktar A & Al Mahtab M (2021). A review of medicinal plants with antiviral activity available in Bangladesh and mechanistic insight into their bioactive metabolites on SARS-CoV-2, HIV and HBV. Frontiers in Pharmacology, 12:732891.

Becker RC (2020). Covid-19 treatment update: follow the scientific evidence. Journal of Thrombosis and Thrombolysis, 50, 43-53.

Bellavite P & Donzelli A (2020). Hesperidin and SARS-CoV-2: New light on the healthy function of citrus fruits. Antioxidants, 9(8), 742.

Brosh-Nissimov T, Orenbuch-Harroch E, Chowers M, ... & Wiener-Well Y (2021). BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully vaccinated hospitalized COVID-19 patients in Israel. Clinical Microbiology and Infection, 27(11), 1652-1657.

Brouqui P, Million M, Parola P, Mccullough PA & Raoult D (2023). Outcomes after early treatment with hydroxychloroquine and azithromycin: An analysis of a database of 30,423 COVID-19 patients. New Microbes and New Infections, 55, 101188.

Caly L, Druce JD, Catton MG, Jans DA & Wagstaff KM (2020). The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Research, 178, 104787.

Cao X (2020). COVID-19: immunopathology and its implications for therapy. Nature Reviews Immunology, 20(5), 269-270.

Cao YC, Deng QX & Dai SX (2020). Remdesivir for severe acute respiratory syndrome coronavirus 2 causing COVID-19: An evaluation of the evidence. Travel Medicine and Infectious Disease, 35, 101647.

CDC (2021a). Centers for Disease Control and Prevention: Understanding mRNA COVID-19 vaccines.

CDC (2021b). Centers for Disease Control and Prevention: Understanding viral vector vaccines.

CDC (2021c). Centers for Disease Control and Prevention: Understanding Protein subunit vaccines.

Chaachouay N, Douira A & Zidane L (2021). COVID-19, prevention and treatment with herbal medicine in the herbal markets of Salé Prefecture, North-Western Morocco. European Journal of Integrative Medicine, 42, 101285.

Chang C-k, Hou M-H, Chang C-F, Hsiao C-D, Huang T-h (2014). The SARS coronavirus nucleocapsid protein – Forms and functions. Antiviral Research, 103, 39-50.

Chowdhury P & Barooah AK (2020). Tea bioactive modulate innate immunity: In perception to COVID-19 pandemic. Frontiers in Immunology, 11, 590716.

Dong L, Hu S & Gao J (2020). Discovering drugs to treat coronavirus disease 2019 (COVID-19). Drug Discoveries & Therapeutics, 14(1), 58-60.

Elmezayen AD, Al-Obaidi A, Şahin AT & Yelekçi K (2021). Drug repurposing for coronavirus (COVID-19): in silico screening of known drugs against coronavirus 3CL hydrolase and protease enzymes. Journal of Biomolecular Structure and Dynamics, 39(8), 2980-2992.

Eynde JJV (2020). COVID-19: An Update about the Discovery Clinical Trial. Pharmaceuticals 13(5), 98.

Fan L, Jiang S, Yang X, Wang Z & Yang C (2020). COVID-19 drug treatment in China. Current Pharmacology Reports, 6(4), 146-154.

Fragkou PC, Belhadi D, Peiffer-Smadja N, ... & Tsiodras S (2020). Review of trials currently testing treatment and prevention of COVID-19. Clinical Microbiology and Infection, 26(8), 988-998.

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

Garcia S (2020). Pandemics and traditional plant-based remedies. A historical-botanical review in the

era of COVID19. Frontiers in Plant Science, 11, 571042.

Gautret P, Lagier JC, Parola P, ... & Raoult D (2020). Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents, 56(1), 105949.

Ghosh AK, Brindisi M, Shahabi D, Chapman ME & Mesecar AD (2020). Drug development and medicinal chemistry efforts toward SARS-coronavirus and Covid-19 therapeutics. ChemMedChem, 15(11), 907-932.

Golechha M (2020). Time to realise the true potential of Ayurveda against COVID-19. Brain, Behavior and Immunity, 87, 130.

Goyal K, Goel H, Baranwal P, ... & Kesari KK (2021). Immunological mechanisms of vaccine-induced protection against SARS-CoV-2 in humans. Immuno, 1(4), 442-456.

Goyal RK, Majeed J, Tonk R, Dhobi M, Patel B, Sharma K & Apparsundaram S (2020). Current targets and drug candidates for prevention and treatment of SARS-CoV-2 (COVID-19) infection. Reviews in Cardiovascular Medicine, 21(3), 365-384.

Haake C, Cook S, Pusterla N & Murphy B (2020). Coronavirus infections in companion animals: virology, epidemiology, clinical and pathologic features. Viruses, 12(9), 1023.

Haque MK, Zaman MRU, Rahman MA, Hossain MY, Shurid TI, Rimi TA, Arby H & Rabbany MG (2022). A review on impacts of COVID-19 on global agricultural system and Scope for Bangladesh after pandemic. Environmental Science and Pollution Research, 29(36), 54060-54071.

Henss L, Auste A, Schürmann C, Schmidt C, von Rhein C, Mühlebach MD & Schnierle BS (2021). The green tea catechin epigallocatechin gallate inhibits SARS-CoV-2 infection. Journal of General Virology, 102(4), 001574.

Hoareau L & DaSilva EJ (1999). Medicinal plants: a re-emerging health aid. Electronic Journal of Biotechnology, 2(2), 3-4.

Hoffmann M, Kleine-Weber H, Schroeder S, ... & Pöhlmann S (2020). SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell, 181(2), 271-280.

Hong-Zhi DU, Xiao-Ying HOU, Yu-Huan MIAO, Huang BS & Da-Hui LIU (2020). Traditional Chinese Medicine: an effective treatment for 2019 novel coronavirus pneumonia (NCP). Chinese Journal of Natural Medicines, 18(3), 206-210.

Islam AR, Ferdousi J & Shahinozzaman M (2021). Previously published ethno-pharmacological reports reveal the potentiality of plants and plant-derived products used as traditional home remedies by Bangladeshi COVID-19 patients to combat SARS-CoV-2. Saudi Journal of Biological Sciences, 28(11), 6653-6673.

Jahan I & Onay A (2020). Potentials of plant-based substance to inhabit and probable cure for the COVID-19. Turkish Journal of Biology, 44(3), 228.

Kapoor KM & Kapoor A (2020). Role of Chloroquine and Hydroxychloroquine in the Treatment of COVID-19 Infection. A Systematic Literature Review. MedRxiv. Retrieved from https://doi.org/10.1101/2020.03.24.20042366

Khadka D, Dhamala MK, Li F ... & Shi S (2021). The use of medicinal plants to prevent COVID-19 in Nepal. Journal of Ethnobiology and Ethnomedicine, 17, 1-17.

Khaerunnisa S, Kurniawan H, Awaluddin R, Suhartati S & Soetjipto S (2020). Potential inhibitor of COVID-19 main protease (M^{pro}) from several medicinal plant compounds by molecular docking study. Retrieved from https://doi.org/10.20944/preprints202003.0226.v1

Klumperman J, Locker JK, Meijer A, Horzinek MC, Geuze HJ & Rottier PJ (1994). Coronavirus M proteins accumulate in the Golgi complex beyond the site of virion budding. Journal of Virology, 68(10), 6523-6534.

Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, ... & Tan W (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The Lancet, 395(10224), 565-574.

Mahase E (2020). Covid-19: what treatments are being investigated? The BMJ, 368, m1252.

Manoharan Y, Haridas V, Vasanthakumar KC, Muthu S, Thavoorullah FF & Shetty P (2020).

Curcumin: a wonder drug as a preventive measure for COVID19 management. Indian Journal of Clinical Biochemistry, 35, 373-375.

Meyer SD, Bojkova D, Cinatl J, ... & Ciesek S (2020). Lack of antiviral activity of darunavir against SARS-CoV-2. International Journal of Infectious Diseases, 97, 7-10.

Nagy PD & Pogany J (2012). The dependence of viral RNA replication on co-opted host factors. Nature Reviews Microbiology, 10(2), 137-149.

Nal B, Chan C, Kien F, ... & Altmeyer R (2005). Differential maturation and subcellular localization of severe acute respiratory syndrome coronavirus surface proteins S, M and E. Journal of General Virology, 86(5), 1423-1434.

Negrut N, Codrean A, Hodisan I, Bungau S, Tit DM, Marin R, ... & Nistor-Cseppento DC (2021). Efficiency of antiviral treatment in COVID-19. Experimental and Therapeutic Medicine, 21(6), 1-7.

NIAID (2021). National Institute of Allergy and Infectious Diseases: Vaccine types. 2021.

Patel MK, Bergeri I, Bresee JS, ... & Feikin DR (2021). Evaluation of post-introduction COVID-19 vaccine effectiveness: Summary of interim guidance of the World Health Organization. Vaccine, 39(30), 4013-4024.

Paules CI, Marston HD & Fauci AS (2020). Coronavirus infections—more than just the common cold. Jama, 323(8), 707-708.

Pediatric oncall (2020). Darunavir. Retrieved from https://www.pediatriconcall.com/drugs/darunavir/464.

Provenzani A & Polidori P (2020). Covid-19 and drug therapy, what we learned. International Journal of Clinical Pharmacy, 42, 833-836.

Rahman MA, Hossain MY, Tanjin S, Mawa Z, Hasan MR & Jasmine S (2021). Effects of COVID-19 pandemic on *Baor* (Oxbow lake) fisheries: Decreased economic livelihoods and food security. Lakes & Reservoirs: Research & Management, 26(3), e12374.

Rahman MH, Akter R, Behl T, ... & Kamal MA (2020). COVID-19 outbreak and emerging management through pharmaceutical therapeutic strategy. Current Pharmaceutical Design, 26(41), 5224-5240.

Ren JL, Zhang A H & Wang XJ (2020). Traditional Chinese medicine for COVID-19 treatment. Pharmacological Research, 155, 104743.

Ren W, Liang P, Ma Y, Sun Q, ... & Yang S (2021). Research progress of traditional Chinese medicine against COVID-19. Biomedicine & Pharmacotherapy, 137, 111310.

Rizzo E (2020). Ivermectin, antiviral properties and COVID-19: a possible new mechanism of action. Naunyn-schmiedeberg's Archives of Pharmacology, 393(7), 1153-1156.

Rouf R, Uddin SJ, Sarker DK, ... & Sarker SD (2020). Antiviral potential of garlic (Allium sativum) and its organosulfur compounds: A systematic update of pre-clinical and clinical data. Trends in Food Science & Technology, 104, 219-234.

Sao A, Nimbekar T, Venkateswarlu G, Mishra M, Kate A, Chauhan MK & Chakole CM (2024). Exploring the Efficacy of Traditional Herbs in Combating COVID-19: A Comprehensive Review. Coronaviruses, 5(2), 8-21.

Schögler A, Kopf BS, Edwards MR, ... & Alves MP (2015). Novel antiviral properties of azithromycin in cystic fibrosis airway epithelial cells. European Respiratory Journal, 45(2), 428-439.

Schwarz S, Sauter D, Wang K, ... & Schwarz W (2014). Kaempferol derivatives as antiviral drugs against the 3a channel protein of coronavirus. Planta Medica, 80(02/03), 177-182.

Shahriar S, Sarker MMR, Soma MA, ... & Rashid MA (2022). Potential of prospective medicinal plants of Bangladesh for the complementary management of COVID-19. Bangladesh Pharmaceutical Journal, 25(1), 89-114.

Shahzamani K, Mahmoudian F, Ahangarzadeh S, ... & Javanmard SH (2021). Vaccine design and delivery approaches for COVID-19. International Immunopharmacology, 100, 108086.

Shang J, Ye G, Shi K, Wan Y, ... & Li F (2020). Structural basis of receptor recognition by SARS-CoV-2. Nature, 581(7807), 221-224.

Silveira D, Prieto-Garcia JM, Boylan F, Estrada O, ... & Heinrich M (2020). COVID-19: is there evidence for the use of herbal medicines as adjuvant symptomatic therapy?. Frontiers in Pharmacology, 11, 581840.

Smith RA, Sidwell RW & Robins RK (1980). Antiviral mechanisms of action. Annual Review of Pharmacology and Toxicology, 20(1), 259-284.

Soheili M, Khateri S, Moradpour F, ... & Moradi Y (2023). The efficacy and effectiveness of COVID-19 vaccines around the world: a mini-review and meta-analysis. Annals of Clinical Microbiology and Antimicrobials, 22(1), 42.

Sruthi D, Jishna JP, Dhanalakshmi M, Deepanraj SP & Jayabaskaran C (2023). Medicinal Plant Extracts and Herbal Formulations: Plant Solutions for the Prevention and Treatment of COVID-19 Infection. Future Integrative Medicine, 2(4), 216-226.

Swartz TS (2020). Can azithromycin treat COVID-19? https://www.optometrytimes.com/view/safe-and-effective-ocular-triage-in-the-covid-19-era.

Tavilani A, Abbasi E, Ara FK, Darini A & Asefy Z (2021). COVID-19 vaccines: Current evidence and considerations. Metabolism Open, 12, 100124.

Touret F & de Lamballeri X (2020). Of chloroquine and COVID-19. Antiviral Research 177, 104762.

Trivedi A, Sharma S & Ashtey B (2020). Investigational treatments for COVID-19. Pharmaceutical Journal, 304, 7938.

Tu YF, Chien CS, Yarmishyn AA, ... & Chiou SH (2020). A review of SARS-CoV-2 and the ongoing clinical trials. International Journal of Molecular Sciences, 21(7), 2657.

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.

Wang M, Cao R, Zhang L, ... & Xiao G (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research, 30(3), 269-271.

WHO (2020). World Health Organization: How do vaccines work? Body's response to vaccines.

WHO (2021a) Collaborating Centre for Vaccine Safety: How do vector vaccines work?

WHO (2021b). Collaborating Centre for Vaccine Safety: How do inactivated vaccines work?

WHO (2024). WHO COVID-19 dashboard. Retrieved from https://data.who.int/dashboards/covid19/

Wu R, Wang L, Kuo HCD, Shannar A, Peter R, Chou PJ, ... & Kong AN (2020). An update on current therapeutic drugs treating COVID-19. Current Pharmacology Reports, 6(3), 56-70.

Xu J, Liu H, Fan Y & Ji B (2022). Traditional Chinese Medicine is effective for COVID-19: a systematic review and meta-analysis. Medicine in Novel Technology and Devices, 16, 100139.

Yang P & Wang X (2020). COVID-19: a new challenge for human beings. Cellular & Molecular Immunology, 17(5), 555–557.

Zhao Z, Li Y, Zhou L, Zhou X, Xie B, Zhang W & Sun J (2021). Prevention and treatment of COVID-19 using Traditional Chinese Medicine: A review. Phytomedicine, 85, 153308.

Zheng C, Shao W, Chen X, Zhang B, Wang G & Zhang W (2022). Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. International Journal of Infectious Diseases, 114, 252–260.

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