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Review article

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A rationalized review on eradication of Covid-19 - targeted herbal products

Dr. S. K. Devipriya^{1*}, Dr. V. Sathyanathan²

¹Siddha Practitioner, Magizham siddha clinic, A.S. Complex Bazar, Sevvapet, Tiruvallur-602025, India

²Principal, Apollo College of Pharmacy, Mevaloorkuppam (V), Valarapuram PO, Sriperumbudur (TK), Kanchipuram-602105, India.

Corresponding author: Dr. S. K. Devipriya
Email: devifeb14siddha@gmail.com

ABSTRACT

Coronavirus disease 2019 (COVID-19) is a recurrent, quickly evolving disease outbreak caused by Coronavirus - 2 Severe Acute Respiratory Syndrome (SARS-CoV2). As of now (December 23, 2020), the cumulative number of known positive cases has been registered to be 78,481,916 in all affected countries around the world and the death toll is 1,726,632. There is no clear therapy to heal COVID-19 at present. No medicines have been developed so far, but people are making tremendous efforts to produce new therapies to disrupt COVID-19. Natural products have been playing an important role in the occurrence of diseases since ancient times. These products can be used as models for developing novel antimicrobial agents with diverse modes of action, as well as opening the door for the study of successful anti-COVID-19 antiviral drugs. The fundamental structure, infection and pathogenesis of the human SARS-CoV2 virus are identified with a focus on this. Due to the structure of these viruses, different natural products or plant extracts/bioactive compounds tested against SARS and MERS coronaviruses are also identified, and SARS-CoV2 may be used to design fresh anti-virus drugs. The antiviral activity against SARS-CoV2 viruses in natural products with the ability to combat SARS, MERS and other viruses illustrated in this article can be specifically used for more preclinical research. Therefore, to save the lives of many people around the world, all efforts should be focused on addressing this serious issue.

Keywords: Coronavirus, COVID-19, Herbal products, SARS-CoV-2, anti-viral, pathogenesis.

INTRODUCTION

The coronavirus outbreak caused by extreme acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in Wuhan, Hubei, China at the end of December 2019[1]. The widespread dissemination of the latest coronavirus (COVID-19) in 2019 has resulted in a pandemic blamed for the ongoing global health crisis[2,3]. Coronaviruses (CoVs) form a broad family of RNA viruses that infect and cause a wide range of diseases in a wide range of mammalian and avian hosts[4]. CoVs contain four genera of a-, b-, g- and d-coronaviruses [5,6] and have a single-stranded, positive-sense RNA genome. The unexpected appearance of a new coronavirus detected at the end of 2019 has triggered a large epidemic of fatal human pneumonia with a widespread global impact, and the World

Health Organisation (WHO) has designated this infectious disease caused by the new coronavirus as coronavirus disease 2019 (COVID-19)[7,8]. The causative agent of this epidemic is now considered to be a novel phylogenetic coronavirus in the SARSCoV clade, known as extreme acute respiratory syndrome coronavirus 2 (SARS-CoV-2). More common is the SARS-CoV-2 than the SARS-CoV[9,10].

Fever, cough, shortness of breath, and dyspnea are the typical respiratory symptoms of a person infected with the coronavirus. Pneumonia, extreme acute respiratory syndrome, organ failure and even death may be caused by infection in more severe cases [11,12]. By 23 Dec 2020, more than 78,481,916 confirmed infected cases were caused by this potentially lethal virus which resulting in more than 1,726,632 deaths worldwide. COVID-19 has spread to more than 250 countries around the world, and no signs of a

decline have been found in its epidemic. Sadly, despite comprehensive efforts to improve anti-coronavirus agents, successful therapeutics for coronavirus infection have so far remained elusive[13]. In existing global attempts to suppress the COVID-19 epidemic, a shortage of successful immunisation and antiviral medications faces a formidable obstacle [14,15]. Therefore, there is obviously an unmet medical requirement for the treatment of the new COVID-19 pandemic for successful antivirals.

Herbal medications and natural compounds dependent on medicinal plants offer a rich resource for the growth of novel antiviral drugs. It has been shown that somnatural drugs exhibit antiviral activities against different strains of viruses. To date, it has been recorded that hundreds of herbal compounds contain antiviral activities. In recent decades, considerable efforts have also been made to expose the antiviral action mechanisms of these natural agents, such as viral entry, replication, assembly, and release, as well as virus-host-specific interactions, on the effect of the viral life cycle. The goal of this analysis is to provide an update on and analyse the molecular targets and pathways of natural products that have promising antiviral effects against coronaviruses.

Covid-19 transmission process

In China, the US, Italy, Iran, Spain, and various different countries, SARS-CoV-2 spread rapidly and causes Coronavirus. A few tests recommended that bat could be the cause for Sars CoV- 2 (16), but there is no indication that bat is the potential SARS-CoV-2 repository (17). If a human event is to occur, CoVs have been recognised as nonlethal microbes that induce only natural colds. SARS-CoV and MERS-CoV are deeply human-pathogenic and occurred in China in 2003 and in Saudi Arabia in 2012 (18). The third CoV, Coronavirus, induces true well-being globally and will be documented throughout humanity's entire lifetime.

Wuhan was accounted for as the original foetal case on 15 January 2020 (19). The scourge grew exponentially and later changed to a pandemic that triggered crises of well-being worldwide. Covid's transmission from human to human touch was detected. There are three basic Coronavirus transmitting courses recommended by Chinese wellness experts, such as transmission of beads, touch transmission and vaporised transmission. The transmission of beads occurs when an infected human hacks or snuffles, respiratory drops are inhaled by people who are closest to the person while the transmission of contact occurs when a person touches their nose, mouth or eyes in the aftermath of touching the surface of the infection toxin or goods and vaporised transmission occurs when the disease causing respiratory beads b (20).

The human stomach-related structure is a perfect way for Coronavirus to propagate within the body by displaying symptoms such as restlessness of the stomach and looseness of the intestines. In this respect, four single cell transcriptome datasets identified with a stomach-related system were investigated and found that angiotensin-changing over compound 2 content (ACE2) was unusually communicated in ileum and colon region absorptive enterocytes (21). The most frequently recognised symptoms reported are fatigue, fever, myalgia or fatigue, pneumonia,

and confounded dyspnea, while nausea, runs, hemoptysis, runny nose and coughing mucus are less usual side effects (22).

Patients with the mellow sign are healed after several weeks, while extreme patients can prompt death due to alveolar damage and respiratory disappointment in this manner. For the most part, death events are observed to be flooded in old mature patients with previous disorders such as tumour, surgical treatment, cirrhosis, arthritis, cardiovascular disease, diabetes, and Parkinson's infectious disease (23). In India pace of pollution is not exactly separate nations and is approximately 1.9 percent . The quantity of infected patients in India is steadily growing (24).

Role of herbal plants in fight against Covid-19

A broad spectrum of integral and complementary medicine is offered by herbal plants which can help solve the many puzzles behind many viral diseases[25]. Herbal remedies such as plant extract, plant-based hybrid (phytoconstituent) extracts of herbal plants from specific parts of the plant (stalk, roots, seeds, bark, food and fowl), nutraceuticals and nutritional supplements are used in the treatment of diseases ranging from frequent to rare infectious and non-infectious diseases [26, 27]. A World Health Organization (WHO) study relies on conventional plants for health requirements for 80% of human beings in developed nations [28, 29]. Many trials have demonstrated promising tools for plant-derived products and their preparations against many viral infectious outbreaks. They can be used extensively to target COVID-19[31], provided the low toxicity screening of herbal medicines[30]. As it is primarily involved in the processing of viral polyproteins translated from viral RNA, the key protease referred to as Mpro (3CLpro) is recognised as a promising target for coronaviruses.

Glycyrrhizin is present widely in the dried roots of Glycyrrhiza uralensis, Glycyrrhiza glabra and Glycyrrhiza inflata, generally referred to as licorice[32, 33]. It is known that glycyrrhizin exhibits potent antiviral activity [34, 35]. Human immunodeficiency virus type 1 (HIV-1) and herpes simplex virus type 1 (HSV-1)[36], hepatitis C virus, varicella-zoster virus and SARS-coronavirus are confirmed to have antiviral efficacy. As licorice has been an abundant and readily available medicinal plant since ancient times, COVID-19 can be due to its possible antiviral function.

Bicylogermecrene is a naturally occurring sesquiterpenoid compound mainly found in some species of eucalyptus, Lantana camara, and other plants belonging to the Verbenaceae family, including Aloysia gratissima. Bicylogermacrene has been delineated to exhibit various activities, including antibacterial, antifungal, antiviral [37, 38] antimicrobial activity.

The key chemical constituents present in Strobilanthes cusia leaf belonging to the Acanthaceae family, mainly found in India, Bangladesh and the Himalayan region, are tryptanthrine and β -sitosterol and indirubin. Anti-Human coronavirus NL63 (HCoV-NL63) (IC₅₀ 1.52 μ M) is reported to exhibit tryptanthrine, suggesting its potent anti-HCoV-NL63 activity. It is also stated that the other portion, indirubin, has antiviral and immunomodulatory effect, mainly against influenza-A[39]. In order to combat COVID-

19, these natural products can serve as promising candidates.

β -sitosterol, a phytosterol known for its SARS coronavirus 3C-like protease and antiHBV (hepatitis B virus) activity in vitro enzyme inhibitory activity. It also demonstrates antibacterial, anti-inflammatory and antitumor behaviours in addition to this[40].

Isatis indigotica containing indigo and indirubin is a popular Chinese medication known as a possible compound for the prevention of SARS-coronavirus, influenza, foot-and-mouth disease, type 1 human immunodeficiency virus and rabies (HIV-1) encephalitis[41].

Hesperetin is an important compound in Chenpi (*Citri Reticulatae Pericarpium*) belonging to the Rutaceae family, a substance belonging to the flavanone class of flavonoids, abundant in citrus fruits which are known to have viral anti-influenza activity and to have a protective effect against fulminant hepatitis[42].

Rhein and crysophanic acid are widely distributed in aloe vera (*Aloe barbadensis*) species belonging to the Asphodelaceae and Rhubarb (*Rheum palmatum*) family belonging to the Polygonaceae family, among which crysophanic acid has been reported to exhibit anti-poliovirus antiviral activity and rhein has been reported to exhibit anti-influenza and anti-human respiratory syncytial virus activity[43].

Berberine is an isoquinoline alkaloid abundant in the category of *Berberis aristata* (Berberidaceae) and other species of berberis. Abundant β -caryophyllene in basil (*Ocimum* spp.), cinnamon (*Cinnamomum* spp.), black pepper (*Piper nigrum*), cannabis (*Cannabis sativa*), cloves (*Syzygium aromaticum*), oregano (*Origanum vulgare*), rosemary (*Rosmarinus officinalis*) and lavender (*Lavandula angustifolia*). Berberine is generally accepted against a number of viruses, including human cytomegalovirus, influenza A/FM1/1/47 (H1N1), enterovirus 71 (EV71), respiratory syncytial virus, chikungunya virus (CHIKV) and herpes simplex virus[44], for its possible broad spectrum action.

Six phytochemicals (Withanoside V [10.32 kcal/mol], Somniferine [9.62 kcal/mol], Tinocordiside [8.10 kcal/mol], Vicenin [8.97 kcal/mol], Isorientin 40-O-glucoside 200-O-phydroxybenzoate [8.55 kcal/mol], and Ursolic corrosive [8.52 kcal/mol]) from restorative plants with probable restraint and high SARS-CoV-2 Mpro affinities, anticipated to limit SARS-CoV-2 Mpro, were identified in the atomic docking investigation. These phytochemicals against COVID-19 can be repurposed. There is a harmless ADMET profile of the best docked mixes with drug-like properties that can help to establish advanced powerful inhibitors of COVID-19. The directions inspecting the contemplated buildings demonstrated simple protection during MD races (45)

In comparison, phytochemicals amentoflavone and galocatechin gallate unambiguously connected to the target proteins balanced the three-dimensional compliances in the wake of authoritative protein structures. In addition, the mixtures' insilico druglikeness and ADMET profiling showed encouraging helpful promise. (46,47). Oleanolic corrosive has a higher limiting ability for SARS-CoV-2 3CL M-master relative to COVID-19 remdesivir. In order to affect apoptosis, these should be paired with ACE2 official to CASP-3 flagging pathway, which merits further analysis

and expects to provide rational guidance. A strong partiality of oleanolic corrosive with the objective proteins was discovered by ongoing atomic docking results. Different organic cycles and mechanisms for the treatment of COVID-19 were used in the synthetic mixes through the consolidation of the fundamental objective proteins CASP-3, CASP-9, and XIAP, which help the clinical treatment of COVID-19 (46)

The SARS-CoV-2 main protease, spike glycoprotein, and RNA subordinate RNA polymerase may be repressed mainly by turmeric mixes anywhere in the range between 1 and 25. Obvious hindrance potential for the theory protease of COVID-19 at a stage equal to ritonavir was seen in mixes 4, 6 and 25. The turmeric aggravates 23, 8, 7 and 14 to the RBD of the spike protein has been shown to be more important in the ability of turmeric mixes to hinder the spike protein of Covid-19. In addition, in RdRp chemical restriction, the mixtures 6, 10 and 11 other than ritonavir and remdesivir are potent. Three mixtures, 1 (Curcumin I), 2 (Curcumin II) and 5 (Curcumin III), which make up company curcumin, have greater capacity for various substances in turmeric. The turmeric mixes bind to selected proteins productively and structure stable protein-ligand structures. The investigation of MD replication of docked buildings confirmed the steadiness of protein-ligand buildings. Turmeric may be an anticipated advantageous or, at any rate, protective specialist against SARS-CoV-2 by repressing the infection's concept protease and spike protein, in particular. (44) Theoretically used to treat an epidemic of COVID-19, pedunculagin, tercatin, and punicalin. The hydrolysable tannins plant's structural relationship behaviour as possible anti-viral components and top three hits that can impede COVID-19's key protease and thus virus replication. (47).

Inhibitory perspectives of *Clerodendrum* spp. phytocomposites. As evidenced by binding energy scores, taraxerol was undoubtedly the most promising inhibitory candidate against the SARS-CoV-2 spike, Mpro and RdRp proteins, followed by friedelin and stigmaterol. The fact that taraxerol has shown a good binding ability against all SARS-CoV-2 proteins included in the present study may provide a basis for its use as a universal SARS-CoV-2 target. (42) Another promising inhibitor of both SARS-COV2 spike protein and Mpro has been demonstrated by coumaroylquinic acid, Hexadecanedioic corrosive free energy official with RBD site was -7,727 and Mpro was -7,663. Cumarylquinic corrosive showed this ability in silico to bring about infection restraint at passage and replication levels (48)

Against the closed and partially open conformers of the PLpro homology models of SARS-CoV-2, alpinia officinarum, ginger and turmeric were coupled. The possible inhibitors of SARS-CoV-2 PLpro were described as eight compounds found in the rhizomes of *Alpinia officinarum* and ginger. Structure-based molecular binding reveals that these natural product inhibitors are promising candidates for medicines and are future consumers of SARS-CoV-2 rhizome extracts. (49).

CONCLUSION

The current situation with covid-19 is a big

problem for the human race. There is no drug/vaccine on the market as of now that will treat Covid-19 patients. Both drugs and vaccines are primarily in the clinical trial stage. Any strategies such as social distancing, staying home stay safe, self-quarantine, preserving grooming, wearing masks and using hand sanitizer may be identified as a preventive measure to fight covid-19. Since they have antiviral effects against covid-19, relying on bioactive molecules from natural products is the only one-way hope for the situation at hand. This could be our only hope of fighting against the

pandemic of Covid-19. Many plants, animals and microbes may be explored in order to produce bioactive compounds that have potent antiviral properties against covid-19. Natural bioactive plant derivative compounds are effective against SARS and MERS, so plants, animals and microbes with antiviral properties should be looked forward to and extensive testing should be performed for the covid-19 drug. It is important to promote corrective measures based on this pandemic bioactive compound and it is high time to investigate such natural products.

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