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## A Brief Review on COVID-19 and Herbs Use for Management of COVID -19



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### ABSTRACT

In the course of recent months, the world has confronted an extraordinary wellbeing risk. The World Health Organization has reported pandemic contamination with obscure types of coronavirus called SARS-CoV-2. Spreading basically through the bead course, the infection causes gentle side effects in most of cases, the most widely recognized being: fever (80%), dry hack or cough (56%), weakness (22%) and pain in muscle (7%); less normal indications incorporate an irritated throat, a runny nose, diarrhea, hemoptysis and chills. A hazardous intricacy of SARS-CoV-2 contamination is an acute respiratory distress syndrome (ARDS), which happens all the more regularly in more seasoned grown-ups, those with insusceptible disarranges and co-morbidities. These types of the disease, being a sign for treatment in the emergency unit, intense lung irritation, ARDS, sepsis and septic shock. Herbal medicines and its secondary metabolites all time promising for health to cure chronic disorder also. The article presents basic information about detail about coronaviruses and prevention, also this review give details about herbs, their secondary metabolites to treat COVID-19.

## INTRODUCTION

First case of coronavirus was notified as cold in 1960. According to the Canadian study 2001, approximately 500 patients were identified as Flu-like system. 17-18 cases of them were confirmed as infected with coronavirus strain by polymerase chain reaction. Corona was treated as simple non-fatal virus till 2002. In 2003, various reports published with the proofs of spreading the corona to many countries such as United States America, Hong Kong, Singapore, Thailand, Vietnam and Taiwan. Several case of severe acute respiratory syndrome caused by corona and their mortality more than 1000 patient was reported in 2003. This was the black year for microbiologist. When microbiologist was started focus to understand these problems. After a deep exercise, they conclude and understand the pathogenesis of disease and discovered as coronavirus. But till total 4421 patient was confirmed as infected with the coronavirus. COVID-19 was first identified and isolated from pneumonia patient belongs to Wuhan, China<sup>[1-2]</sup>.

### Humans Coronavirus

Coronavirus sickness was first in 1931<sup>[3]</sup>, with the first coronavirus (HCoV-229E) disengaged from people in 1965. Until the flare-up of extreme intense respiratory disorder in late 2002, just two human coronaviruses (HCoV) were known HCoV-229E and HCoV-OC43. When the SARS coronavirus (SARS-CoV) had been distinguished, two further human coronaviruses were recognized. Three groups of coronaviruses are as follows:

- Group 1 (HCoV-229E and HCoV-NL63),
- Group 2 (HCoVOC43 and HCoV-HKU1),
- Group 3 (no human CoVs as yet).

### Microbiology

Coronavirus is spherical or pleomorphic, single stranded, enveloped RNA and covered with club shaped glycoprotein. Coronaviruses are four subtypes such as alpha, beta, gamma and delta coronavirus. Each of subtype coronaviruses has many serotypes<sup>[4-6]</sup>.

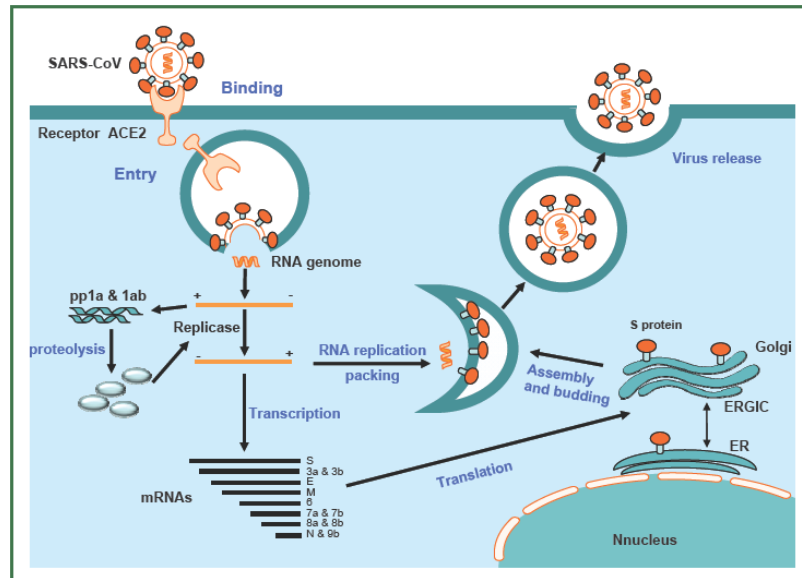
## Taxonomy

*Coronaviruses and toroviruses* are two virus genera within the virus family Coronaviridae, order Nidovirales. Coronaviruses are well developed pathogens of humans and animals while the toro viruses are recognized as causes of animal diarrhoea. Toroviruses have also been found in human faeces but their etiological role remains unclear<sup>[7-8]</sup>.

## Structure, Pathogenesis and immune response SARS-CoV-2

Coronavirus is spherical or pleomorphic, single stranded, enveloped RNA and covered with club shaped glycoprotein. Coronaviruses are four subtypes such as alpha, beta, gamma and delta coronavirus. Each of subtype coronaviruses has many serotypes<sup>[9-11]</sup>. From SARS-CoV and MERS-CoV, and becomes the seventh member of the coronavirus family to infect humans<sup>[12]</sup>. Envelope spike proteins (S) protein on the surface of SARS-CoV-2 that binds to angiotensin-converting enzyme 2 (ACE2) receptor on the target cells. The spike protein of coronavirus is divided into the S1 and S2 domain, in which S1 is responsible for receptor binding and S2 domain is responsible for cell membrane fusion. Spikes bind with host receptor ACE2 to enter the cells, the same receptor facilitating transcription with host RNA and creat 1000s of viral partical they infects bronchii, reach to alveoli and other extrapulmonary organs causes pneumonia. It is also found it infect 100 times more frequent to GIT, kidney, testes<sup>[13]</sup>.

In COVID-19 lowers adaptive immunity as it facilitates severity and fatality symptoms. As pulmonary inflammation and lungs infection, it produce pre and pro-inflammatory mediators shows high levels of IL-1 $\beta$ , IFN- $\gamma$ , IP-10, and MCP-1 in their serum, leading to activation of the Th1 cell responses. The counts of peripheral CD4+ and CD8+ T lymphocytes were substantially reduced, cytokine storms that hampers immunity and cause tissue injury<sup>[14-15]</sup>.



**Figure No. 1: Life cycle of SARS CoV**

### Sign and symptoms

Mild respiratory tract infection, fever on an average after 5-6 days of infection (mean range for incubation 1-14 days) along with dry cough, dyspnoea, chest pain, fatigue and myalgia. Less common symptoms include headache, dizziness, abdominal pain, diarrhea, nausea, and vomiting. Severe complications such as hypoxemia, acute ARDS, arrhythmia, shock, acute cardiac injury, and acute kidney injury have been reported among COVID-19 patients [16-17]. Some cases in China at first gave just chest snugness and palpitation [18]. In March 2020 there were reports showing that loss of the feeling of smell (anosmia) might be a typical manifestation among the individuals who have gentle disease, despite the fact that not as basic as at first reported. In a few, the infection may advance to pneumonia, multi-organ disappointment, and death. In the individuals who create extreme side effects, time from side effect beginning to requiring mechanical ventilation is ordinarily 8 days [18].

As is basic with diseases, there is a deferral between the minute when an individual is tainted with the infection and when they create symptoms. This is known as the brooding time frame or incubation period. The brooding time frame for COVID-19 is ordinarily five to six days however may run from two to 14 days.[19]

### Diagnosis

The WHO has distributed a few testing conventions for the disease. The standard technique for testing is continuous reverse interpretation polymerase chain response (rRT-PCR)[20]. The

test is normally done on respiratory examples acquired by a nasopharyngeal swab, anyway, a nasal swab or sputum test may likewise be used. Blood tests can be utilized, but these require two blood tests dismantled two weeks and the outcomes have little immediate value. A March 2020 review concluded that chest X rays are of little value in early stages, whereas CT scans of the chest are useful even before symptom occur typical features on CT include bilateral multilobar ground-glass opacifications with a peripheral, asymmetric and posterior distribution. Subpleural dominance, crazy paving and consolidation develop as the disease evolves. As of March 2020, the American College of Radiology recommends that "CT should not be used to screen for or as a first-line test to diagnose COVID-19"<sup>[21]</sup>. Now test kit is available for COVID-19.

### **Treatment of COVID-19**

Different antiviral regimens are being attempted to assist patients with extreme manifestations of the infection. Lopinavir and ritonavir have been utilized in some clinical preliminaries<sup>[22]</sup>. Neuraminidase inhibitors, chloroquine, and arbidol have additionally been proposed. There are different research groups attempting to explore a potential immunization for the infection<sup>[23]</sup>. Till date not proper treatment for Covid 19.

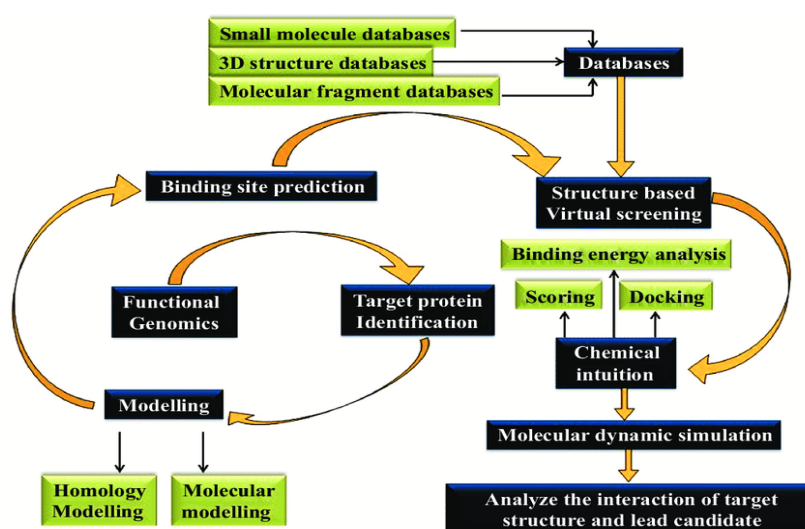
### **Preventive measures of COVID-19**

There is currently no vaccine to prevent coronavirus disease 2019 (COVID-19). The best way to prevent illness is to avoid being exposed to this virus. The virus is thought to spread mainly from person-to-person, between people who are in close contact with one another (within about 6 feet). Through respiratory droplets produced when an infected person coughs or sneezes, these droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs wash your hands often with soap and water for at least 20 seconds especially after you have been in a public place or after blowing your nose, coughing, or sneezing. If soap and water are not readily available, use a hand sanitizer that contains at least 60% alcohol. Cover all surfaces of your hands and rub them together until they feel dry. Avoid touching your eyes, nose, and mouth with unwashed hands. Avoid close contact with people who are sick, Put distance between yourself and other people if COVID-19 is spreading in your community<sup>[24]</sup> you should wear a facemask when you are around other people (e.g., sharing a room or vehicle) and before you enter a healthcare provider's office. If you are not able to wear a facemask (for example, because it causes trouble breathing), then

you should do your best to cover your coughs and sneezes, and people who are caring for you should wear a facemask if they enter your room. If you are not sick: You do not need to wear a facemask unless you are caring for someone who is sick (and they are not able to wear a facemask). Facemasks may be in short supply and they should be saved for caregivers. Clean and disinfect frequently touched surfaces daily. This includes tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks. If surfaces are dirty, clean them: Use detergent or soap and water prior to disinfection<sup>[25]</sup>.

### Bioactive compounds use as preventive Measures in COVID- 19

No specific therapies are available and investigations regarding COVID-19 treatment are lacking. Liu *et al.* (2020) successfully crystallised the COVID-19 main protease (Mpro), which is a potential drug target. Several popular antiviral secondary metabolites have been screened by molecular docking in comparison with nelfinavir, lopinavir. Several compounds, such as flavonoids, from medicinal plants, have been reported to show antiviral bioactivities<sup>[25-27]</sup>. The binding energies obtained from docking 6LU7 with the native ligand, nelfinavir, lopinavir, kaempferol, quercetin, luteolin-7-glucoside, demethoxycurcumin, naringenin, apigenine-7-glucoside, oleuropein, curcumin, catechin, epicatechin-gallate, zingerol, gingerol, and allicin were -8.37, -10.72, -9.41, -8.58, -8.47,-8.17, -7.99, -7.89, -7.83, -7.31, -7.05, -7.24, -6.67, -5.40, -5.38, -5.40, and -4.03 kcal/mol, respectively<sup>[28]</sup>.



**Figure No. 2: Flow chart shows Traditional medicine database screened with protein database of COVID-19 by molecular modeling**

Table No. 1: Properties of some plants to fight against COVID-19<sup>[28-29]</sup>

No	Plant Scientific Name	Secondary Metabolite	Activity
1	<b>Ashwagandha</b> <i>Withania somnifera</i> (Apocynaceae)	Serpentine, Withanone	Adaptogenic property, AEC2-RBD complex inhibitor, ↑nitric oxide <sup>[30-32]</sup>
2	<b>Berberin</b> <i>Berberis aristata</i> (Berberidaceae)	Berberin	Inhibit inflammatory mediators <sup>[29]</sup>
3	<b>Cardamom</b> <i>Elettaria cardamomum</i> (Zingiberaceae)	Limonene, lemonene	Anti-cancer properties, Antiviral <sup>[29]</sup>
4	<b>Celery</b> <i>Apium graveolen</i> (Apiaceae)	Apigenin-7- glucoside	Contain abundant amount of minerals and vitamins. effectively strengthens the stomach, liver, and kidneys <sup>[33]</sup>
5	<b>Cinnamon</b> <i>Cinnamomum zeylanicum</i> (Lauraceae)	Cinnamic aldehyde	Modulate cytokine responses, Block viral attachment to ACE-2 linkages <sup>[33]</sup>
6	<b>Citrus fruit</b> <i>Citrus sinensis</i> (Rutaceae)	Naringenin	Antioxidant, antiviral, antibacterial, naringenin ability to improve endothelial function <sup>[34]</sup>
7	<b>Dill</b> <i>Anethum graveolens</i> (Umbelliferaceae)	Kaempferol	Antioxidant, Thrombus preventive, slowdowns coagulation system <sup>[35-36]</sup> .
8	<b>Fennel leaves</b> <i>Foeniculum vulgare</i> (Umbelliferaceae)	Quercetin	Antioxidant, Thrombus preventive <sup>[37]</sup>
9	<b>Garlic</b> <i>Allium sativum</i> (Alliaceae)	Diallyl Disulfide, Allicine	Natural antibiotic, anti-virus, cures respiratory infections, capable of eliminating the biofilms of this bacterium <sup>[38]</sup>
10	<b>Ginger</b> <i>Zingiber officiale</i> (Zingiberaceae)	Zingerol, Gingerol	Work against GI disturbances, cancer, inflammation, nausea, vomiting <sup>[28]</sup>
11	<b>Ginkgo</b> <i>Ginkgo biloba</i> (Ginkgoaceae)	<u>Ginkgolides</u> , ginkgolic acid and <u>bilo</u> <u>balides</u>	Upregulate and protect ACE-2 expression, increase its activity (esp in the aged) <sup>[29]</sup>
12	<b>Ginseng</b> <i>Panax ginseng</i> (Araliaceae)	Ginsenosides and Gintonin	Boosting the immune system <sup>[29]</sup>
13	<b>Green tea</b> <i>Camellia sinensis</i> (Theaceae)	Epicatechinal late, Catechin	Antioxidant, reduce inflammation <sup>[34]</sup>
14	<b>Kalmegh</b> <i>Andrographis paniculata</i> (Acanthaceae)	Kalmeghin, andrographol ides	Potent inhibitory effect on the NF-κB and STAT3 signaling pathways in inflammation <sup>[29]</sup>

15	<b>Liquorice</b> <i>Glycyrrhiza glabra</i> (Leguminosae)	Coumarin, Glycerhizine	Glycyrrhizin, inhibiting its replication. Block viral attachment to ACE-2 linkages <sup>[40]</sup>
16	<b>Ma- Hung</b> <i>Ephedra gerardiana</i> (Ephedraceae)	Ephedrine	Decongestant and bronchodilator <sup>[29]</sup>
17	<b>Olive</b> <i>Olea europaea</i> L(Oleaceae)	Luteolin-7- glucoside, Oleuropein	Antioxidant <sup>[36]</sup>
18	<b>Pennyroyal</b> <i>Mentha pulegium</i> (Lamiaceae)	Thymol	Useful for dealing with nausea, vomiting, gastrointestinal problems, flu, asthma, cough and pertussis <sup>[41]</sup>
19	<b>Pepper</b> <i>Capsicum annum</i> (Solanaceae)	Capsaicin	Reduce severity and duration of the cold, stimulates the immune system <sup>[42]</sup>
20	<b>Rubarb</b> <i>Rheum emodii</i> (Polygonaceae)	Emodin	Inhibit the 3a ion channel of coronavirus SARS-CoV and HCoV-OC43 as well as virus release from HCoV-OC43 <sup>[43]</sup>
21	<b>Tragacanth</b> <i>Astragalus gossypinus</i> (Fabaceae )	Glucuronic acid	Used as a soothing and anti-cough agent in the common cold medication <sup>[28-29]</sup>
22	<b>Turmeric</b> <i>Curcuma longa</i> (Zingiberaceae)	Curcumin, Demethoxyc urcumin	Anti-inflammatory and immunomodulatory effects. Potent Natural Antibiotic <sup>[44-47]</sup>

Kaempferol, quercetin, luteolin-7-glucoside, apigenin-7-glucoside, naringenin, oleuropein, demethoxycurcumin, curcumin, catechin, and epigallocatechin were the most recommended compounds found in medicinal plants as potential inhibitors of COVID-19 M<sub>pro</sub>, which should be explored in future research. In this table, we mention most used herbal medicine to fight against COVID -19. Some of them inhibitors of COVID-19 M<sub>pro</sub>, some traditional Chinese medicine such as Ginseng, Rhubarb, cinnamomum, liquorice and Ephedra. This all medication gives symptomatic relief and boost immunity for this globally spreading infection. Along with this cannabinoids is also use given in literature.

## CONCLUSION

On current literature review, it have seen that nelfinavir and lopinavir may represent potential treatment options, and kaempferol, quercetin, luteolin-7 glucoside, demethoxycurcumin, naringenin, apigenin-7-glucoside, oleuropein, curcumin, catechin, and epicatechin-gallate appeared to have the best potential to act as COVID-19 M<sup>pro</sup> inhibitors. However, further research is necessary to investigate their potential medicinal use and some Chinese medicines such as Ginseng, Rhubarb, cinnamomum, liquorice and Ephedra will help to give



symptomatic relief and boost immunity to fight against this globally spread infection.

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