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POTENTIAL MEDICINAL PLANT REMEDIES AND THEIR POSSIBLE MECHANISMS AGAINST COVID-19: A REVIEW

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ABSTRACT

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) outbreak was first reported in Wuhan, a city in Hubei Province of China in December, 2019 and is known to be responsible for the novel coronavirus disease (COVID-19). COVID-19 was declared a pandemic in March, 2020 and since then, it has caused a number of deaths in over 200 countries around the world. Extensive researches have continued in the search of effective vaccines or drug compounds against SARS-CoV-2 and a total of 64 vaccines are currently in clinical trials with 12 currently approved for use by different regulatory bodies, depending on the country. Since the outbreak of SARS-CoV-2, many countries have utilised traditional herbal medicines alongside conventional drugs for the treatment of infected patients. In this review, traditional medicines used to prevent or treat SARS-CoV-2 infection are listed along with the plant parts as used by the traditional healers. Additionally, the possible mechanisms responsible for this preventive or therapeutic outcome are also identified and listed. Our literature search was conducted using Google Scholar, PubMed, Scopus and WHO website. Unpublished reports such as dissertations and theses are not included. Plant parts including roots, leaves, flowers, seeds and so on have been used in the treatment of COVID-19. These traditional medicinal herbs may exert their anti-COVID-19 activity by direct inhibition of the virus replication or entry. Some may act by blocking the ACE-2 receptor, SARS-CoV helicase, Type II Transmembrane Serine Protease (TMPRSS2) and RNA-dependent RNA polymerase (RdRp) activities which are required by SARS-CoV-2 in order to infect human cells. Others act by inhibiting the SARS-CoV-2 life-cycle related proteins, namely chymotrypsin-like cysteine protease (3CL-pro) and Papain-like protease (PL-pro). Medicinal plants are promising alternative medicines for the treatment or prevention of SARS-CoV-2 infection. Further researches, are needed to decipher their active components and structures which may suggest clues for the development of drugs against this novel coronavirus.

Keywords: Severe Acute Respiratory Syndrome (SARS-CoV-2), COVID-19, medicinal plants, plant parts, mechanism of action, pandemic, 3-chymotrypsin-like cysteine protease

INTRODUCTION

The novel coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was first reported in Wuhan, a city in Hubei Province of China in December, 2019. The World Health Organization (WHO) declared COVID -19 outbreak a pandemic on March 11th 2020 and has since been an enormous challenge for the global public health systems, having affected about two hundred and thirteen (213) countries and territories in the world (WHO, 2020[a]). This viral infection is considered the first pandemic due to a coronavirus (Boukhatem and Setzer, 2020). The WHO report as at 21st March, 2021 shows a cumulative total of one hundred and twenty two million five hundred and twenty four thousand four hundred and twenty four (122,524,424) confirmed cases; Two million seven hundred and three thousand six hundred and twenty (2,703,620) confirmed deaths globally since the start of the outbreak (WHO, 2021[a]). Extensive researches have continued in the search of effective vaccines or drug compounds against SARS-CoV-2 and a total of 64 vaccines are currently in clinical trials and 12 are currently approved for use by different regulatory bodies, depending on the country; with those developed by Pfizer (BioNtech), Moderna (mRNA-1273) and Johnson&Johnson/Janssen (Ad26-COV2,S) approved for use in the United States (WHO, 2021[b]; CDC, 2021). A lot of current research have also focused on repurposed drugs such as antivirals, antimalarials, anti-inflammatory and immune modulators while some potential therapies act in different ways or through multiple mechanisms (Robinson, 2020). The United States Food and Drug Agency, US-FDA recently created a new emergency program; Coronavirus Treatment Acceleration Program (CTAP) aimed at speeding up research for the development of COVID-19 treatment (FDA, 2020[a]).

Medicinal plants have been used against SARS-CoV-2. This is majorly inspired by the success reported in the treatment of severe acute respiratory syndrome (SARS) caused by the outbreak of SARS coronavirus (SARS-CoV) between 2002 and 2003. There were compelling evidences supporting the beneficial effect in the use of numerous herbal formulas, especially in China and in the Middle East (Chen and Nakamura, 2004; Lau *et al.*, 2005; Hsu *et al.*, 2006). In 2003 for instance, the fatality rate at the outbreak of at SARS-CoV was more than 52% in Beijing and about 18% in Singapore and Hong Kong. However in Beijing, this reduced dramatically to 1%–4% just after 10 days, which was believed to be as a result of using plant-based traditional Chinese medicines as a supplement medication with conventional therapy (Chen and Nakamura, 2004). The major druggable targets of SARS-CoV-2 include 3-chymotrypsin- like protease (3CLpro), papain like protease (PLpro), RNA-dependent RNA polymerase (RdRp), angiotensin-converting enzyme 2 (ACE2), SARS-CoV helicase and Type II Transmembrane Serine Protease (TMPRSS2) (Wu *et al.*, 2020). Other mechanisms have also been postulated for some medicinal plants such as Immunomodulatory activities. Immunomodulatory agents are compounds that are non-specific and exert their activities without antigenic specificity. These compounds are similar to the adjuvants that are related to some vaccines (Liu *et al.*, 2020). Some medicinal plants with possible immunomodulatory activities have been utilised in traditional medicine for the treatment/prevention of coronavirus. The aim of this review therefore is to document the medicinal herbs that have been reported to be effective against SARS-CoV-2 and their proposed mechanism(s) of action.

Structure and Pathogenesis of SARS-CoV-2

Coronaviruses belonging to the family Coronaviridae, subfamily Coronavirinae are large non- segmented positive-sense single-stranded ribonucleic acid (RNA) viruses with a viral RNA genome of diameter of 80-120 nm and ranging between 26-32 kb in length. At this length, the coronavirus genome is the largest among RNA viruses (Mittal *et al.*, 2020; Wu *et al.*, 2020). (Fig. 1). They are subdivided into four genera, namely: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*. Presently all identified coronaviruses that are capable of infecting humans belong to the first two genera (Chu *et al.*, 2020). SARS-CoV-2 is a *Betacoronavirus* and belongs to the subgenus Sarbecovirus and mostly bear resemblance to a bat coronavirus, with which it shares about 96.2% sequence homology (Chan *et al.*, 2020[a]). In addition to SARS-CoV-2, the *Betacoronavirus genus* has two other highly pathogenic coronavirus, namely; the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). SARS-CoV and MERS-CoV infections result in higher mortality rates compared to SARS-CoV-2, but only SARS-CoV-2 is capable of establishing sustained human-to human-transmission (da Silva *et al.*, 2020; Mittal *et al.*, 2020).

The coronavirus genome encodes several structural and non-structural proteins. The structural proteins which are responsible for host infection, membrane fusion, viral assembly, morphogenesis, and release of virus particles, among other functions include Spike (S) protein, envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein while the non-structural proteins (Nsp) which are not incorporated within the virion particles facilitate viral replication and transcription and are expressed as two huge poly-proteins that are then cleaved into 16 smaller proteins (Nsp1-16). This group of proteins include the main protease (Nsp5) and RNA polymerase (Nsp12) (Yoshimoto, 2020). Among the four structural proteins, the N and S are the most important. The former helps the virus to develop the capsid and the entire viral structure appropriately and the later helps in the attachment of virus to the host cells (Walls *et al.*, 2020).

Coronaviruses (corona=crown) actually got their name from the crown-shaped appearance of the virus which is as a result of the large Spike (S) glycoprotein, which forms extended homotrimers. It is this spike protein that binds to the animal host cell by interacting with specific anchoring proteins, typically proteinases, such as angiotensin-converting enzyme 2 (ACE-2) or aminopeptidase N. This binding of the spike (S) protein facilitates viral entry into the host cell and the release of the viral genome. Current reports have shown that the SARS CoV and SARS-CoV-2 have similar kind of receptors, particularly the receptor binding domain (RBD) and the receptor binding motif (RBM) present in the viral genome (Yin and Wunderink, 2018). In the course of the SARS infection, the RBM of the S protein gets directly attached to ACE-2 in the host cells. Since ACE-2 protein is expressed in various organs of the human body chiefly in the lungs, kidney and intestine, these organs become the prime targets of the coronavirus (Zhao *et al.*, 2020).

Following the attachment, the host protease usually influences the cleaving of the receptor attached spike protein and the fusion of virus into host cell. Based on the protease type, SARS coronaviruses follow two different paths to penetrate into the host cell. Firstly, a SARS virus may enter into the cell through endocytosis at the presence of host's pH-dependent cysteine protease cathepsin L, which leads to formation of a membrane bounded endosome (Figure 2A). This protease induces the activation of the attached spike protein which leads to changes in shape of endosome and helps the viral envelope to fuse with the endosomal wall (Simmons *et al.*, 2013). Secondly, the presence of type II transmembrane serine protease (TMPRSS2) at the outer membrane of some epithelial tissues such as respiratory, urogenital and gastrointestinal induces proteolytic cleavage of viral spike protein. The S2'site of the S protein comprises single lysine or arginine residues which can be targeted by TMPRSS2 for cleaving, hence SARS and other respiratory viruses can penetrate into the host cell directly by a fusion of viral envelope and host cell membrane (Figure 2B) (Heurich *et al.*, 2014). When the fusion is completed, the virus releases its nucleocapsid into the cytoplasm where the viral genome mimics the messenger RNA and takes part in the translation process by cell ribosome (Figure 2A). The mRNAs further translates accessory proteins and structural proteins. The structural proteins (envelope glycoproteins), nucleocapsid proteins and newly synthesized genomic RNA reorganize to form progeny viruses. Finally, the virion containing viral particles discharge from the infected cell through secretory vesicles by exocytose process (Figure 2A), (Zhang *et al.*, 2020).

Symptoms and Risk of COVID-19 Infection

The current coronavirus disease affects different people in different ways, the presentation ranging from asymptomatic/mild symptoms to severe illness and death (Esakandari *et al.*, 2020). Most common symptoms include fever, dry cough, and tiredness while the less common symptoms include aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, a rash on skin, or discolouration of fingers or toes. Serious symptoms are difficulty in breathing or shortness of breath, chest pain or pressure and loss of speech or movement (WHO, 2020[b]). At the early stage of the pandemic, an analysis of some patients showed that 17.6% were severe cases while 82.4% were common cases, which include 73.3% mild cases, 4.2% non-pneumonia cases and 5.0% asymptomatic cases respectively (Tian *et al.*, 2020). The most common symptoms at the onset of illness were fever (82.1%), cough (45.8%), fatigue (26.3%), dyspnea (6.9%) and headache (6.5%) with a reported fatality of 0.9% (Tian *et al.*, 2020). In another systematic review and meta analysis, Jain and Yuan (2020) found that cough, fever and fatigue were the most prevalent symptoms in the severe disease while cough, fever and dyspnoes were the symptoms that warranted intensive care unit admission. Older population have a higher risk of serious illness from COVID-19, and this risk is known to increase with age (CDC, 2020[a]). Another factor that may increase risk of serious illness include pre- existing chronic medical conditions such as heart diseases, cancer, diabetes, severe obesity, chronic kidney disease, sickle cell disease, weakened immune system from solid organ transplants, HIV or some medications and high blood pressure (CDC, 2020[b]).

Current conventional treatment and the Role of Traditional Medicine in the search for agents against SARS-CoV-2

Quite a number of conventional/ Orthodox medicine treatment are under investigations and at different phases of clinical trials; Remdesivir, was given an emergency use authorization (EUA) on 1st May, 2020, being the drug that has gone furthest along in clinical trials (FDA, 2020[b]). Other drugs that are being used include corticosteroids such as Dexamethasone (Horby *et al.*, 2020), Tocilizumab (Samaee *et al.*, 2020; Potere *et al.*, 2020), Hydroxychloroquine and Chloroquine (Gao *et al.*, 2020), Azithromycin (Bleyzac *et al.*, 2020), Lopinavir/Ritonavir (Lu, 2020), Abidol (Lu, 2020) Oseltamivir (Chiba, 2020), Favipiravir (De Clercq, 2019), Colchicine (Schlesinger *et al.*, 2020, Ivermectin (Chaccour *et al*, 2020) and Convalescent plasma (FDA, 2020[c]). There are thousands of clinical trials of COVID-19 therapies taking place across the world. Updated list of these numerous trials are available at World Health Organization's International Clinical Trials Registry Platform (WHO ICTRP, 2020) and at ClinicalTrials.gov (2020).

The use of traditional medicine for the treatment of various ailments/ diseases is dated back to 4000-5000 BC (Hosseinzadeh *et al.*, 2015). The WHO in recognition of the important role of traditional medicine, developed a strategy in response to the World Health Assembly resolution on traditional medicine (WHA62.13) aimed at supporting member states in developing proactive policies and implementing action plans that will strengthen the role traditional medicine plays in keeping the population healthy (WHO, 2013). Since the prehistoric times, people from different parts of the world have been utilizing medicinal plants to mitigate against infectious diseases (Andrighetti-Frohner *et al.,* 2005; Yang *et al.*, 2020). For instance, Indian herbs have been used as a treatment and preventive strategy for several diseases, including respiratory viral infections (Vellingiri, 2020), Traditional Chinese Medicine (TCM) has played an essential role in treating epidemic diseases in the long history of China. Also, At least eighty per cent (80%) of African populations use some form of traditional herbal medicine (Willcox and Bodeker, 2004). The WHO has estimated that the worldwide annual market for medicinal plant product approaches US$ 60 billion (Linde and Jonas, 1999). The popularity of traditional medicine has been attributed to some of its advantages such as affordability, availability, acceptability, and apparently low toxicity compared to orthodox medicine (Sofowora, 1993).

Medicinal plants contain diverse secondary metabolites, some of which are believed to have the ability to interfere with viral protein and enzyme activities hence prevent viral entry/penetration into the host cells and replication within it (Li and Peng, 2013). The efficacies of some of these plant-based therapies were confirmed in combating SARS in 2003 (Zhang, *et al*, 2004). With many similarities being found between SARS-CoV and SARS-CoV-2 (e.g both of them belonging to the same beta family and containing the same genetic material i.e. RNA; both attaching to the host cell through same ACE2 receptor and with an eighty-six percent (86%) identity and ninety-six percent (96%) similarity of genome); previously employed plant metabolites for SARS-CoV in 2003 can be considered as emerging drug candidates for COVID-19 (Bhuiyan *et al.*, 2020).

At the early stage of the COVID-19 pandemic in China, the treatment protocol of COVID-19 highlights the combination of TCM with conventional/Western therapy. Yang *et al.* (2020) reported that greater than 85% of SARS-CoV-2 infected patients in China were receiving TCM treatment. This practice has demonstrated that TCM intervention is effective in the management of COVID-19. This is evident in the improvement of the cure rate, shortened course of the disease/delayed disease progression and a reduction in mortality rate (Chan *et al.*, 2020[b], Luo *et al.*, 2020[a], Luo *et al*, 2020[b], Ren *et al.*, 2020, Wan *et al.*, 2020[a]).

Table 1 consist of a list of medicinal plants that has been reportedly used in the prevention and treatment of COVID-19 in different parts of the world.

Table 1: Medicinal plants with activity against SARS-CoV-2

S/N	Botanical name	Family	Common name/ Local name	Part used	Reference
1	*Saxifraga spinulosa*	Saxifragaceae	Spider plant/spider –legged saxifrage	Aerial parts	Takeda *et al.*, 2020
2	*Strobilanthes callosa*	*Acanthaceae*	Karvi	Leaf	
3	*Strobilanthes cusia*	*Acanthaceae*	Assam Indigo	Leaf	Tsai *et al.*, 2020
4	*Astragalus membranaceus*	Fabaceae	Mongolian milkvetch	Root	
5	*Glycyrrhiza glabra)*	Fabaceae	Liquorice	Root	
6	*Saposhnikovia divaricate*	Apiaceae	fang feng Siler	Root	Luo *et al*, 2020[c]
7	*Atractylodes lancea*	Asteraceae	Cang Zhu.	Rhizome	
8	*Lonicera japonica*	Caprifoliaceae	Japanese honeysuckle	Leaves and Flowers	Yang *et al.*, 2020
9	*Forsythia* suspensa	Oleaceae	Golden Bell	Fruit	
10	*Capsicum annuum*	Solanaceae	Sweet Pepper , Cayenne Pepper, Chili Pepper	Seed	
11	*Mentha*	Lamiaceae	Horse mint	Aerial part (Stem and leaf)	Khaerunnisa *et al.*, 2020
12	*Olea europaea*	Oleaceae	Olive	Leaf	
13	*Lindera aggregate*	Lauraceae	Spicewood	Root	Suryanarayana and Banavath, 2020
14	*Pynosia lingua*	Polypodiaceae	Tongue Fern	Rhizome	
15	*Lycoris radiate*	Amaryllidaceae	*Red spider lily*	Bulb	
16	*Stephania tetrandra*	*Menispermaceae*	*Stephania*/ Fen Fang Ji	Root	Kim *et al.*, 2014
17	*Clivia miniata*	Amaryllidaceae	Natal lily or bush lily	Rhizome	
18	*Carapichea ipecacuanha*	Rubiaceae	*Ipecac.*	Root	Shen *et al.*, 2019
19	*Broussonetia papyrifera*	Moraceae.	Paper mulberry	Root	Park *et al.*, 2017
20	*Citrus sinensis*	Rutaceae	Sweet orange	Peel (Pericarp)	Ulasli *et al.*, 2014
21	*Nigella Sativa*	Ranunculaceae	Black cumin, Black seed, Black caraway	Seed	
22	*Anthemis Hyaline*	Asteraceae	Chamomile	Flower and buds	
23	*Paulownia tomentosa*	*Paulowniaceae*	Paulownia, empress tree or Princess tree	Fruit	Cho *et al.*, 2013
24	*Pelargonium sidoides*	*Geraniaceae*	African geranium and South African geranium.	NA	Michaelis *et al.*, 2011
25	*Cibotium barometz*	Dicksoniaceae	Chain Fern _Golden Hair Dog Fern, Golden Moss	Rhizome	
26	*Gentiana scabra*	Gentianaceae	Japanese gentian	Rhizome	
27	*Taxillus chinensis*	Loranthaceae	Chinese Mistletoe	Stem and Leaf	Wen *et al.*, 2011
28	*Cassia tora,*	Leguminosae	Sickle Senna, Sickle pod	Seed	
29	*Dioscorea batata,*	*Dioscoreaceae*	Chinese Yam	Tuber	
30	*Torreya nucifera*	Taxaceae	Japanese nutmeg - yew or Japanese *torreya*	Leaf	Ryu *et al.*, 2010
31	*Houttuynia cordata*	Saururaceae	Fish mint , Rainbow plant, Chameleon plant	NA	Lau *et al.*, 2008

32	*Rheum officinale*	Polygonaceae	Chinese rhubarb	Tuber	
33	*Polygonum multiflorum*	Polygonaceae	Tuber fleeceflower, Chinese knotweed.	Tuber and Vines	Ho *et al*., 2007
34	*Pogostemon cablin*	Lamiaceae	Patchouli	Aerial part	
35	*Perilla Frutescens*	Lamiaceae	Perilla or Korean perilla	Leaf	
36	Angelica dahurica	Umbelliferae	Bai Zhi	Root	
37	*Atractylodes macrocephala*	Compositae	Largehead atractylode , Bai Zhu	Rhizome	
38	*Citrus reticulata*	Rutaceae	Mandarin	Peel (Pericarp)	Pan *et al*., 2020
39	*Pinellia ternata*	Araceae	Crow-dipper	Tuber	
40	*Magnolia officinalis*	Magnoliaceae	Houpu magnolia	Bark	
41	*Lonicera Japonica*	Caprifoliaceae	*Japanese honeysuckle*	Leaf and Flowers	
42	*Fritillaria thunbergii*	Liliaceae	Zhe Bei Mu	Bulb	
43	*Scutellariae* baicalensis	Lamiaceae	Baikal skullcap, Chinese skullcap	Root	
44	*Arctium lappa*	Asteraceae	Greater burdock	Fruit	
45	*Artemisia annua,*	Asteraceae	Sweet wormwood	Leaf	
46	*Forsythia suspensa,*	Oleaceae.	Weeping forsythia	Fruit	
47	*Ephedra sinica*	Ephedraceae	Ma huang , Yellow horse, Sea grape	Stem/ Aerial part	
48	*Prunus armeniaca*	Rosaceae	Siberian apricot	Seed	
49	*Isatis indigotica*	Brassicaceae	Woad	Root	
50	*Dryopteris crassirhizoma*	Dryopteridaceae.	Male fern	Rhizome	
51	*Pogostemon cablin*	Lamiaceae	Mint	Aerial part	
52	*Polygonum cuspidatum*	Polygonaceae	Asian knotweed/ Japanese knotweed.	Rhizome and root	
53	*Bupleurum chinense*	Apiaceae/ Umbelliferae.	Bei Chai Hu.	Root	Pan *et al*., 2020
54	*Glycyrrhiza uralensis*	Leguminosae	*Licorice*	Rhizome and Root	
55	*Schizonepeta tenuifolia*	Lamiaceae.	Japanese mint/ Japanese catnip	Spike	
56	*Menthae haplocalyx*	Lamiaceae	Mentha/ Peppermint	Aerial part	
57	*Carthamus tinctorius*	Asteraceae	Safflower	Flower	
58	*Ligusticum chuanxiong*	Umbelliferae	Szechuan lovage C huānxiōng	Rhizome	
59	*Salvia miltiorrhiza*	Lamiaceae	Red sage, Chinese sage	Rhizome and Root	
60	*Panax ginseng*	*Araliaceae.*	Asian ginseng, Chinese ginseng, or Korean ginsen	Rhizome and root	
61	*Ophiopogon japonicus*	Liliaceae	Mondo grass	Root	
62	*Schisandra chinensis*	Schisandraceae	Magnolia-vine	Fruit	
63	*Aconitum carmichaelii*	Ranunculaceae	Chinese aconite, Carmichael's monkshood or Chinese wolfsbane	Root	
64	*Forsythia suspensa*	Oleaceae	Lianqiao	Fruit	
65	*Gardenia jasminoides*	Rubiaceae	Cape jasmine	Fruit	Pan *et al*., 2020

66	*Trichosanthes kirilowii*	Cucurbitaceae	Chinese snake gourd, Chinese cucumber	Fruit	Luo *et al.*, 2020[c]
67	*Coptis chinensis*	Ranunculaceae	Huang Lian	Rhizome	
68	*Rheum palmatum*	Polygonaceae	Rhubarb	Root and Rhizome	
69	*Lophatherum gracile*	Poaceae	Bamboo-leaf	Leaf	
70	*Pogostemon cablin*	Lamiaceae	Patchouli	Leaf	
71	*Coix lacryma*	Gramineae	Coix seed	Seed	
72	*Amomum compactum*	Zingiberaceae	Round cardamom	Fruit	
73	*Medulla Tetrapanacis*	Amaranthaceae	Rice Paper Plant Pith, *Tong Cao*	Leaf	
74	*Glycine max*	Fabaceae	Soybean	Seed	
75	*Alisma orientale*	Alismataceae	Asian water plantain,	Rhizome	
76	*Magnolia officinalis*	Magnoliaceae	Houpu magnolia, Magnolia-bark	Bark	
77	*Cyrtomium fortunei*	Dryopteridaceae	Holly fern	Aerial part	
78	*Rhodiola crenulata*	Crassulaceae	*Stonecrops*	Root and Rhizome	
79	*Aucklandia lappa*	Asteraceae	Costus, Mu Xiang	Root	
80	*Aquilaria agallocha*	Thymelaeaeeae	Agarwood, Aloeswood	Rhizome	
81	*Scrophularia ningpoensis*	*Scrophulariaceae*	Ningpo figwort or Chinese figwort, Xuanshen	Root	
82	*Cimicifuga racemosa*	Ranunculaceae	Black Cohosh	Rhizome	
83	*Syzygium aromaticum*	Myrtaceae	Clove	Flower buds	
84	*Lanxangia tsaoko*	Zingiberaceae	Cardamom *Tsao-ko*	Fruits	
85	*Anemarrhena asphodeloides*	Asparagaceae	Zhi Mu	Rhizome	
86	*Paeonia lactiflora*	Paeoniaceae	Chinese peony	Root	
87	*Bupleurum falcatum*	Apiaceae	Sickle-leaved hare's-ear, Chinese Thoroughwax, Sickle hare's ear	Root	
88	*Ziziphus jujuba*	Rhamnaceae	Chinese date tree, Common *jujube*	Fruit	Luo *et al.*, 2020[c]
89	*Descurainia sophia*	Brassicaceae	Flixweed	Seed	
90	*Fritillaria thunbergii*	Liliaceae	Zhe Bei Mu	Bulb	
91	*Cimicifuga heracleifolia*	Ranunculaceae	Black Cohosh	Rhizome	
92	*Notopterygium incisum*	Apiaceae	Qiang Huo.	Rhizome and Root	
93	*Curcuma longa*	Zingiberaceae	Turmeric	Rhizome and Root	
94	*Withania somnifera*	Solanaceae	Ashwagandha, Indian ginseng, Poison gooseberry or Winter cherry	Root	
95	*Tinospora cordifolia*	Menispermaceae	Guduchi	Root	
96	*Ocimum sanctum*	Lamiaceae	Holy basil, Tulsi	Leaf	
97	*Leptadenia reticulata*	Apocynaceae	Dori	Root, Aerial parts	
98	*Pavonia odorata*	*Malvaceae*	Fragrant Sticky Mallow.	Root	

99	*Cedrus deodara*	Pinaceae	Deodar Cedar	Heart wood	Balkrishna *et al.*, 2020
100	*Cyperus scariosus,*	Cyperaceae	Cypriol, Nutgrass	Root	
101	*Cinnamomum verum*	Lauraceae	True cinnamon tree or Ceylon cinnamon tree	Bark	
102	*Chrysopogon zizanioides*	Poaceae	Vetiver,	Whole plant	
103	*Hemidesmus indicus*	Apocynaceae ·	Indian sarsaparilla	Root	
104	*Santalum album*	Santalaceae	Indian *sandalwood*	Heartwood	
105	*Berberis aristata*	Berberidaceae	Indian barberry, "chutro" or Tree turmeric	Root bark	
106	*Aquilaria agallocha*	Thymelaeaceae	Agarwood, Aloeswood	Root	
107	*Solanum indicum*	Solanaceae	Indian Night Shade, Poison Berry	Root, Fruit	
108	*Pluchea lanceolata*	Asteraceae	Indian fleabane	Leaf	
109	*Nelumbo nucifera*	Nelumbonaceae	Sacred lotus	Rhizomes, Leaves and Seed	
110	*Pistacia integerrima*	Anacardiaceae	Zebrawood	Gall	Balkrishna, 2020
111	*Cressa cretica*	Convolvulaceae	Salt Cresse	Fruit	
112	*Piper nigrum*	Piperaceae	Black pepper	Fruit	
113	*Anacyclus pyrethrum*	Asteraceae	Spanish chamomile	Root	
114	*Embelia ribes*	Myrsinaceae	False black pepper	Fruit	Rastogi *et al.*, 2020
115	*Terminalia chebula*	Combretaceae	Black- or chebulic myrobalan	Fruit	
116	*Emblica officinalis*	Euphorbiaceae	Indian gooseberry	Fruit	
117	*Acorus calamus*	Acoraceae	Sweet flag or Calamus	Root	
118	*Aconitum heterophyllum*	Ranunculaceae	Aconite, Monkshood, Wolf's-bane, Leopard's bane	Root	
119	*Cynanchi Stauntonii*	Asclepiadaceae	Cynanchum Root and Rhizome Prime White Root	Rhizome and Root	Ang *et al.*, 2020
120	*Fritillariae Thunbergii*	Liliaceae	Zhe bei mu	Bulb	

*NA = Not available

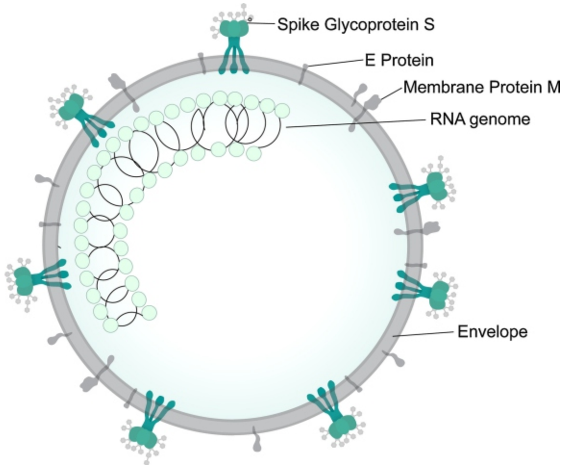

Figure 1: The general structure of a SARS-CoV-2 (reproduced from Wikipedia under CC licence 4.0). E protein = envelope protein (Mani *et al.*, 2020)

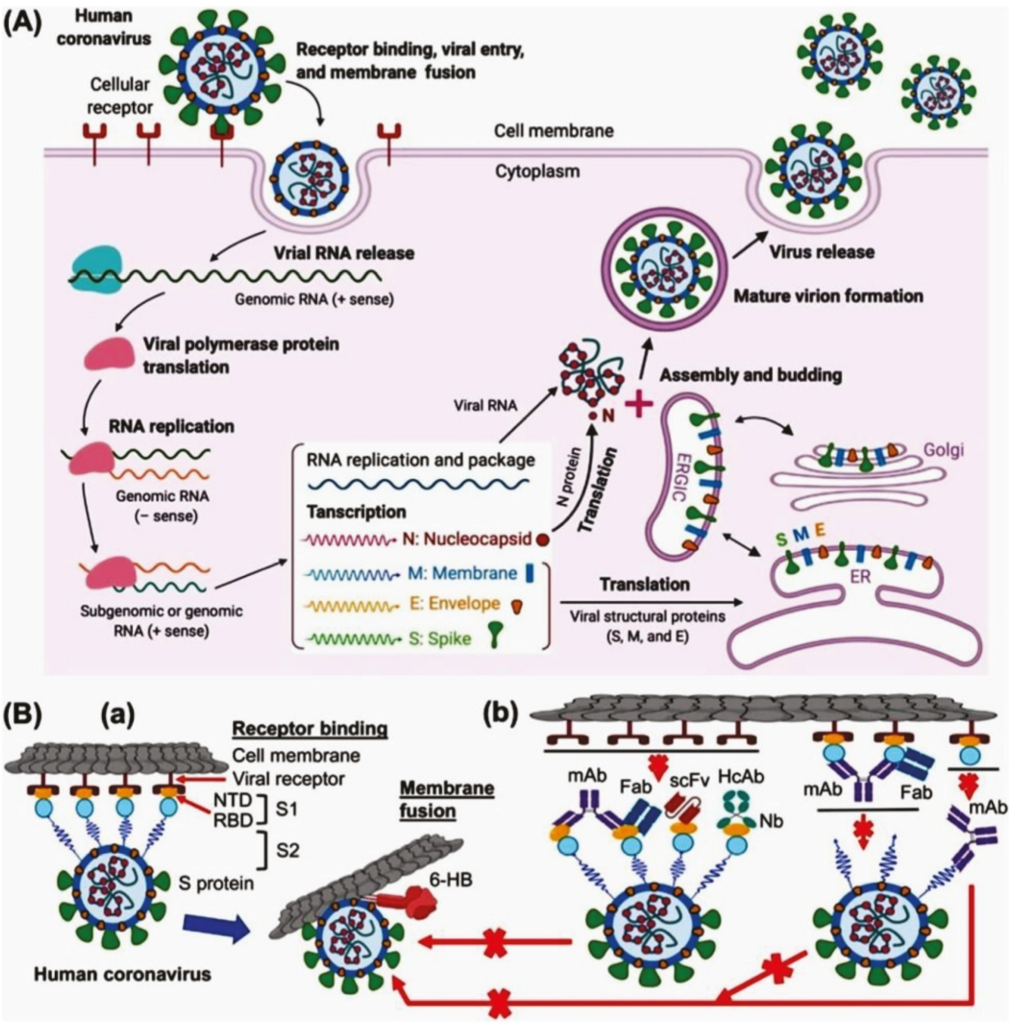

Figure 2. (A) Replication cycle of human coronavirus; (B) host cell receptor and viral protein (S-protein) binding and membrane fusion mechanism (Jiang *et al.*, 2020).

Potential mechanism of action of plants used against SARS-CoV-2

Medicinal plants with potential activity against 3-chymotrypsin-like cysteine protease (SARS-CoV 3CLpro) abound (Upadhyay *et al.*, 2020; ul Qamar *et al.*, 2020; Benarba and Pandiella, 2020) (Table 2). 3-Chymotrypsin-like protease is necessary for viral replication and as such an important drug target for SARS-CoV-2 therapeutic agents. Other potential mechanisms through which medicinal plants act which are also important targets for therapeutic agents include angiotensin-converting enzyme 2 (ACE2) (Table 3), SARS-CoV- PLpro activity (Table 4), SARS-CoV helicase (Table 5), Type II Transmembrane Serine Protease (TMPRSS2) (Table 6), RNA-dependent RNA polymerase (RdRp) (Table 7) and Immunomodulatory activities (Table 8).

Table 2: Medicinal plants with potential activity against 3-chymotrypsin-like cysteine protease (SARS-CoV 3CLpro) of SARS-CoV-2

S/N	Medicinal plant	Family	Other Pharmacologic action	References
1.	*Psorothamnus arborescens*	Fabaceae	Anti-SARS-CoV-2 activity	Idrees *et al.*, 2020
2.	*Myrica cerifera*	Myricaceae	Anti-cancer and Antioxidant activities	Paul *et al.*, 2013 Zhang et al., 2016
3.	*Cassine xylocarpa*	Celastraceae	Anti-HIV activity	Osorio et al., 2011
4.	*Phyllanthus emblica*[a]	Phyllanthaceae	Antimicrobial and Anti - inflammatory activities	Gaire and Subedi, 2014; Asmilia *et al.*, 2020
5.	*Tinospora cordifolia*[e,f]	Menispermaceae	Immunomodulatory activity; Anti-HIV	Kalikar *et al* ., 2008; Akhtar, 2010
6.	*Commiphora wightii*	Burseraceae	Anti-cancer activity	Uzma *et al.*, 2020
7.	*Curcuma longa*	Zingiberaceae	Anti-allergic and Anti -cancer activities	Choi *et al.*, 2010; Kuttan *et al.*, 1985
8.	*Terminali chebula*	Combretaceae	Anti-HSV-2 and Antitussive activities	Kesharwani *et al*., 2017; ul Haq *et al.*, 2013
9.	*Glycyrrhiza glabra*[a,c]	Fabaceae	Antitussive, Expectorant and Antiviral activities	Kamei *et al* ., 2003; De Clercq, 2000; Lalita,1994
10.	*Azadirachta indica*	Meliaceae	Antimalarial and Antiviral activities	Deshpande *et al.* , 2014; Badam *et al.,* 1999
11.	*Boswellia serrate*	Burseraceae	Immunomodulatory and Anti - inflammatory activities	Beghelli *et al.,* 2017; Siddiqui, 2011
12.	*Zingiber officinale*	Zingiberaceae	Antiviral, Immunomodulatory and Anti -inflammatory activities	San *et al.*, 2013; Carrasco *et al.,* 2009; Ezzat *et al*., 2018
13.	*Helianthus annuus*	Asteraceae	Anti-asthmatic and Antiviral activities	Heo *et al.,* 2008; Oliveira et al., 2009
14.	*Ocimum sanctum*	Lamiaceae	Immunomodulatory, Antiviral and Anti-asthmatic activities	Jeba and Rameshkumar, 2011; Ghoke *et al.*, 2018; Vinaya, 2017
15.	*Hyptis atrorubens Poit*	Lamiaceae	Antimicrobial activity	Kerdudo *et al* ., 2016; Abedini *et al.,* 2013
16.	*Phaseolus vulgaris*	Fabaceae	Antiviral, Antioxidant and Anti-inflammatory activities	Ye *et al.*, 2001; Oomah *et al.*, 2010
17.	*Fraxinus sieboldiana*	Oleaceae	Anti-HIV and other Antiviral activities	Kim *et al.,* 2001; Lin *et al.*, 2010
18.	*Glycyrrhiza uralensis*	Fabaceae	Antiviral, Anti -inflammatory, and Anti-asthmatic activities	Alfajaro *et al.,* 2012; Shin *et al*., 2008; Huang *et al.,* 2019
19.	*Amaranthus tricolor*	Amaranthaceae	Antioxidant activity	Pulipati *et al.,* 2017
20.	*Camellia sinensis*[e]	Theaceae	Anti-inflammatory and Immunomodulatory activities	Chattopadhyayet al., 2004; Chattopadhyay *et al.*, 2012
21.	*Andrographis paniculata*	Acanthaceae	Antiviral, Immunostimulatory, Antioxidant and anti - inflammatory activities	Pongtuluran and Rofaani, 2015; Sheeja *et al.*, 2006

22.	*Angelica keiskei*[a]	Umbelliferae	Anti-inflammatory and Immunomodulatory activities	Lee *et al.,* 2010; Sudira and Merdana, 2017
23.	*Ecklonia cava*	Laminariaceae	Antimicrobial, Antioxidant and Antiviral activities	Venkatesan *et al.,* 2016; Yang *et al*., 2018
24.	*Torreya nucifera*[d]	Taxaceae	Anti-inflammatory and Antioxidant activities	Kim *et al*., 2016; Jeon *et al*., 2009
25.	*Rheum palmatum*	Polygonaceae	Antifungal activity	Shang *et al*., 2019
26.	*Withania somnifera*[e]	Solanaceae	anti-inflammatory and anti-microbial activities	Dar *et al*., 2015
27.	*Strychnos usambarensis*	*Loganiaceae*	Antimalarial activity	Frédérich *et al*., 2004
28.	*Cryptolepis sanguinolenta*	Periplocaceae	Antimalarial activities	Ansha and Mensah, 2013
29.	*Teclea trichocarpa*	Rutaceae	Antiprotozoal and cytotoxic activity	Mwangi *et al.,* 2010
30.	*Fagara zanthoxyloides*	Rutaceae	Antimalarial activity	Enechi *et al*., 2019
31.	*Ancistrocladus tanzaniensis*	Acistrocladaceae	Antimalarial activity	Bringmann *et al*., 1999
32.	*Monodora angolensis*	Annonaceae	Antimalarial activity	Nkunya *et al*., 2004
33.	*Toddalia asiatica*	Rutaceae	Anti-HIV and Antimalarial activities	Rashid *et a* l., 1995; Borah *et al*., 2010
34.	*Glossocalyx brevipes*	Siparunaceae	Antiplasmodial activity	Mbah *et al.,* 2004
35.	*Triphyophyllum peltatum*	Dioncophyllaceae	Antimalarial activity	Bringmann *et al*., 1997
36.	*Anastatica hierochuntica*[a]	Brassicaceae	Antioxidant and antimicrobial activities	Mohamed *et al*., 2010
37.	*Allium myrianthum*	Liliaceae	Antioxidant activity	Petropoulos *et al*., 2020
38.	*Cichorium intybus*[a,c]	Asteraceae	Antimalarial and hepatoprotective activities	Bischoff *et al*., 2004; Atta *et al.,* 2010
39	*Marrubium vulgare*[a,c]	Lamiaceae	Hypotensive activity	Bardai *et al*., 2001
40.	*Olea europaea*[a,c]	Oleaceae	Anti-hypertensive activity	Somova *et al*., 2003
41.	*Hibiscus sabdariffa*[e]	Malvaceae	Anti-inflammatory and Antihypertensive activities	Dafallah and Al-Mustafa, 1996; Onyenekwe *et al*., 1999
42.	*Sonchus macrocarpus*	Asteraceae	Antioxidant and anti-inflammatory activities	Li and Yang, 2018
43.	*Tamarix nilotica*	Tamaricaceae	Antioxidant and hepatoprotective activities	AbouZid and Sleem, 2011
44.	*Quercus suber*	Fagaceae	Antioxidant activity	Fernandes *et al.,* 2009
45.	*Artemisia herba-alba*	Asteraceae	Antioxidant and antifungal activities	Boukhennoufa *et al.,* 2020
46.	*Schinus molle*	Anacardiaceae	Anti-inflammatory and Antioxidant activities	Feriani *et al*., 2020
47.	Lepidium sativum	Brassicaceae	Anti-inflammatory and Antioxidant activities	Alqahtani *et al*., 2019
48.	*Crataegus sinaica*	Rosaceae	Antioxidant, Cytotoxic and Antimicrobial activities	El-Hela *et al*., 2017
49.	*Cicer arietinum*	Fabaceae	Anti-inflammatory and Antifungal activities	Milán-Noris *et al*., 2018; Bajwa *et al*., 2006
50.	*Artemisia judaica*[a,c]	Asteraceae	Antioxidant, Antimicrobial and Anti-inflammatory activities	Nasr *et al* ., 2020; Abu - Darwish *et al*., 2016
51.	*Isatis Indigotica*	Brassicaceae	Anti-inflammatory and Anti-viral activities	Meng *et al*., 2017
52.	*Dioscorea batatas*[e]	Dioscoreaceae	Anti-SARS-CoV Immunomodulatory, Anti-inflammatory and Antioxidant activities	Wen et al., 2011; Choi et al., 2004; Lim *et al*., 2019
53.	*Cassia tora*	Caesalpinaceae	Anti-SARS-CoV; Anti-inflammatory, Antioxidant and Antibacterial activities	Wen et al., 2011; Antonisamy *et al*., 2017; Sharma *et al*., 2010
54.	*Taxillus Chinensis*	Loranthaceae	Immunomodulatory, Anti-SARS-CoV activities	Zhang *et al*., 2013; Wen et al., 2011
55.	*Cibotium barometz*	Dicksoniaceae	Anti-SARS-CoV and Anti-inflammatory activities	Wen et al., 2011; Lee *et al*., 2010

a= Plant with PL pro activity; c= Plant with RdRp activity; d= Plant with helicase activity; e= Plants with Immunomodulatory activity; f= Plant with ACE2 activity

Table 3: Medicinal plants with potential activity against SARS-CoV-2 Receptor, angiotensin-converting enzyme 2 (ACE2), binding activity

S/N	Medicinal plant	Family	Other Pharmacologic action	References
1.	*Quercus infectoria*	Fagaceae	Hepatoprotective and immunomodulatory activities	Pithayanukul *et al*., 2009; Yahya *et al.,* 2018
2.	Rheum emodin	Polygonaceae	Antiviral, Anti -airway inflammation activities	Ho *et al*., 2007; Zhong *et al*., 2017
3.	*Ipomoea obscura*	Convolvulaceae	Anti-inflammatory and anti - tumour, Hepatoprotective and antioxidant activities	Hamsa and Kuttan, 2011; Ramachandran *et al*., 2019
4.	*Berberis integerrima*	Berberidaceae	Anticonvulsant, Antibacterial activities	Hosseinzadeh *et al*., 2013; Azimi et al., 2018
5.	*Crataegus laevigata*	Rosaceae	Anti-inflammatory and Anti - microbial activities	Tadić *et al*., 2008
6.	*Onopordum acanthium*	Asteraceae	Anti-inflammatory and Antibacterial activities	Lajter *et al*., 2014
7.	*Cheyniana microphylla*	Myrtaceae	Antioxidant activity	Renda *et al.,* 2018
8.	*Scutellaria baicalensis*[d]	Lamiaceae	Anti-SARS CoV-2, Antiallergic, Immunomodulatory Anti - inflammatory and antioxidant activities	Liu *et al.,* 2020; Jung *et al*., 2012; Huang *et al*., 2006; Yang *et al*., 2007
9.	*Veronicalina Riifolia*	Veronicellidae	Anti-SARS CoV activity	Goel and Goel, 2020
10.	*Galla chinensis*	Anacardiaceae	Antibacterial and Anti - inflammatory activities	Zheng *et al.,* 2011
11.	*Glycyrrhizae radix*	Leguminosae	Antiviral, Antiiflammatory and Antioxidant activities	Parizipour and Shahriari, 2020; Yang *et al*., 2013
12.	*Polygonum multiflorum*[e]	Polygonaceae	Immunomodulatory, Antiiflammatory and Antioxidant activities	Zhang *et al*., 2018; Park et al., 2017; Ip *et al.,* 1997

Table 4: Medicinal plants with potential activity against SARS-CoV-2 Receptor, SARS CoV- PLpro activity

S/N	Medicinal plant	Family	Other Pharmacologic action	References
1.	*Alnus japonica*	Betulaceae	Anti-influenza; Antioxidant and Anti-inflammatory activities	Tung *et al* ., 2010; Ibrahim *et al*., 2017
2.	*Cullen corylifolium*	Leguminosae	Antiviral activity	Kim *et al*., 2014;
3.	*Paulownia tomentosa*	Scrophulariaceae	Antioxidant and Anti - inflammatory activities	Jo and Kim, 2019
4.	*Salvia miltiorrhiza*[b]	Lamiaceae	Antioxidant; Hepatoprotective effect; Anti-HIV-1 activities	Zhao *et al.,* 2006; Lee *et al.,* 2003; Abd-Elazem *et al*., 2002
5.	*Tribulus terrestris*[c]	Zygophyllaceae	Antihypertensive; Anticholinergic; Antibacterial activities	Ahmed *et al*., 2020
6.	*Psoralea corylifolia*	Leguminosae	Anti-inflammatory activity	Neve *et al*., 2018
7.	*Cynara scolymus*[e]	Asteracea	Immunomodulatory, Anti - inflammatory and Antioxidant activity	Hueza *et al* ., 2019; Majeed *et al*., 2015
8.	*Ephedra alata*	Ephedraceae	Anti-inflammatory and Antioxidant activity	Soumaya *et al.,* 2020
9.	*Salvia triloba*[c]	Labiatae	Anti-inflammatory and Antioxidant activity	Risaliti *et al*., 2019
10.	*Centaurea furfuracea*	Asteraceae	Antioxidant activity	Chemsa *et al*., 2018
11.	*Matricaria chamomilla*[c]	Asteraceae	Anti-inflammatory, antioxidant and antiviral activities	Satyal *et al*., 2015
12.	*Globularia alypum*	Globulariaceae	Antibacterial, Anti - inflammatory and Antioxidant activities	Ghlissi *et al*., 2016
13.	*Tetraclinis articulata*[e]	Cupressaceae	Immunomodulatory Antioxidant, antibacterial, anti - inflammatory activities	Daoudi *et al* ., 2013; Rached *et al.,* 2018
14.	*Podocarpus gracilior*	Podocarpaceae	Antioxidant activity	Kamal *et al.,* 2012
15.	*Epilobium hirsutum*[b]	Onagraceae	Antiviral and Antioxidant activities	Todorov *et al.,* 2014; Karakurt *et al*., 2016
16.	Cicer arietinum[b,e]	Fabaceae	Antiviral and Antioxidant activities	Kan and Kartal, 2009; Kou *et al*., 2013
17.	*Centaurea incana*[b]	Asteraceae	Antioxidant activity	Bouafia *et al*., 2018
18	*Broussonetia papyrifera*	Moraceae	Antioxidant and anti - inflammatory activities	Malaník *et al*., 2020

b= activity against 3CLPro; c= Plant with RdRp activity; e= Plants with Immunomodulatory activity

Table 5: Medicinal plants with potential activity against the SARS-CoV helicase

S/N	Medicinal plant	Family	Other Pharmacologic action	References
1.	*Aglaia perviridis*	Meliaceae	Anti-inflammatory activity	An *et al*., 2020;
2.	*Isatis indigotica*[b,e]	Brassicaceae	Antiviral; Anti - inflammatory and Antipyretic activities	Meng *et al*., 2017; Ho *et al*., 2002
3.	*Griffithsia spp*	Wrangeliaceae	Anti-HIV1 activity	Vamvaka *et al.,* 2016

b= activity against 3CLPro

Table 6: Medicinal plants against Type II Transmembrane Serine Protease (TMPRSS2)

S/N	Medicinal plant	Family	Other Pharmacologic action	References
1.	*Strobilanthes cusia*[a]	Acanthaceae	Antiviral activity	Tsai *et al*., 2020
2.	*Fumaria indica*	Papaveraceae	Antypyretic, Anti -cough activities	Gupta *et al.,* 2012
3.	*Strychnos nux-vomica*	Loganiaceae	Anti-inflammatory, Antypyretic and Anti - oxidant activities	Eldahshan *et al*., 2015
4.	*Corydalis govaniana*	Papaveraceae	Anti-oxidant and Analgesic activities	Shrestha and Adhikari, 2017; Muhammad *et al*., 2015
5.	*Nerium oleander*	Apocynaceae	Anti-inflammatory, Anti - poliovirus activities	Balkan *et al.* , 2018; Sanna *et al.,* 2019
6.	*Strychnos ignatii*	Loganiaceae	Anti-inflammatory activity	Kim *et al*., 2009
7.	*Strychnos colubrina*	Loganiaceae	Antypyretic activity	Karthikeyan *et al* ., 2011
8.	*Fumaria vaillantii*	Papaveraceae	antifungal, anti - inflammatory activities	Moghtader, 2013
9.	*Edgeworthia gardneri*	Thymelaeaceae	Antidiabetic activity	Gao *et al*., 2016

a= Plant with PL pro activity

Table 7. Medicinal plants against RNA-dependent RNA polymerase (RdRp)

S/N	Medicinal plant	Family	Other Pharmacologic action	References
1.	*Trigonella foenum-graecum*[e]	Papilionaceae	Immunomodulatory, Antioxidant, Anti - inflammatory and Antipyretic activities	Ahmadiani *et al.,* 2001; Bhanger *et al.,* 2008; Anarthe *et al*., 2014
2.	*Eruca sativa*	Brassicaceae	Antioxidant, Antimicrobial, Antiplatelet and Antithrombotic activities	Fuentes *et al* ., 2014; Koubaa *et al*., 2015
3.	*Medicago sativa*[a]	Leguminosae	Analgesic, anti -inflammatory, Antioxidant and cytotoxic activities	Seddighfar *et al* ., 2020; Zagórska-Dziok *et al*., 2020
4.	*Cleome species*[e]	Capparaceae	Antimalarial, Anti - inflammatory, Antipyretic, Antiviral and immunomodulatory activities	Abdullah *et al* ., 2016; Samra *et al*., 2020; Rastogi *et al*., 2009
5.	*Fraxinus oxycarpa*	Oleaceae	Antioxidant activity	Jiménez-López *et al*., 2017
6.	*Scrophularia saharae*	Scrophulariaceae	Anti-inflammatory and Neuroprotective activities	Pasdaran and Hamedi, 2017
7.	*Daucus carota*[b,e]	Apiaceae	Antiviral, Antioxidant, Anti - inflammatory, and Immunomodulatory activities	Shebaby, 2014; Torky, 2013; Patil *et al*., 2012
8.	Apium graveolens[a]	Apiaceae	Anti-inflammatory activity	Ramezani *et al*., 2009
9.	*Houttuynia cordata*[b,e]	Saururaceae	Anti-inflammatory, AntiSARS and Immunomodula tory activities	Choi *et al.,* 2010; Lau *et al.,* 2008
10.	*Sinomenium acutum*[e]	Menispermaceae	Anti-inflammatory activity	Zhao *et al*., 2015
11.	*Coriolus versicolor*[e]	Polyporaceae	Immunomodulatory, antioxidant and antimicrobial, Anti-HIV1 activities	Saleh *et al*., 2017; Han *et al.,* 2015; Collins and Ng, 1997
12.	*Ganoderma lucidum*	Ganodermataceae	Antioxidant, Anti - inflammatory Immunomodulatory and Antiviral activities	Shi *et al.,* 2013; Cai *et al.,* 2016; Zhang *et al*., 2014

a= Plant with PL pro activity; b= activity against 3CLPro

Table 8: Medicinal plants with Immunomodulatory activities

S/N	Medicinal plant	Family	Other Pharmacologic action	References
1.	*Astragalus mongholicus*	Fabaceae	Antioxidant, Anti -inflammatory activities	Schinella *et al.,* 2002
2.	*Lonicera japonica*	Caprifoliaceae	Antioxidant, Anti-inflammatory, Antiviral activities	Hsu *et al.,* 2016; Liu *et al.*, 2020
3.	*Panax ginseng*	Araliaceae	Neuroprotective and anti - inflammatory activities, Antiviral Activities	Kong *et al.,* 2009; Baek *et al.,* 2010
4.	*Astragalus membranaceus*	Fabaceae	Antiviral, Antioxidant, Anti - inflammatory activities	Khan *et al.* , 2019; Lee *et al.,* 2013
5.	*Echinacea purpurea*	Asteraceae	Antioxidant, Anti -inflammatory and Antiviral activities	Aarland *et al*., 2017; Signer *et al*., 2020
6.	*Allium sativum*	Alliaceae	Antimalarial, Antioxidant, Anti-inflammatory and Antiviral activities	Adebayo and Motunrayo, 2018; Tsai *et al*., 2005
7.	*Psidium guajava*	Myrtaceae	Anti-cough, Anti -inflammatory, Antioxidant and antimicrobial activities	Fernandes *et al* ., 2014; Jaiarj *et al.,* 1999; Sen *et al.,* 1995
8.	*Cymbopogon citratus*	Poaceae	Antimalaria, Antioxidant, Anti - inflammatory and Antiviral activities	Tchoumbougnang *et al.,* 2005; Lu, *et al.* , 2014; Abraham - Oyiguh *et al*., 2019
9.	*Cinnamomum zeylanicum*	Lauraceae	Anti-inflammatory, Antioxidant and Antimicrobial activities	Joshi *et al* ., 2010; Tepe and Ozaslan, 2020; Alizadeh Behbahani *et al* ., 2020
10.	*Acacia concinna*	Fabaceae	Antibacterial, Anti -coagulant, Anti-platelet and Anti - thrombotic activities	Todkar *et al.,* 2010; Boonmee *et al*., 2017
11.	*Lawsonia inermis*	Lythraceae	Anti-inflammatory, antipyretic, Antimicrobial Antimalarial activities	Alia *et al.,* 1995; El-Hag *et al.,* 2007; Afolayan *et al*., 2016
12.	*Piper longum*	Piperaceae	Antioxidant, Anti -inflammatory and Antiallergic activities	Jin *et al* ., 2013; Dahanukar *et al.,* 1984
13.	*Gelidium amansii*	Gelidiaceae	Anti-inflammatory, Antibacterial and Antifungal activities	Park and Yoon, 2018; Nagalingam *et al.,* 2019
14.	*Petroselinum crispum*	Apiaceae	Antioxidant, Anti-inflammatory, Antihypertensive and Antibacterial activities	Petrolini, et al., 2013; Ajebli et al., 2019; Slighoua *et al*., 2020
15.	*Plantago major*	Plantaginaceae	Anti-inflammatory, Antioxidant and Antiviral activities	Zubair *et al* ., 2019; Stanisavljević *et al.* , 2008; Chiang *et al.,* 2002
16.	*Adenocarpus mannii*	Faboideae	Antioxidant and Antimicrobial activities	Ndjateu *et al*., 2014
17.	*Caucalis melanantha*	Umbelliferae	Antibacterial activity	Djeussi *et al.,* 2016
18.	*Ocimum gratissimum*	Lamiaceae	Antimalarial, Anti - inflammatory, Antioxidant and Antimicrobial activities	Tchoumbougnang et al., 2005; Joshi, 2013
19.	*Asystasia intrusa*	Acanthaceae	Anti-inflammatory and Antimicrobial Activities	West *et al* ., 2011; Dian, 2016
20.	*Clematis chinensis*	Ranunculaceae	Anti-inflammatory and Antioxidant activities	Peng *et al* ., 2012; Chen *et al.,* 2005
21.	*Pouteria cambodiana*	Sapotaceae	Antioxidant activity	Chaisri and Laoprom, 2017
22.	*Clausena excavata*	Rutaceae	Anti-HIV-1, Antiplatelet activity, Anti -inflammatory and Antioxidant activities	Kongkathip *et al.,* 2005; Wu et al., 1994; Albaayit *et al.*, 2020
23.	*Limoniastrum guyonianum*	Plumbaginaceae	Anti-inflammatory, Antioxidant and Antimicrobial activities	Krifa *et al* ., 2015; Bouzidi *et al*., 2016
24.	*Codium fragile*	Codiaceae	Anti-inflammatory, Antioxidant, Thrombolytic and Antiviral activities	Choi *et al.,* 2013; Koz *et al.,* 2009; Ohta *et al.,* 2009; Han *et al*., 2010
25.	*Acacia catechu*	Mimosoideae	Anti-inflammatory, Antioxidant, Antiallergic and Antiviral activities	Stohs and Bagchi, 2015; Patel and Patel, 2019; Gupta and Chaphalkar, 2016

CONCLUSION AND PROSPECTS

In the present review, we have shown the various medicinal plants which have been utilised in the prevention and treatment of COVID-19. Majority of the plants have also been shown to possess other pharmacological activities which may contribuite to their ability to alleviate the symptoms and treat coronavirus disease. This medicinal plants use has been regarded among the principal factors that contributed to the containment of the COVID-19 in China (Salzberger et al., 2020). Existing information have shown that the possible mechanism of action of anti-COVID-19 medicinal plants were inhibition of 3-chymotrypsin- like protease (3CLpro), papain like protease (PLpro), RNA-dependent RNA polymerase (RdRp), angiotensin-converting enzyme 2 (ACE2) and immunomodulatory activities. These proposed mechanisms target multiple components pathways in the life cycle of SARS-CoV-2 for the treatment of COVID-19. However, the bulk of the understanding of the mechanisms of medicinal plants is mainly produced following virtual simulations (molecular docking and network pharmacology analysis). In order to confirm these predicted mechanisms, it is of paramount importance that well designed experiments (both *in vitro* cell and *in vivo* animal studies) be conducted to validate these predictions. Finally, tissue samples as well as the biofluids from medicinal plant-treated COVID-19 patients should be collected and analysed using appropriate instruments and controlled clinical trial parameters to further validate the proposed possible mechanisms.

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