

## Review Article

# Traditional to Recent Approaches in Herbal Medicine Therapy of COVID-19

### ABSTRACT

The novel coronavirus pneumonia that broke out and invaded the whole world since 2019 where deaths reached millions. Still, no vaccine is available, therefore, developing effective programs for therapy is of high priority. Chinese herbal medicine has succeeded in the treatment of other coronavirus pneumonia such as SARS, MERS and, avian influenza which gives us hope to find the targeted remedy in the natural herbs consumed by natives from different regions. This work aims to provide a documented data base and highlight the use of natural traditional remedies in the treatment of COVID-19 and other related viruses. Although promising results were obtained in many cases, few studies reported the characterization of bioactive principles and/or mechanisms. It is requested that pharmaceutical industries and the scientific community focus on some of these plants for future research to discover a promising effective drug for the development of anti-SARSCoV-2 therapeutics soon.

**Keywords:** COVID-19, Traditional Medicine, SARS, Influenza, Rhinovirus, pneumonia.

### INTRODUCTION

Viruses are considered as a reason for many ailments that affect humans worldwide. Most of these ailments are very complex and hard to cure, these viruses include coxsackievirus (CV), dengue virus (DENV), enterovirus 71 (EV71), hepatitis B virus (HBV), hepatitis C virus (HCV), herpes simplex virus, human immunodeficiency virus (HIV), influenza virus, measles virus (MV), and respiratory syncytial virus (RSV) in addition to coronavirus [1]. Coronavirus (COVID-19), pandemic 2019, is considered a newly recognized strain of coronavirus that causes severe illness varying from symptoms like flu and reaches to be fatal in a considerable percentage of people across the world [1]. This represents a global challenge as cases are increasing rapidly especially critical cases with pneumonia. Recently, over 81,000 cases have been confirmed, with over 2700 deaths [2]. The mortality rate is around 2%, most of them need ICU admission while about 20.1 % developed acute respiratory distress syndrome [2]. Therefore, there is an urgent demand to find a quick protocol and strategy for therapy for mild and severe cases. Herbal medicines and purified natural products provide a rich resource for novel remedies where some antiviral drugs have been developed and used in many herbal preparations for therapy. In China, traditional Chinese medicine was widely used and has already played an important role during SARS-CoV and SARSCoV2 outbreak [3]. Besides, there are some herbal formulae following the Chinese guidelines in terms of the composition of herbs for the treatment of pediatric COVID-19 [4]. However, the herbs used frequently in the proposed herbal formulae for the treatment of pediatric COVID-19 lack diversity in comparison to that of the adults [4]. In the recommendations on adult treatment for COVID-19, the herb *Glycyrrhiza* root and rhizome was one of the highest frequency used herbs [4]. There is also an extensive dependence on traditional medicine in Africa [5] and India [6] and many of them were related to SARS-CoV therapy. This review aimed to systematically summarize and analyze the herbs that have been traditionally used in the treatment of coronavirus and some related diseases in many regions of the world to try to participate in finding a suitable therapy for this fatal virus.

### METHODOLOGY

Database searches using PubMed, Elsevier, Scopus, Google Scholar and Web of Science were conducted till 10th June 2020 to include up-to-date documented information in the present review article. For mining data, the following MESH words were used in the databases mentioned above: traditional herbal medicinal plants for COVID-19, antiviral effects of coronavirus, Chinese herbal medicine, natural products for coronavirus, as well as recently reported mechanisms of action were all gathered from the online bibliographical databases.

## DISCUSSION

Since there are no treatments specific for CoV infection and the production of a preventive vaccine is still under investigation. Thus, comes the urgent need to produce effective antivirals for prophylaxis and effective treatment of CoV infection to try to reduce the mortality it causes. The exploration of already used therapies in the treatment of this epidemic resembles a quick way to overcome this situation. This study will include a wide overall survey for the effects of traditional herbal medicine, some herbal formulae including their ingredients in addition to recent approaches for the herbal treatment of COVID-19. The use of traditional herbal medicine for the prevention or treatment of this novel viral infection including pneumonia will be investigated. Our research was extended to include most herbs used in this aspect in most regions of the world to provide a collective review with all data required in this field. In searching for the traditionally used therapies some Chinese formulae were found listed in (Table 1) that seem to be effective [7]. It was found that *Glycyrrhizae* spp. root and rhizome is considered as one of the most used herbs in several herbal formulas followed by *Scutellariae* root and rhizome then come *Rheum* spp. and other herbs listed. These formulas were used for the treatment of several symptoms of some patients of COVID-19 as high fever and diarrhea syndromes [7].

It was declared at a press conference in April 2020 by a Chinese official that three patent drugs of herbal constituents were approved for the treatment of COVID-19 manifestations. These include Xuebijing injections when the cases are severe in addition to Jinhuaqinggan granules and Lianhuaqingwen capsules indicated for moderate cases. After this approval, these drugs were propagated and widely used in China for the treatment of COVID-19. It was stated that these patents relieve some symptoms as fever, cough, fatigue also it decreases the risk that these cases develop to be severe but no other details were added [8].

*Glycyrrhizae* Radix et Rhizoma is considered from the highly effective herbs widely used whatever is the stage of infection. It is approved by the China Food and Drug Administration (SFDA) as antiviral herbal therapy. Its mechanism was reported by many studies as it inhibits attachment, entry, and replication of the virus which was earlier used in treating SARS [9, 10]. In addition, *Glycyrrhizae* Radix et Rhizoma possesses an anti-inflammatory effect which is useful in the treatment of lung inflammatory cases associated with COVID-19 [4, 11].

In the Korean guidelines, an herbal formula called Qingfei Paidu Tang was recommended for the treatment of severe conditions of COVID-19 as well as its recommendation by the national Chinese guidelines for diagnosis and treatment. This formula consists of (*Ephedrae* Herba 9g, *Glycyrrhizae* Radix et Rhizoma 6g, *Armeniacae* Semen amarum 9g, *Gypsum fibrosum* 15~30g, *Cinnamomi ramulus* 9g, *Alismatis* Rhizoma 9g, *Polyporus* 9g, *Atractylodis macrocephalae* Rhizoma 9g, *Poria sclerotium* 15g, *Bupleuri* Radix 16g, *Scutellariae* Radix 6g, *Pinelliae* Rhizoma 9g, *Zingiberis* Rhizoma Recens 9g, *Asteris* Radix 9g, *Farfarae* Flos 9g, *Belamcandae* Rhizoma 9g, *Asari* Herba 6g, *Dioscoreae* Rhizoma

12g, *Aurantii fructus* 6g, *Citri unshius* Pericarpium 6g and *Agastachis* Herba 9g). Recently, it was reported by [12], that this formula boosts immunity and decreases inflammation through its effect on the lung and spleen which are considered the pathways of COVID-19. In addition, the Korean guidelines removed the *Farfarae* Flos herb due to its safety and toxicity [4].

Ang *et al*, presented several herbal formulas used in traditional medicine for pediatric COVID-19 cases (Table 2). They mentioned 13 herbal formulas approved by the Chinese guidelines which consist totally of 56 herbs. According to the authors, clusters of herbal pairs were used *Artemisiae annuae* herb and *Scutellariae* root in a cluster, *Armeniaca* seeds, and *Coicis* seeds in another and *Ephedrae* with *Gypsum fibrosum*. [13].

In Africa, traditional medicine play an important role in providing care to populations. Medicinal herbal plants as *Artemisia annua* are considered as one of the possible treatments for COVID-19 where efficacy and adverse side effects should be tested for. The WHO recommended testing herbs for their efficacy and safety before traditional practice through rigorous clinical trials is critical [14], at the meanwhile traditional medicine continues to be widely used across Africa. President Rajoelina stated that 80% of Madagascar's population uses 'COVID Organics' [15]. A biochemist researcher in traditional medicine at North-West University in South Africa, Professor Chrisna Gouws, reported about the use of *Artemisia annua* in herbal medicine "It's a very popular herbal medicine. It's one of the most frequently used herbs in parts of the world. The scientific community became interested because it contains artemisinin, which is a recognized anti-malarial treatment" [15]. A state of art, The Max Planck Institute of Colloids and Interfaces, Potsdam (Germany) will collaborate with ArtemiLife Inc., a US based company and medical researchers in Denmark and Germany to test *Artemisia annua* extract and artemisinin derivatives in laboratory cell studies against the novel coronavirus Sars-CoV-2 [16].

Furthermore, there are several medicinal plants and many secondary metabolites that were reported effective against viral respiratory tract infections. For example, (Table 3) explains some of medicinal plants that possessed antiviral activity against different coronavirus types and their possible mechanism of actions. While (Tables 4 and 5) included various herbal medicines and different secondary metabolites which reported to have activity against causes of viral respiratory infection, specially corona virus. Among these plants, the Lamiaceae family herbs, which have a completely different chemistry, primarily monoterpenoids. According to [17] *Salvia apiana* (white sage), *S. officinalis* (garden sage), *Thymus vulgaris* (thyme), *Rosmarinus officinalis* (rosemary), and *Prunella vulgaris* (heal-all) are among the many other mints with antiviral and other beneficial effects relevant to viral respiratory infections. Generally, these are received well by patients based on taste [17]. Trees from two evergreen families, the Pinaceae and Cupressaceae, make up another family groups of antivirals. *Pinus spp.* (pine), *Abies spp.* (true firs), *Picea spp.* (spruces), *Thuja spp.* (cedars), and *Juniperus spp.* (junipers) resin and branch tips are all antiviral and inflammatory modulators with a respiratory tract affinity. All these groups are inflammation modulators, which is important for two reasons. The symptoms of viral respiratory infections are significantly due to immune responses to the infecting virus. More importantly, severe influenza is in part due to what has been dubbed "cytokine storm": a hyper-reaction of the immune system to certain influenza strains. Thus, inflammation-modulating herbs are significant to decrease symptoms and to prevent severe consequences, at least in the case of influenza infection. Additionally, these herbs considerably have immune-stimulating effects, running the risk of rising symptoms of viral respiratory infections or making cytokine storms worse [17].

In India, Balachandar and his colleagues reported a strategy to develop an efficient viral inactivation system by exploiting active compounds from naturally occurring medicinal plants and infusing them into nanofiber-based respiratory masks. They listed some of the Indian medicinal plants (Table 6) that could be used as potent antiviral agents [18]. Moreover, Thangadurai *et al.* reported that Siddha or Ayurvedha traditional medicine validated a polyherbal formulation Deva chooranam (DC) with proven preclinical safety and activity against HIV and may have possible activity for the prevention and management of 2019-nCoV infection. This herbal formula includes three medicinal herbs: *Cedrus deodara* (Devadaru), *Alpinia galanga* (Arathai) and *Cinnamomum tamala* (Lavanga pathiri) [19].

### Recent approaches for corona virus treatment

Recently, a study reported by Ren *et al* indicated that, among 96606 classical prescriptions, 574 prescriptions with the key words to treat “Warm diseases (Wenbing)”, “Pestilence (Wenyi or Yibing)” or “Epidemic diseases (Shiyi)” were obtained [7]. Meanwhile, 40 kinds of Chinese Medicines (CMs), 36 CMs-pairs, 6 triple-CMs-groups existed with high frequency among the 574 prescriptions. Also, the key targets of SARS-COV-2, namely 3CL hydrolase (Mpro) and angiotensin-converting enzyme 2 (ACE2), were used to dock the main constituents from the 40 kinds by the Ligand FitDock method. A total of 66 compounds with higher frequency were docked with the COVID-19 targets, which were distributed in 26 kinds of CMs, among which Gancao (*Glycyrrhizae Radix et rhizoma*), HuangQin (*Scutellariae radix*), Dahuang (*Rhei radix et rhizome*) and Chaihu (*Bupleuri radix*) contain more potential compounds. As well, the network pharmacology results showed that Chinese medicine pairs Gancao (*Glycyrrhizae radix et rhizoma*) and HuangQin (*Scutellariae radix*) could interact with the targets involving in immune and inflammation diseases [7].

Another study carried out by chen *et al*, stated that two main proteins, 3C-like protease (3CLpro) and angiotensin-converting enzyme 2 (ACE2), could be used as targets for *in silico* screening active constituents that stops the replication and proliferation of SARS-COV-2, benefit from rapid sequencing of SARS-COV-2 coupled with molecular modelling depending on the genomes of related viral proteins [20, 21]. Owis *et al*, reported that ten flavonoids that were isolated from *Salvadora persica* L. aqueous extract showed remarkable binding stability at the N3 binding site of main protease of the COVID-19 to different degrees when compared with the currently used darunavir, a COVID-19 main protease inhibitor. The isolated and identified flavonoids were similar in structure which gave the opportunity to deduce the relation between their structure and the affinity to the receptors of the N3 binding site. The results indicated that the basic flavonol as a nucleus itself possesses an activity, in addition, the presence of rutinose in position 3 in this nucleus and the lack of O-CH<sub>3</sub> group in ring B may be a reason to increase the binding stability [22]. According to Khattab *et al.*, cathepsins and furin, may be used for developing broad-spectrum anti-SARS CoV therapies which target multiple viral and non-viral proteins [23]. A recent study by Qamar and his colleagues analyzed the 3CLpro sequence of CoV-19, constructed its 3D homology model, and screened it against a medicinal plant library containing 32,297 potential anti-viral phytochemicals/ traditional Chinese medicinal compounds and selected the top nine hits that may inhibit SARS-CoV-2 3CLpro activity and hence virus replication [24]. These compounds were 5,7,3',4'-Tetrahydroxy-2'-(3,3-dimethylallyl) isoflavone, myricitrin, methyl rosmarinate, 3,5,7,3',4',5'-hexahydroxy flavanone-3-O-β-D-glucopyranoside, (2S)-eriodictyol 7-O-(6''-O-galloyl)-β-D-glucopyranoside, calceolarioside B, myricetin 3-O-β-D-glucopyranoside, licoleafol and amaranthin with docking scores -16.35, -15.64, -15.44, -14.42, -14.41, -14.36, -13.70, -13.63 and -12.67, respectively, compared to nelfinavir (-12.20), prulifloxacin (-11.32) and colistin (-11.73). The screened phytochemicals displayed higher docking scores, stronger binding energies,

and closer interactions with the conserved catalytic dyad residues (Cys-145 and His-41) than nelfinavir, prulifloxacin and colistin [24].

### Conclusion:

From the above reviewed studies, it is evident that different countries around the world have abundance of antiviral plants resources based on scientific findings. There are several medicinal plants traditionally used by the local people of many countries all over the world to treat coronavirus. However, there is a great deficiency to find enough studies considering the chemistry and pharmacological effects of these herbal plants. Therefore, carrying detailed ethnomedicinal studies is of great demand to discover novel active principles with promising activity against this fatal virus. Besides, very few herbs have been screened *in vitro* and *in vivo* against viruses including coronavirus, so, pharmaceutical industries and/or government agencies should support more research activities in this area in order to utilize these antiviral medicinal plants for a solution against the global fatal illness (COV-19) or any threaten viral infections.

### Conflicts of interest

The authors have no conflicts to report.

### Disclosure statement

The study had no ethical approval requirements.

**Table 1:**List of some Formulas used in Traditional Chinese Medicine for COVID-19

No.	Chinese Name	Plant Latin name	Part used
1	Gancao	<i>Glycyrrhiza uralensis</i> Fisch	Rhizome
		<i>Glycyrrhiza inflata</i> Batalin	
		<i>Glycyrrhiza glabra</i> L.	
2	Huangqin	<i>Scutellaria baicalensis</i> Georgi	Root
		<i>Rheum palmatum</i> L.	
3	Dahuang	<i>Rheum tanguticum</i> Maxim. ex Balf.	Rhizome
		<i>Rheum officinale</i> Baill.	
4	Baishao	<i>Paeonia lactiflora</i> Pall.	Root
5	Chenpi	<i>Citrus reticulata</i> Blanco	Fruit
6	Chaihu	<i>Bupleurum chinense</i> DC.	Root
		<i>Bupleurum scorzonerifolium</i> Willd	
7	Jiegeng	<i>Platycodon grandiflorus</i> (Jacq.) A.DC	Root
8	Cangzhu	<i>Atractylodes lancea</i> (Thunb.) DC.	Rhizome
		<i>Atractylodes chinensis</i> (DC.) Koidz	
9	Danggui	<i>Angelica sinensis</i> (Oliv.) Diels	Root
10	Shengdi	<i>Rehmannia glutinosa</i> (Gaertn.) DC	Root
11	Shigao	Gypsum	
12	Gegen	<i>Pueraria lobata</i> (Willd.) Ohwi	Root
13	Houpu	<i>Magnolia officinalis</i> Rehder & E.H.Wilson	Bark
		<i>Magnolia officinalis</i> var. <i>biloba</i> Rehder & E.H.Wilson	
14	Chuanxiong	<i>Ligusticum chuanxiong</i> Hort.	Root

15	Fangfeng	<i>Saposhnikovia divaricata</i> (Turcz.) Schischk.	Root
16	Sbexiang	<i>Moschus berezovskii</i> Flerov. <i>Moschus sifanicus</i> Przewalski <i>Moschus moschiferus</i> Linnaeus	Musk bag
17	Huanglian	<i>Coptis chinensis</i> Franch. <i>Coptis deltoidea</i> C.Y.Cheng et Hsiao <i>Coptis teeta</i> Wall.	Rhizome
18	Qianghuo	<i>Notopterygium incisum</i> K.C.Ting ex H.T.Chang <i>Notopterygium franchetii</i> H.Boissieu	Rhizome
19	Xuanshen	<i>Scrophularia ningpoensis</i> Hemsl.	Root
20	Baizhi	<i>Angelica dahurica</i> (Hoffm.) Benth. & Hook.f. ex Franch. & Sav.	Root
21	Renshen	<i>Panax ginseng</i> C.A.Mey.	Root
22	Xionghuang	Realgar	
23	fuling	<i>Poria cocos</i> (Schw.)Wolf	Scleroaum
24	Zhiqiao	<i>Citrus aurantium</i> L.	Fruit
25	Maidong	<i>Ophiopogon japonicus</i> (Thunb.) Ker Gawl.	Root
26	Jiangcan	<i>Beauveria assiana</i> (Bals.)Vuillant	Silkwormbod y
27	Lianqiao	<i>Forsythia suspensa</i> (Thunb.) Vahl	Fruit
28	Zhimu	<i>Anemarrhena asphodeloides</i> Bunge	Rhizome
29	Banxia	<i>Pinellia ternata</i> (Thunb.) Makino	Rhizome
30	Bohe	<i>Mentha haplocalyx</i> Briq.	Stem
31	Zhusha	Cinnabar	
32	Shengma	<i>Cimicifuga heracleifolia</i> Kom. <i>Cimicifuga dahurica</i> (Turcz.) Maxim. <i>Cimicifuga foetida</i> L.	Rhizome
33	Mahuang	<i>Ephedra sinica</i> Stapf <i>Ephedra intermedia</i> Schrenk & C.A.Mey. <i>Ephedra equisetina</i> Bunge	Stem
34	Zhizi	<i>Gardenia jasminoides</i> J. Ellis	Fruit
35	Chantui	<i>Cryptotympana pustulata</i> Fabricius	
36	Tianhuafen	<i>Trichosanthes kirilowii</i> Maxim. <i>Trichosanthes rosthornii</i> Harms	Root
37	Shengjiang	<i>Zingiber officinale</i> Roscoe	Rhizome
38	Xixin	<i>Asarum sieboldii</i> Miq. <i>Asarum heterotropoides</i> F.Schmidt	Rhizome
39	Huashi	Talcum	
40	Huoxiang	<i>Pogostemon amaranthoides</i> Benth.	Stem

**Table2:** Chinese herbal medicines recommendation for pediatric COVID-19

Stages	Name of herbal formula	Pattern Identification	Composition of herbal formula
Mild	Yin Qiao San	Seasonal epidemic	# <i>Lonicerae Flos, Forsythiae fructus, Platycodonis Radix, Menthae Herba, Lophatheri Herba, Schizonepetae spica, Glycine Semenpreparatum, Arctii Semen, Phragmitis Rhizoma</i>
	Xiang Su San	invading the exterior-defense	<i>Cyperi Rhizoma, Perillae folium, Citrericulatae Pericarpium, Glycyrrhizae Radix et Rhizoma, Bupleuri Radix, Cinnamomi ramulus, Saposhnikoviae Radix, Osterici seu notopterygii Radix et Rhizoma</i>
Moderate	Ma Xing Shi Gan Tang + San Ren Tang	Dampness-heat blocking the lung	# <i>Ephedrae Herba, Armeniacae Semen amarum, Glycyrrhizae Radix et Rhizoma, Gypsum fibrosum, Amomi Fructus rotundus, Coicis Semen, Pinelliae Rhizoma praeparatum, Magnoliae Cortex, Talcum, Stachyuri Medulla, Helwingiae Medulla, Lophatheri Herba</i>
	Buhuan Jin Zhengqi San	Dampness-heat in the spleen and stomach	# <i>Citri Reticulatae Pericarpium, Atractylodis Rhizoma, Magnoliae Cortex, Glycyrrhizae Radix et Rhizoma, Amomi tsao-ko Fructus, Pinelliae Rhizoma, Agastachis Herba</i>
Severe	Xuanbai Chengqi Tang + Ganlu Xiaodu Dan	Heat toxin blocking the lung	# <i>Gypsum fibrosum, Rhei Radix et Rhizoma, Armeniacae Semen amarum, Trichosanthis fructus, Talcum, Scutellariae Radix, Artemisiae scopariae Herba, Acori tatarinowii Rhizoma, Fritillariae cirrhosae Bulbus, Akebiae caulis, Agastachis Herba, Forsythiae fructus, Amomi fructus Rotundus, Menthae Herba, Belamcandae Rhizoma</i>
	Not available	Intense heat toxin with blockage of bowel Qi and dysphagia	<i>Rhei Radix et Rhizoma</i> (Enema using herbal decoction)
Recovered	Liu Junzi Tang + Yu Ping Feng San	Unclear residual heat	# <i>Ginseng Radix, Atractylodis macrocephalae Rhizoma, Poria sclerotium, Glycyrrhizae Radix et Rhizoma, Citri reticulatae Pericarpium, Pinelliae Rhizoma, Saposhnikoviae</i>

		Radix, <i>Astragali</i> Radix
Ma Xing Shi Gan Tang*	Heat toxin fettering the lung	<i>Ephedrae</i> Herba 4g, <i>Gypsum fibrosum</i> 20g, <i>Anemarrhenae</i> Rhizoma 9g, <i>Armeniacae Semen amarum</i> 10g, <i>Coicis Semen</i> 10g, <i>Phragmitis</i> Rhizoma 10g, <i>Platycodonis</i> Radix 6g, <i>Mori radice</i> s Cortex 10g, <i>Lonicerae</i> Flos 10g
Ma Xing Shi Gan Tang*	Epidemic toxin blocking the lung	<i>Ephedrae</i> Herba 4g, <i>Gypsum fibrosum</i> 20g, <i>Anemarrhenae</i> Rhizoma 9g, <i>Armeniacae Semen amarum</i> 10g, <i>Coicis Semen</i> 10g, <i>Trichosanthis fructus</i> 10g, <i>Rhei Radix et Rhizoma</i> 5g, <i>Mori radice</i> s Cortex 10g, <i>Lepidii seu descurainiae</i> Semen 6g, <i>Bubali cornu</i> 10g, <i>Pheretima</i> 10g, <i>Ginseng</i> Radix 6g
Yin Qiao San	Wind-heat invading the lung	<i>Lonicerae</i> Flos 15g, <i>Forsythiae fructus</i> 15g, <i>Schizonepetae spica</i> 10g, <i>Menthae</i> Herba 10g, <i>Arctii Semen</i> 10g, <i>Platycodonis</i> Radix 10g, <i>Scutellariae</i> Radix 10g, <i>Trichosanthis pericarpium</i> 15g, <i>Angelicae decursivae</i> Radix 15g, <i>Belamcandae</i> Rhizoma 10g, <i>Eriobotryae folium</i> 15g, <i>Artemisiae annuae</i> Herba 21g
Ma Xing Shi Gan Tang	Wind-heat blocking the lung	<i>Ephedrae</i> Herba 5g, <i>Armeniacae Semen amarum</i> 10g, <i>Gypsum fibrosum</i> 15g, <i>Scutellariae</i> Radix 10g, <i>Trichosanthis pericarpium</i> 15g, <i>Angelicae decursivae</i> Radix 15g, <i>Belamcandae</i> Rhizoma 10g, <i>Eriobotryae folium</i> 15g, <i>Pumex</i> 20g, <i>Lepidii seu descurainiae</i> Semen 10g, <i>Pheretima</i> 10g, <i>Artemisiae annuae</i> Herba 21g
Qianjin Weijing Tang + Shangjiao Xuanpi Tang	Dampness-heat fettering the lung	<i>Phragmitis</i> Rhizoma 15g, <i>Benincasae pericarpium</i> 15g, <i>Coicis semen</i> 15g, <i>Armeniacae Semen amarum</i> 10g, <i>Scutellariae</i> Radix 10g, <i>Trichosanthis pericarpium</i> 15g, <i>Angelicae decursivae</i> Radix 15g, <i>Belamcandae</i> Rhizoma 10g, <i>Eriobotryae folium</i> 15g, <i>Curcumae longae</i> Radix 15g, <i>Lepidii seu descurainiae</i> Semen 10g, <i>Artemisiae annuae</i> Herba 21g
San Ren Tang	Dampness-heat fettering the spleen	<i>Armeniacae Semen amarum</i> 10g, <i>Amomi fructus</i> Rotundus 5g, <i>Coicis semen</i> 15g, <i>Pinelliae</i> Rhizoma <i>praeparatum</i> 10g, <i>Magnoliae</i> Cortex 15g, <i>Talcum</i> 10g, <i>Stachyuri</i> Medulla <i>Helwingiae</i> Medulla 5g, <i>Agastachis</i> Herba 10g, <i>Poria sclerotium</i> 15g, <i>Arecae pericarpium</i> 15g, <i>Scutellariae</i> Radix 10g, <i>Artemisiae annuae</i> Herba 21g

Not reported

\* Name of the herbal formula is originally not reported, and the authors named them based on Dictionary of Traditional Chinese Medicine Formula.

# The compositions of the herbal formula is originally not reported, and the authors added them based on Dictionary of Traditional Chinese Medicine Formula



**Table 3:** Medicinal plants reported in the treatment of COVID-19 and their mechanism of action

Plant name	Responsive virus	Mechanism of action	References
<i>Rosa nutkana</i> C. Presl	Corona virus (CoV)	The extract was very active against an enteric corona virus	[25]
<i>Amelanchier alnifolia</i> (Nutt.) Nutt. ex M. Roem.	Corona virus (CoV)	The extract was very active against an enteric corona virus	[25]
<i>Houttuynia cordata</i> Thunb.	SARS-CoV	- It inhibited two key proteins of SARS-CoV, namely chymotrypsin-like protease (3CLpro) and RNA-dependent RNA polymerase (RdRp) - It increased CD4+ and CD8+ cell count in test animals suggesting its immunostimulatory effect	[26]
<i>Toona sinensis</i> (Juss.) M. Roem.	SARS-CoV	It inhibited SARS-CoV replication	[27]
<i>Rheum officinale</i> Baill., <i>Polygonum multiflorum</i> Thunb.	SARS-CoV	inhibited the interaction of SARS-CoV (S) protein and ACE2	[28]
<i>Cibotium barometz</i> (L.) J. Sm. and <i>Dioscorea batatas</i> Dence.	SARS-CoV	significant inhibition of SARS-CoV 3CLpro activity	[29]
Extracts of ( <i>Anthemis hyaline</i> DC., <i>Nigella sativa</i> L., and <i>Citrus</i>	CoV	They decreased the replication of virus. They increased IL-8 level. They significantly	[30]

<i>sinensis</i> (L.) Osbeck)		changed the expression of TRPA1, TRPC4, TRPM6, TRPM7, TRPM8 and TRPV4 genes.	
<i>Isatis indigotica</i> Fortune ex Lindl.	CoV	3CL protease inhibition	[31]
<i>Houttuynia cordata</i> Thunb.	CoV	3CL protease and viral polymerase inhibition.	[26]
Extracts of ( <i>Gentiana scabra</i> Bunge, <i>Dioscorea batatas</i> Dence., <i>Cassia tora</i> L., <i>Taxillus chinensis</i> (DC.) Danser, <i>Cibotium barometz</i> (L.) J.Sm.)	CoV	3CL protease inhibition.	[29]
<i>Cimicifuga rhizoma</i> , <i>Meliae cortex</i> , <i>Coptidis rhizoma</i> and <i>Phellodendron cortex</i>	mouse hepatitis virus A59 (MHV-A59)	They decreased the MHV production and the intracellular viral RNA and protein expression with EC <sub>50</sub> values ranging from 2.0 to 27.5 g/ml. These extracts also significantly decreased PEDV production and less dramatically decreased vesicular stomatitis virus (VSV) production <i>in vitro</i> .	[32]
<i>Sophorae radix</i> , <i>Acanthopanax cortex</i> , <i>Torilis fructus</i> and <i>Sanguisorbae radix</i>	MHV-A59	They reduced intracellular viral RNA levels with comparable reductions in viral proteins and MHV-A59 production. The extracts also reduced the replication of the John Howard Mueller strain of MHV, porcine epidemic diarrhoea virus and vesicular stomatitis virus <i>in vitro</i> .	[33]

**Table 4:** Medicinal plants used in traditional medicine to treat upper respiratory viral infections

No.	Plant name	Responsive virus	Mechanism of action	References
1	Polyphenols from <i>Punica granatum</i> L.	Influenza A virus	Viral replication suppression against influenza A virus	[34, 35]
2	Polyphenols of <i>Berries</i> extract	Influenza virus	Immunity modification and improvement of T cells function against influenza virus and common cold	[36-41]
3	Glycyrrhizin isolated from <i>Glycyrrhiza uralensis</i> Fisch, <i>Glycyrrhiza inflata</i> Batalin and <i>Glycyrrhiza glabra</i> L.	influenza virus A2 (H2N2), H5N1 virus	Stimulation of interferon-gamma production by T cell, immunomodulation, antiinflammation reduction of virus uptake by host cells against influenza virus A2 (H2N2), H5N1 virus and influenza A	[7, 42-44]
4	Maoto ( <i>Ehedra</i> herba, <i>Cinnamomi</i> cortex, <i>Armenicae</i> semen and <i>Glycyrrhizae</i> radix)	Influenza virus	They help virus-bound natural antibodies against seasonal influenza	[45, 46]
5	<i>Echinacea</i> spp.	Influenza, rhinovirus	inflammation modulators in cells infected with influenza, rhinovirus, and	[17]

			other respiratory viruses	
6	<i>Camellia sinensis</i> (L.) Kuntze	Influenza	Influenza Increase levels of T- lymphocytes	[26]
7	<i>Potentilla arguta</i> Pursh	Syncytial virus (RSV)	completely inhibited respiratory syncytial virus (RSV)	[25]
8	<i>Sambucus racemosa</i> L.	Syncytial virus (RSV)	completely inhibited respiratory syncytial virus (RSV)	[25]
9	<i>Ipomopsis aggregate</i> (Pursh) V.E. Grant	Parainfluenza	It demonstrated good activity against parainfluenza virus type 3.	[25]
10	<i>Lomatium dissectum</i> (Nutt.) Mathias & Constance	Rotavirus	completely inhibited the cytopathic effects of rotavirus	[25]
11	Berries extract	Influenza virus	Immunity modification and improvement of T cells function against influenza virus and common cold	[36-41]
12	<i>Clinacanthus siamensis</i> Bremek.	Influenza virus	Enhancement of anti-influenza virus IgG and IgA antibodies production against influenza virus	[47]
13	<i>Punica granatum</i> L.	Influenza A virus	Viral replication suppression against influenza A virus	[34, 35]
	<i>Psidium guajava</i> L.	Influenza A (H1N1)	virucidal inhibition	[48]

14			of viral hemagglutination against influenza A (H1N1)	
15	<i>Epimedium koreanum</i> Nakai	Influenza A subtypes (H1N1, H5N2, H7N3, H9N2)	Reduction in viral replication, enhancement secretion of type I interferon and pro-inflammatory cytokines, immunomodulation against influenza A subtypes (H1N1, H5N2, H7N3, H9N2)	[49]
16	<i>Scutellaria baicalensis</i> Georgi	Influenza A virus	Neuraminidase inhibitor, virus budding prevention against influenza A virus and common cold	[50]
17	<i>Paeonia lactiflora</i> Pall.	Influenza virus	Against influenza virus, it causes inhibition of viral RNA and viral protein synthesis, viral hemagglutination, viral binding to and penetration into host cells	[51]
18	<i>Allium sativum</i> L.	Parainfluenza, rhinovirus	-	[17, 52]
19	<i>Forsythia suspense</i> (Thunb.) Vahl	RSV	-	[53]
20	<i>Geranium sanguineum</i> L.	Influenza	-	[54]
21	<i>Lonicera japonica</i> Thunb.	Influenza	-	[55]
	<i>Pelargonium sidoides</i> DC.	Influenza	-	[56, 57]

22		Coronavirus, Coxsackie, parainfluenza Rhinovirus, RSV		
23	<i>Pinus</i> spp.	Influenza	-	[58, 59]
24	<i>Prunella vulgaris</i> L.	Influenza	-	[60]
25	<i>Rosmarinus officinalis</i> L.	RSV	-	[61]
26	<i>Salvia</i> spp.	Influenza	-	[62]
27	<i>Sambucus</i> spp.	Influenza (fruit) Rhinovirus (fruit) RSV (branch tip) Parainfluenza, adenovirus, Coxsackie virus (flower)	-	[63-65]
28	<i>Thuja</i> spp.	Influenza	-	[58]

**Table 5:**List of some secondary metabolites against viral respiratory tract infections

No.	Compound name	Responsive virus	Mechanism of action	References
1	<b>Concanavalin A</b> isolated from <i>Canavalia</i>	CoV	It caused inactivity of hemagglutinating	[66]

*ensiformis*(L.)DC.

encephalomyelitis  
CoV, possibly  
through binding with  
glycosylated  
membrane proteins  
that help virus in  
host cell recognition

2      **Lycorine** isolated from  
*Lycoris radiata*(L'Hér.) Herb.      SARS-CoV      It inhibited SARS-  
CoV with an EC<sub>50</sub>  
value of 5.7 nM      [31]

3      **Emodin** isolated from *Rheum*  
*officinale* Baill.and  
*Polygonum*  
*multiflorum*Thunb.      SARS-CoV      It inhibited the  
interaction of SARS-  
CoV (S) protein and  
ACE2 with IC<sub>50</sub>  
values ranging  
between 1 and 10  
µg/mL for extracts,  
and 200 µM for  
emodin      [28]

4      **Tetrandrine**      HCoV-OC43-  
infected MRC-5  
human lung cells      It significantly  
inhibited early stage  
viral-induced cell  
death in HCoV-  
OC43-infected  
MRC-5 human lung  
cells with IC<sub>50</sub>  
values 0.33, 1.01,  
and 0.83 µM,  
respectively      [67]

5      **Fangchinoline**      HCoV-OC43-  
infected MRC-5  
human lung cells      It significantly  
inhibited early stage  
viral-induced cell  
death in HCoV-  
OC43-infected  
MRC-5 human lung  
cells with IC<sub>50</sub>  
values 0.33, 1.01,  
and 0.83 µM,  
respectively      [67]

6      **Cepharanthine**      HCoV-OC43-  
infected MRC-5  
human lung cells      It significantly  
inhibited early stage  
viral-induced cell      [67]

			death in HCoV-OC43-infected MRC-5 human lung cells with IC50 values 0.33, 1.01, and 0.83 $\mu\text{M}$ , respectively	
7	<b>8<math>\beta</math>-Hydroxyabieta-9(11),13-dien-12-one</b>	SARS-CoV	It inhibited SARS-CoV 3CLpro activity with a SI > 667	[68]
8	<b>Savinin</b>	SARS-CoV	It inhibited SARS-CoV 3CLpro activity with a SI > 667	[68]
9	<b>Betulinic acid</b>	SARS-CoV	It was competitive inhibitors of SARS-CoV 3CLpro with Ki values of 8.2 and 9.1 $\mu\text{M}$	[68]
10	<b>Halituna</b> isolated from marine alga <i>Halimeda tuna</i>	Coronavirus A59	It exhibited antiviral effect against murine coronavirus A59	[69]
11	<b>Tanshinone I</b> isolated from <i>Salvia miltiorrhiza</i> Bunge	SARS-CoV 3	It inhibited SARS-CoV 3CLpro and papain-like protease (PLpro) infection and replication at 1–1000 $\mu\text{M}$	[70]
12	<b>Tannic acid</b> isolated from black tea	SARS-CoV	It exerted inhibitory effects on SARS-CoV 3CLpro with IC50 value of 3 $\mu\text{M}$ , respectively	[71]
13	<b>3-Isotheaflavin-3-gallate</b> isolated from black tea	SARS-CoV	It exerted inhibitory effects on SARS-CoV 3CLpro with IC50 value of 7 $\mu\text{M}$ , respectively	[71]



14	<b>Theaflavin-3,3'-digallate</b> isolated from black tea	SARS-CoV	It exerted inhibitory effects on SARS-CoV 3CLpro with IC <sub>50</sub> value of 9.5 μM,	[71]
15	<b>Theaflavin</b> isolated from black tea	bovine CoV, bovine rotavirus	It was able to neutralize bovine rotavirus and bovine corona virus infections	[72]
16	<b>Sinigrin</b> isolated from <i>Isatis indigotica</i> Fortune ex Lindl.	SARS-CoV	It displayed an inhibitory effect on SARS-CoV 3CLpro with IC <sub>50</sub> value of 217 μM.	[73]
17	<b>Indigo</b> isolated from <i>Isatis indigotica</i> Fortune ex Lindl	SARS-CoV	It displayed an inhibitory effect on SARS-CoV 3CLpro with IC <sub>50</sub> value of 752 μM.	[73]
18	<b>Aloe emodin</b> isolated from <i>Isatis indigotica</i> Fortune ex Lindl	SARS-CoV	It displayed an inhibitory effect on SARS-CoV 3CLpro with IC <sub>50</sub> value of 8.3 μM.	[73]
19	<b>Hesperetin</b> isolated from <i>Isatis indigotica</i> Fortune ex Lindl	SARS-CoV	It displayed an inhibitory effect on SARS-CoV 3CLpro with IC <sub>50</sub> value of 365 μM.	[73]
20	<b>β-sitosterol</b> isolated from <i>Isatis indigotica</i> Fortune ex Lindl	SARS-CoV	It displayed an inhibitory effect on SARS-CoV 3CLpro with IC <sub>50</sub> value of 1210 μM.	[73]
21	<b>Amentoflavone</b> isolated from <i>Torreya nucifera</i> (L.) Siebold & Zucc.	SARS-CoV	It exhibited inhibitory effects on SARS-CoV 3CLpro with IC <sub>50</sub> value of 8.3 μM.	[74]

22	<b>Apigenin</b> isolated from <i>Torreya nucifera</i> (L.) Siebold & Zucc	SARS-CoV	It exhibited inhibitory effects on SARS- CoV 3CLpro with, IC <sub>50</sub> value of 280.8 μM.	[74]
23	<b>Luteolin</b> isolated from <i>Torreya nucifera</i> (L.) Siebold & Zucc	SARS-CoV	It exhibited inhibitory effects on SARS- CoV 3CLpro with, IC <sub>50</sub> value of 20.2 μM.	[74]
24	<b>Quercetin</b> isolated from <i>Torreya nucifera</i> (L.) Siebold & Zucc	SARS-CoV	It exhibited inhibitory effects on SARS- CoV 3CLpro with, IC <sub>50</sub> value of 23.8 μM.	[74]
25	<b>Myricetin</b>	SARS-CoV	It exerted SARS-CoV 3CLpro inhibitory effect at 0.01–10 μM	[75]
26	<b>Scutellarein</b>	SARS-CoV	It exerted SARS-CoV 3CLpro inhibitory effect at 0.01–10 μM	[75]
27	<b>Brousochalcone B</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
28	<b>Brousochalcone A</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
29	<b>4-Hydroxyisolonchocarpin</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
30	<b>Papyriflavonol A</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro. It showed the highest inhibition among isolated compound from the same plant	[76]

			against PLpro with an IC <sub>50</sub> value 3.7 μM	
31	<b>3'-(3-methylbut-2-enyl)-3',4,7-trihydroxyflavane</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
32	<b>Kazinol A</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
33	<b>Kazinol B</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
34	<b>Brousoflavan A</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
35	<b>Kazinol F</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
36	<b>Kazinol J</b> isolated from <i>Broussonetia papyrifera</i> (L.) L'Hér. ex Vent.	SARS-CoV	It inhibited both SARS-CoV 3CLpro and PLpro	[76]
37	<b>Saikosaponin A</b>	CoV- 229E	It exhibited activity against human CoV- 229E, with EC <sub>50</sub> value of 8.6 μM.	[77]
38	<b>Saikosaponin B<sub>2</sub></b>	CoV- 229E	It exhibited activity against human CoV- 229E, with EC <sub>50</sub> value of 8.6, 1.7μM. It inhibited viral attachment and penetration stages.	[77]
39	<b>Saikosaponin C</b>	CoV- 229E	It exhibited activity against human CoV- 229E, with EC <sub>50</sub> value of 19.9 μM.	[77]

40	<b>Saikosaponin D</b>	CoV- 229E	It exhibited activity against human CoV- 229E, with EC <sub>50</sub> value of 13.2 μM.	[77]
41	<b>Ginsenoside Rb1</b> isolated from <i>Panax ginseng</i> C.A.Mey.	SARS-CoV	exhibited antiviral activity at 100 μM	[78]
42	<b>Actinomycin D</b> isolated from <i>Streptomyces parvulus</i> bacteria	CoV	inhibited CoV attachment and penetration stages at 5–25 μM with an EC <sub>50</sub> value of 0.02 μM	[77]
43	<b>Homoharringtonine</b>	Murine coronavirus	It was the most potent alkaloid among 727 compounds with an IC <sub>50</sub> of ~11 nM	[79]
44	<b>Tylophorine</b> isolated from <i>Tylophora indica</i> (Burm. f.) Merr.	CoV	It inhibited N and S protein activity as well as viral replication of enteropathogenic coronavirus transmissible gastroenteritis virus	[80]
45	<b>7-Methoxycryptopleurine</b> isolated from <i>Tylophora indica</i> (Burm. f.) Merr.	CoV	It inhibited N and S protein activity as well as viral replication of enteropathogenic coronavirus transmissible gastroenteritis virus	[80]
46	<b>Cepharanthine</b>	SARS-CoV	It inhibited SARS-CoV protease enzyme at 0.5–10 μg/mL	[81]
47	<b>Berbamine</b>	HCoV-NL63	It inhibited HCoV-NL63 with an IC <sub>50</sub> value 1.48 μM	[82]

48	<b>Lycorine</b>	HCoV-OC43	inhibited cell division, and inhibited RNA, DNA, and protein synthesis, respectively	[82]
49	<b>Emetine</b>	HCoV-OC43	inhibited cell division, and inhibited RNA, DNA, and protein synthesis, respectively	[82]
50	<b>Mycophenolate mofetil</b>	HCoV-OC43	exerted an immune suppressing effect on the CoV species	[82]
51	<b>Eckol</b> isolated from <i>Ecklonia cava</i>	Porcine epidemic diarrhea coronavirus	It blocked the binding of virus to porcine epidemic cells at 1– 200 $\mu$ M with IC50 values of 22.5, 18.6, 12.2, and 14.6 $\mu$ M, respectively	[83]
52	<b>7-phloroeckol</b> isolated from <i>Ecklonia cava</i>	Porcine epidemic diarrhea coronavirus	It blocked the binding of virus to porcine epidemic cells at 1– 200 $\mu$ M with IC50 values of 22.5, 18.6, 12.2, and 14.6 $\mu$ M, respectively	[83]
53	<b>Phlorofuofuroeckoln</b> isolated from <i>Ecklonia cava</i>	Porcine epidemic diarrhea coronavirus	It blocked the binding of virus to porcine epidemic cells at 1– 200 $\mu$ M with IC50 values of 22.5, 18.6, 12.2, and 14.6 $\mu$ M, respectively	[83]
54	<b>Dieckol</b> isolated from <i>Ecklonia cava</i>	Porcine epidemic diarrhea coronavirus	It blocked the binding of virus to	[83]

			porcine epidemic cells at 1–200 $\mu\text{M}$ with IC <sub>50</sub> values of 22.5, 18.6, 12.2, and 14.6 $\mu\text{M}$ , respectively	
55	<b>Procyanidin A2</b> isolated from <i>Cinnamomi cortex</i>	SARS-CoV	It inhibited SARS-CoV infection at 0–500 $\mu\text{M}$	[84]
56	<b>Procyanidin B1</b> isolated from <i>Cinnamomi cortex</i>	SARS-CoV	It inhibited SARS-CoV infection at 0–500 $\mu\text{M}$	[84]
57	<b>Cinnamtannin B1</b> isolated from <i>Cinnamomi cortex</i>	SARS-CoV	It inhibited SARS-CoV infection at 0–500 $\mu\text{M}$	[84]
58	<b>Tetra-O-galloyl-beta-D-glucose</b>	SARS-CoV	It blocked the host cell entry of SARS-CoV at 0–10 <sup>-3</sup> mol/L	[85]
59	<b>Luteolin</b>	SARS-CoV	It blocked the host cell entry of SARS-CoV at 0–10 <sup>-3</sup> mol/L	[85]
60	<b>Tetra-O-galloyl-beta-D-glucose</b>	SARS-CoV	It blocked the host cell entry of SARS-CoV at 0–10 <sup>-3</sup> mol/L	[85]
61	<b>Bavachinin</b> isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It inhibited papain-like protease of SARS-CoV	[86]
62	<b>Neobavaisoflavone</b> isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It inhibited papain-like protease of SARS-CoV	[86]
63	<b>Isobavachalcone</b> isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It inhibited papain-like protease of SARS-CoV	[86]
64	<b>4'-O-methylbavachalcone</b> isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It inhibited papain-like protease of SARS-CoV	[86]

65	<b>Psoralidin</b> isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It inhibited papain-like protease of SARS-CoV	[86]
66	<b>Corylifol</b> isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It inhibited papain-like protease of SARS-CoV	[86]
67	Psoralidin isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It exhibited a strong protease inhibitory effect on SARS-CoV with an IC <sub>50</sub> value 4.2 μM	[28]
68	Emodin isolated from <i>Psoralea corylifolia</i> L.	SARS-CoV	It inhibited interaction of SARSCoV (S) protein and ACE2 at 0–400 μM	[28]
69	<b>Juglanin</b>	SARS-CoV	It blocked the 3a channel of SARSCoV with an IC <sub>50</sub> value of 2.3 μM	[87]
70	<b>Tomentin A</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 μM	[88]
71	<b>Tomentin B</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 μM	[88]
72	<b>Tomentin C</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 μM	[88]
73	<b>Tomentin D</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 μM	[88]
74	<b>Tomentin E</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 μM	[88]
75	<b>3'-O-methyldiplacol</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 μM	[88]

76	<b>4'-O-methyldiplacol</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 $\mu$ M	[88]
77	<b>3'-O-methyldiplacone</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 $\mu$ M	[88]
78	<b>4'-O-methyldiplacone</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 $\mu$ M	[88]
79	<b>Mimulonediplacone</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 $\mu$ M	[88]
80	<b>6-geranyl-4',5,7-trihydroxy-3',5'- dimethoxyflavanone</b> isolated from <i>Paulownia tomentosa</i> Steud.	SARS-CoV	It inhibited PLpro of SARSCoV at 0–100 $\mu$ M	[88]
81	<b>(-)-Catechin gallate</b>	SARS-CoV	It inhibited nanoparticle-based RNA oligonucleotide of SARS-CoV at 0.001–1 $\mu$ g/mL	[89]
82	<b>(-)- Gallocatechin gallate</b>	SARS-CoV	It inhibited nanoparticle-based RNA oligonucleotide of SARS-CoV at 0.001–1 $\mu$ g/mL	[89]
83	<b>Quercetin</b> isolated from <i>Houttuynia cordata</i> Thunb.	murine CoV	It act against murine CoV at 15.63–500 $\mu$ g/mL	[90]
84	<b>Rutin</b> isolated from <i>Houttuynia cordata</i> Thunb.	murine CoV	It act against murine CoV at 15.63–500 $\mu$ g/mL	[90]
85	<b>Cinanserin</b> (1 and 2 dpi) isolated from <i>Houttuynia cordata</i> Thunb.	murine CoV	It act against murine CoV at 15.63–500 $\mu$ g/mL	[90]



86	<b>Sivestrol</b> isolated from <i>Aglaia foveolata</i> Pannell	HCoV-229E	It inhibited cap-dependent viral mRNA translation of HCoV-229E at 0.6–2 $\mu$ M with an IC <sub>50</sub> of 40 nM	[91]
87	<b>Ferruginol</b> isolated from <i>Sequoia sempervirens</i> (D. Don) Endl.	SARS-CoV	It significantly inhibited SARS-CoV replication at 0–80 $\mu$ M	[92]
88	<b>3<math>\beta</math>,12-diacetoxyabieta-6,8,11,13-tetraene</b> isolated from <i>Sequoia sempervirens</i> (D. Don) Endl.	SARS-CoV	It significantly inhibited SARS-CoV replication at 0–80 $\mu$ M	[92]
89	<b>Betulonic acid</b> isolated from <i>Sequoia sempervirens</i> (D. Don) Endl.	SARS-CoV	It significantly inhibited SARS-CoV replication at 0–80 $\mu$ M	[92]
90	<b>Betulinic acid</b> isolated from <i>Sequoia sempervirens</i> (D. Don) Endl.	SARS-CoV	It significantly inhibited SARS-CoV replication at 0–80 $\mu$ M	[92]
91	<b>Hinokinin</b> isolated from <i>Sequoia sempervirens</i> (D. Don) Endl.	SARS-CoV	It significantly inhibited SARS-CoV replication at 0–80 $\mu$ M	[92]
92	<b>Savinin</b> isolated from <i>Sequoia sempervirens</i> (D. Don) Endl.	SARS-CoV	It significantly inhibited SARS-CoV replication at 0–80 $\mu$ M	[92]
93	<b>Curcumin</b> isolated from <i>Sequoia sempervirens</i> (D. Don) Endl.	SARS-CoV	It significantly inhibited SARS-CoV replication at 0–80 $\mu$ M	[92]
94	<b>Ouabain</b>	Gastroenteritis coronavirus (TGEV)	It diminished both the viral titers and viral yields, and reduced the number of viral RNA copies at 0–3000 nM	[93]

95	<b>Tylophorine</b> isolated from <i>Tylophora indica</i> (Burm. f.) Merr.	CoV	It inhibited viral replication in CoV-infected swine testicular cells	[80]
96	<b>7-methoxycryptoleurine</b> isolated from <i>Tylophora indica</i> (Burm. f.) Merr.	CoV	It inhibited viral replication in CoV-infected swine testicular cells	[80]
97	<b>Tylophorine</b>	CoV	It targeted viral RNA replication and cellular JAK2 mediated dominant NF-κB activation in CoV at 0–1000 nM	[94]

**Table 6:**List of Indian medicinal plants and their active compounds as a best therapeutic tool to treat different viral diseases

Medicinal Plant	Active principle	Antiviral mechanism of action	Ref.
<i>Vitex trifolia</i> L.	Casticin	Immunomodulatory & Anti-inflammatory effect on lungs	[6]
<i>Punica granatum</i> L.	Punicalagin	Inhibited viral Glycoprotein & Anti-HSV-1	
<i>Euphorbia granulata</i> Forssk.	Gallic acid	HIV inhibitory	
<i>Allium sativum</i> L.	Allicin	Proteolytic and hemagglutinating activity and viral replication	
<i>Acacia nilotica</i> (L.) Delile	Quercetin	Inhibition HIV-PR	
<i>Andrographis paniculata</i> (Burm.f.) Nees	Andrographolide	Antiviral potential	
<i>Cynara scolymus</i> L.	Cynaratriol	ACE inhibitor	
<i>Sphaeranthus indicus</i> L.	Tartaric acid	Inhibition of Mouse corona virus Various compositions and Herpes virus -	

		Bronchodilation
<i>Strobilanthes cusia</i> (Nees) Kuntze	Lupeol	Inhibitory action towards HCoV-NL63
<i>Vitex negundo</i> L.	Sabinene	Inhibitory action against HIV
<i>Ocimum kilimandscharicum</i> Gürke	Camphor	Inhibitory action towards HIV-1
<i>Clitoria ternatea</i> L.	Delphinidin-3-O-glucoside	Antiviral properties
<i>Embelia ribes</i> Burm.f.	1,4- benzoquinone	Inhibition of ACE
<i>Hyoscyamus niger</i> L.	hyoscyamine	Viral Inhibition and Bronchodilator
<i>Eugenia jambolana</i> Lam.	Ellagic acid	Protease Inhibitor
<i>Gymnema sylvestre</i> (Retz.) R.Br. ex Sm.	Tartaric acid	Inhibition of viral DNA synthesis

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