

Current Medical and Drug Research

(Contents available at www.globalscitechocean.com)



Review article

Therapeutic potential of medicinal herbs in the management of COVID-19

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Article history

Received : November 25, 2021 Accepted : December 18, 2021

Keywords

Coronavirus Herbal drugs Mechanism of action Phytochemicals Symptoms Transmission

DOI: 10.53517/CMDR.2581-5008.522021218

ABSTRACT

Medicinal plants have been in constant use since ancient times and are proven to be effective from time to time and even today, herbs are in great demand due to their high therapeutic values. The present paper highlights the usage of medicinal herbs against COVID-19 (SARS-CoV-2) which has brought on a global outbreak of severe respiratory disease. The Indian device of holistic medicine regarded as "Ayurveda" is playing a key role in controlling COVID-19 and its associated symptoms. Nutraceuticals and natural medicines can act as complementary preventive remedies for COVID-19. The literature survey presented several plant secondary metabolites that confirmed significant antiviral activity against SARS-CoV-2 through inhibiting the main proteins used in their pathogenesis and replication. This evaluation specializes in interpreting the capability of various secondary metabolites from medicinal herbs as healing alternatives, both as inhibitors of healing goals of SARS-CoV-2 or as blockers of viral debris access through host molecular receptors. The use of medicinal plants containing specific phytochemicals can be seen in offering a more secure and long-lasting answer for the population with lesser side effects. This review suggests certain Indian traditional medicinal plants as possible therapeutic targets exclusively against SARS-CoV-2.

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INTRODUCTION

Covid-19 (coronavirus disease 2019) is a major concern for global public health, in December 2019, first reported a pneumonia case having a high potential to invade from human to human in Wuhan, China (Mpiana et al., 2020). Initially, some investigators promoted that the suspicion might be initiating for infection. On 7 January 2020, the Chinese Centre for Disease Control and Prevention identified the pathogen responsible for the infection and named it COVID-19. On 30 December 2019 and on 30 January 2020, W.H.O. issued alerts covid-19 as a Public Health Emergency for International Concern. On 11 February 2020. ICTV (International Committee of Taxonomy of Viruses) named the virus SARS-CoV-2 (Wang et al., 2021). In India, the first COVID-19 case was reported in Kerala on 27 January 2020. The cases of COVID-19 in India crossed 9.74 M after reporting the first case in Kerala (Jabaris and Ananthalakshmi, 2021). COVID-19 is a viral infection and are responsible for the mortality or morbidity of human being universally. The pandemic of the COVID-19 has challenged the healthcare system not only in India but all over the world including developed countries. Starting from 2019, COVID-19 caused massive economical loss and health crises across the world (Huang et al., 2020a).

There is no particular treatment available for the covid-19, but in different countries, people used medicinal plants for the prevention and management of COVID-19.

Plants or natural products used in the treatment and management of viral infection from ancient times and many plants are highly effective against the covid-19 infection. In the pandemic of COVID-19 situation, the use of herbal medicine is more e.g., ginger, tulsi, turmeric and decoction of different herbs. Different secondary metabolites like flavonoids, polyphenols, alkaloids, terpenoids, stilbenes, coumarins and lignin from the plant assert to be effective against the viral protein and prevent viral replication in the host cell. Currently, the known herbal drugs which show antiviral activity are used as a supplementary treatment for the coronavirus (Bergmann and Silverman, 2020).

GENOMIC STRUCTURE OF SARS-CoV-2

SARS-CoV-2 enters in the body through the mouth and nose, and enters into the lungs through the trachea and causes respiratory failure by decreasing the oxygen saturation level below 90%. The virus enters in the body and comes in contact with the mucous membrane further affecting the respiratory tract and causing breathing problems associated with difficulty in breathing, sputum, dry mouth, etc. (Vimalanathan and Hudson, 2014; Tahir UI Qamar et al., 2020). The coronavirus is still unknown for most scientists because of its mutation property but scientists are more focused on different strains of coronavirus and their management. So, the patients suffering from respiratory disorders they are more prone to covid-19 as compared to others (Hoever et al., 2005). Common coronavirus contains double strand RNA and it belongs to the family Coronaviridae. All around the world scientists have discovered six types of human infected coronavirus at present and the newly discovered strain of SARS-CoV-2 become the seventh that affect humans (Huang et al., 2020b) (Fig. 1).

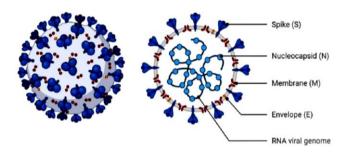


Fig. 1. Structure of SARS-CoV-2 showing spikes by which the virus directly attach to the host receptor and penetrate (Mittal et al., 2020).

Coronaviruses are spherical oval viruses containing the sRNA having the length of RNA is approximately 26-32kb. The diameter of the virus is about 50-200 nm. Covid-19 has a unique spike projection on its surface like club-shaped. The projections from the viral surface resemble a crown and they are made up of highly glycosylated proteins named spike(S) protein. Other structural components are membrane(M), envelop(E) and nucleocapsid(N) proteins. This RNA virus contains the largest genome (26.4-31.7kb) among all viruses known to date (Kumar et al., 2021).

For entry of viruses into the cell, glycosylated S proteins that cover the SARS-CoV-2 binds to the ACE2 receptor (angiotensin-converting enzyme). after binding the virus TMPRSS2, a type 2 TM serine protease in the host cell promote the entry of the virus into the cell by the breakdown of spike protein its help in the fusion of the virus to the host. S protein size is 180-200kDa and it consists of extracellular N terminus, a transmembrane domain, intracellular C terminal segment (Holmes, 2003). S1 recognizes the ACE-II receptors in the lungs, kidney and liver (V'kovski et al., 2021).

The transmission of the SARS-CoV-2 is very fast and also unique from the other SARS-CoV it may be due to the structural difference in proteins. covid-19 include four genera i.e., alpha, beta, gamma and delta. In which betacoronavirus comprising SARS (severe acute respiratory syndrome). The total length of the virus spike is 1273 amino acids. Coronaviruses changed themselves by mutations in the S gene. Envelop(E) protein responsible for assembling and release of virus from the host cell. membrane (M) protein helps to form and give shape to the virus envelope. Nucleocapsid (N) proteins help in cleavage of defense mechanism in host cell also pack genome of viral in capsid to protect it (Alipoor et al., 2021).

SYMPTOMS AND TRANSMISSION MECHANISM

Symptoms of COVID-19 appear 2 to 14 days after exposure to the virus. Symptoms are ranging from mild to severe illness. Older people or persons who have severe conditions like lungs disease, heart disease or diabetes seems to be at high risk of developing serious complication due to covid -19. Some people experience worsened symptoms of covid-19 like worse shortness of breath and pneumonia and the risk of severity is also increased with age. So, preventive measures should be considered to stop the spreading of infection (Fig. 2).

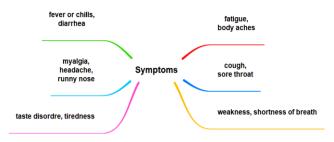


Fig. 2. Common symptoms associated with COVID-19 (Rodriguez-Morales et al., 2020).

Transmission of Covid-19 occurs mainly via close contact with an infected person due to the presence of virus in droplets and touching infected surfaces and then touching eyes, nose or mouth without cleaning hands (Keni et al., 2020). The process of transmission of virus involves many steps from attachment to exocytosis, each step exhibits a particular period of time to accelerate the process of transmission. Firstly, viruses enter in the body through the nose, mouth or eyes. Then spike proteins of virus attach to the host cell receptor (ACE2). After binding of the virus with the host cell, protease present in the host cell cleaves spike protein so the fusion of virus and host cell occurs. Thereafter, uncoating of virus genome into the host cell takes place. Viral RNA translated into pp1a and pp1ab polyproteins. These help in the replication and also the transcription of the viral genome. Replication of positive (+) sense RNA by RNA dependent RNA polymerase which gives negative (-) sense RNA. It replicated into + sense RNA and incorporated into the viral genome. Further transcribed RNA produces viral proteins i.e., spike protein, membrane, envelop, and nucleocapsid protein. host cell endoplasmic reticulum carries proteins towards Golgi apparatus for assembling viral genome. so, the new virus is formed or released by exocytosis and infect other cells. The whole process causes death of the host cell (Utku et al., 2020; Keni et al., 2020) (Fig. 3).

MEDICINAL HERBS USED IN MANAGEMENT OF SARS-COV-2 INFECTION

A number of approaches have been used for the treatment of COVID-19 infection but the morbidity and mortality were found to be very high. Several antibiotics and other synthetic compounds were found to be ineffective to control the menace of COVID-19. Considering the therapeutic potential of herbal drugs in the management of a number of diseases, herbal drugs were considered to be used in the treatment of COVID-19. More than 80% population worldwide relies on herbal drugs.

Cinchona officinalis

Cinchona officinalis is a pharmacologically active plant belonging to Rubiaceae family having antipyretic and antimalarial activity but nowadays plants are widely used for the treatment of coronavirus because of chloroquine and quinine (present all over the plant but the high amount present in bark) which increases the pH of the host cell lysosomes and thus interferes with the virus strategy to acidify the lysosome, which is a requirement for the creation of autophagosomes where a cell start to eat themselves. The plants are basically highly acidic in nature and are needed an acidic solvent to extract the chemical constituents (Gachelin et al., 2017).

Commiphora molmol

Commiphora molmol is a plant belonging to the *Burseraceae* family and having bitter in nature. The resin of the plant is prepared for pharmacological use. The plant is accepted for widespread use of different diseases like anti-fungal, anti-parasitic, anti-bacterial, anti-septic, to treat the wound and is now highly acceptable to treat coronavirus by inhibiting the DNA polymerase in viral strains (Tariq et al., 1986).

Ephedra sinica

Ephedra is a pharmaceutical formulation prepared from the plant *Ephedra sinica* belonging to the family *Ephedraceae*. The plant is known for its important chemical constituent's ephedrine, pseudoephedrine and feruloyl histamine. widely used for health-promoting effect, it stimulates the heart and brain cause death in some patients so banned by sports authorities for further use of ephedrine. But recent scientific data shows that catechin present in ephedra has an anti-viral activity to teat coronavirus by inhibiting SARS-CoV viral adsorption and penetration (González-Juárez et al., 2020).

Eucalyptus globulus

Eucalyptus globulus is a commonly available plant used for various tooth problems and herbal remedies to treat open wound infection belonging to the family *Myrtaceae*. Eucalyptol is the major chemical constituent having anti-viral activity used for the treatment of coronavirus by Innate cell-mediated immune response (Ait-Ouazzou et al., 2011).

Glycyrrhiza glabra

Glycyrrhiza glabra is known for its hypokalaemic, increased blood pressure and muscle weakness activity which is belonging to the family *Fabaceae*. Scientists claim that glycyrrhizin, the main constituent, has the potency to inhibit coronavirus by inhibiting SARS-CoV viral adsorption and penetration (Lim, 2015).

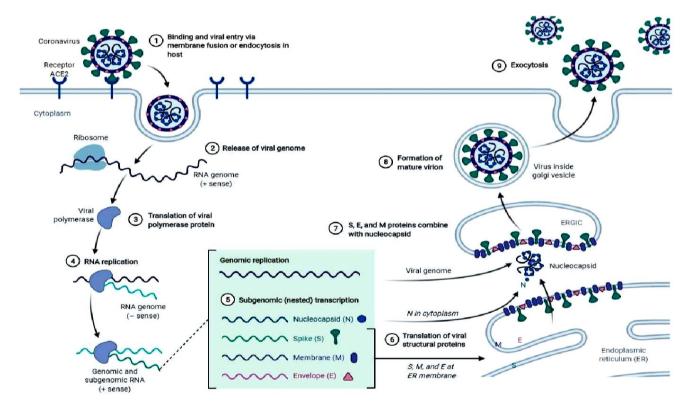


Fig. 3. Mechanism of transmission of SARS-CoV-2.

Hedera helix

Hedera helix is a flowering plant belonging to the family *Araliaceae*, widely used for cough and watering eye but recent studies show that the stigmasterol present in the *Hedera helix* is also used for the treatment of corona virus-highly replicated virus by maintaining the alveolar function by the expansion of bronchial tubes (Rai, 2013)

Justicia pectoralis

Justicia pectoralis, a herb that belongs to the family *Acanthaceae* is used as a muscle relaxant. It is used in the form of a tea. The herb is having potent activity against SARS-CoV-2 by acting as an immunomodulator via reducing the hyper-responsiveness of sensitized antigen (Nunes et al., 2018).

Magnolia officinalis

Magnolia officinalis is found in high altitude regions belonging to the family *Magnoliaceous*, the bark and leaves are used for pharmacological activity. The plant contains two highly potent chemical constituents magnolol and honokiol having activity against coronavirus by Inhibiting the protease in virus and mediating cell signalling pathway (Poivre and Duez, 2017).

Pimpinella anisum

Pimpinella anisum is commonly known as anise or aniseed belonging to the family *Apiaceae* which is widely used for its carminative and flatulence effect. But recent studies show that anise is having antiviral activity and is used for coronavirus treatment by interfering with virus adsorption to the host cell surface and directly inactivating viruses (Shojaii and Fard, 2012).

Pimpinella anisum

Sambucus nigra is a flowering shrub belonging to the family *Adoxaceae* is commonly used in dietary supplements and traditional medicine. The shrub is also used for its antiviral activity by inhibiting the replication and viral attachment of coronavirus (Młynarczyk et al., 2018).

Curcuma xanthorrhizza

Curcuma xanthorrhizza is commonly known as Javanese turmeric or java ginger belonging to the family *Zingiberaceae* and is used for dyspepsia and in some cases as a pesticide for mites but nowadays, the same shrub is used for the treatment of coronavirus with a selective affinity towards specific protein present on the cell wall of the virus and act as an immunosuppressant by Inhibiting proinflammatory cytokines (Oon et al., 2015).

Vernonia amygdalina

Vernonia amygdalina, a common shrub belonging to the family *Asteraceae*, is used for the treatment of malaria, intestinal parasites, diarrhoea, diabetes and stomach upset. The leaves of the shrub contain vernodalin, vernodalol and vernolide, all these compounds having high activity for a coronavirus membrane protein, they attach or bind with the protease protein and penetrate into the intracellularly and disrupts the membrane, at last, the rupturing of the cell wall of virus causes the death of the virus. This dead body of the virus is further engulfed through the phagocytosis process (Momoh et al., 2012).

Artemisia annua

Artemisia annua is commonly known as sweet wormwood belonging to the family Asteraceae which is used for the treatment of malaria. Artemisinin is a famous compound from the shrub used for anti-malarial activity as well as anti-viral activity and further used for the treatment of coronavirus through inhibiting the replication of coronavirus by inhibiting the enzyme CLPro (Septembre-Malaterre et al., 2020).

Tinospora cordifolia

Tinospora cordifolia is a herb belonging to the family *Menispermaceae*. Nowadays, the herb is used as an immune suppressant to treat coronavirus. The herb is recommended to use by consulting an expert to avoid any side effects. It acts by inhibiting the protease enzyme present in the coronavirus. The main chemical constituent tinosporide penetrates inside the cell wall of the virus and binds with the protease enzyme. Further, it inhibits virus replication (Saha and Ghosh, 2012).

Ocimum sanctum

Ocimum sanctum is a tremendous holy plant belonging to the family *Lamiaceae*, widely known as tulsi in India. In India, the plant is widely known for its holy phenomenon or the title of God. Leaves of the plant are highly active to treat cough, cold, sinusitis and headache. New advancement on tulsi shows that the plant is also having activity against coronavirus by inhibiting the viral replication by binding to the spike protein of the virus (Cohen, 2014).

Laurus nobilis

Laurus nobilis is an aromatic evergreen plant belonging to the family *Lauraceae*. The plant is famous for its massage and aromatherapy. The two chemicals 1,8-cineole and R-terpinyl are found highly efficacious and potent in the treatment of coronavirus (Caputo et al., 2017).

Aegle marmelos

Aegle marmelos is commonly known as golden apple and Bengal quince, and belongs to the family *Rutaceae*. The plant is recommended by FDA and CDC for dietary supplements and especially for weight loss. But new studies have shown that the drug is active against various targets of SARS-COV-2 such as spike protein, protease (Rahman and Parvin, 2014).

Anacyclus pyrethrum

Anacyclus pyrethrum is a flowering plant belonging to the family Asteraceae, widely popular as a traditional remedy. In new research, scientists found that plant is highly effective against the virus by preventing the binding of the viral protein to the host receptor. Among others, Pyrethrin is the most abundant constituent responsible for anti-viral activity (Jawhari et al., 2020).

Cocculus hirsutus

Cocculus hirsutus is a tropical invasive creeper commonly known as patalgarudi and belongs to the family *Menispermaceae*. Due to the presence of the phenolic compounds in the plant, it is widely used as an antimicrobial and in some instances anti-viral. Phenolic group attach with the sarcoplasm layer of the virus and then further causes rupturing of the wall and inhibit the viral replication (Logesh et al., 2020).

Curcuma longa

Curcuma longa is a flowering plant commonly known as curcumin belonging to the family *Zingiberaceae*. The root of the plant is ground and converted to powder form which is widely used in households. The powder of curcumin is used as a peripheral analgesic and as an anti-cancer agent. Scientists are more focussing on curcumin to treat coronavirus by preventing the replication of the virus and also inhibiting the protease enzyme (Kocaadam and Şanlier 2017). Selected medicinal plants having anti-SARS-CoV-2 activity are shown in Table 1.

|--|

Botanical	Common	Chemical constituents	Anti-SARS-	Mechanism of	Reference
name	name and		CoV-2	action	
<i>C</i> : 1	part used	· · · · · · · ·	constituent	·	
Cinchona	Cinchona	quinine, cinchonine,	chloroquine	increases the pH of	(Tahir Ul
officinalis	(bark)	cinchonidine, quinidine,	(synthetic	the host cell	Qamar et al.,
		cinchotannic acid	analogue),	lysosomes and thus	2020)
			quinine	interferes with the	
				virus strategy to	
				acidify the lysosome,	
				which is a	
				requirement for the	
				creation of	
				autophagosomes	
				where a cell start to	
				eat themselves.	
commiphora	Myrrh	curzerene, furanoeudesma-	-	inhibits DNA	(Tonkal and
molmol	(Gum resin)	1,3diene, β-elemene, 2-0-acetyl-		polymerase in viral	Morsy, 2008)
		8,12-epoxygermacra-1		strains	
		(10),4,7,11-tetraene			
Ephedra sinica	Mormon-	N-methyl ephedrine, herbacetin,	catechin	inhibits SARS-CoV	(Hoever et al.,
	tea or Brigha	cathine, feruloylhistamine,		viral adsorption and	2005)
	m tea	ephedrine, pseudoephedrine		penetration	
eucalyptus	Blue gum	eucalyptol, alpha-pinene,	eucalyptol	innate cell-mediated	(Li et al., 2020)
globulus	(leaves and	aromadendrene, limonene,		immune response	
	bark)	alpha-terpineol			
Glycyrrhiza	Liquorice	saponin, flavonoids,	glycyrrhizin	inhibits SARS-CoV	(Negri et al.,
glabra	(root)	isoflavonoids, stilbenoids,		viral adsorption and	2013)
		coumarins, glycyrrhizin		penetration	
Hedera helix	Ivy	rutin, quercetin, kaempferol,	stigmasterol	Maintain alveolar	(Liu et al.,
	(Leaves and	stigmasterol, alpha & beta		function by the	2006)
	berry)	amyrin		expansion of	
				bronchial tubes	
Justicia	Tilo	coumarin, umbelliferone,	-	reduces the hyper-	Venâncio et al.,
pectoralis	(leaves)	quercetin, kaempferol, swertisin		responsiveness of	2011
				sensitized antigen	
Magnolia	Mangolia	magnolol, honokiol,	-	inhibits the protease	(Weng et al.,
officinalis	(bark)	isomagnolol,		in virus and mediate	2019)
		trihydroxyhonokiol,		cell signalling	
		dihydroxyhonokiol,		pathway	
<u></u>		polymagnolol A & C			
Pimpinella	Anise	eugenol, <i>trans</i> -anethole,	-	interferes with virus	(Shojaii and
anisum	(seed)	methylchavicol, anisaldehyde,		adsorption to the host	Fard, 2012)
		estragole, coumarins, scopoletin,		cell surface and	
		umbelliferone, estrols, terpene		directly inactivate	
		hydrocarbons, polyenes,		viruses.	
C 1	Eldert	polyacetylenes		intitute no the sta	(A.J., 1.)
Sambucus	Elderberry	lectin, rutin, lupeol, β -sitosterol,	-	inhibits replication	(Ademola et
nigra	(berries)	tannic acid, choline chloride		and viral attachment	al., 2021)
0	T			of coronavirus	
Curcuma	Java turmeric	phelandren, camphor, tumerol,	xanthorrhizol	acts as	(Cheah et al.,
xanthorrhizza	(root)	sineol, borneol, xanthorrhizol,		immunosuppressant	2009)
Roxb		curcuminoids like curcumine &		by inhibiting	
		desmetoxicurcumine		proinflammatory	
Vernonia	Bitterleaf	ovalata phylota tanning	vomodalia	cytokines	(Ling 2000)
vernonta amygdalina		oxalate, phylate, tannins,	vernodalin,	bind to coronavirus	(Ling, 2006)
	(leaves)	saponins, flavonoid, cyanogenic	vernodalol,	protease and do	
		glycosides, alkaloids,	vernolide	penetration	
A	Correct t	anthraquinone, steroid, phenol		intribute of	(Ó / 1
Artemisia	Sweet	terpenes, polysaccharides,	artemisinin	inhibits the	(Ćavar et al.,
annua	wormwood,	artemisinin, sesquiterpene,		replication of	2012; Law et
	sweet Annie,	monoterpenoids (camphor, 1,8-		coronavirus by	al., 2020; Saha

	sagewort, mugwort (leaves)	cineole, camphene) artemether, artesunic acid, artelinic acid, artemisinic acid		inhibiting the enzyme CLPro (chymotrypsin-like protease)	and Ghosh 2012; Gaur et al., 2014)
Tinospora cordifolia	Guduchi, gurcha, garo, Amritavalli, Giloya, Madhupa, Vatsadaan (Stem, root)	berberine, magnoflorine, choline, palmatin, tembetarine, tinosporine, isocolumbin, aporphine alkaloids, jatrorrhizine, tetrahydropalmatine, tinosporon, columbin, jateorine, tinosporides, diterpenoids, steroids	tinosporides	immunomodulator, inhibits the main protease of SARS- CoV-2	(Upadhyay et al., 2010; Khan and Rathi, 2020; Sethi and Bhadra, 2020; Kumar et al., 2020)
Ocimum sanctum	Tulsi, holly basil (leaf and stem)	eugenol, euginal, urosolic acid, carvacrol, linalool, limatrol, methyl carvicol, rosmarinic acid, cirsimaritin, vicenin, orientin, dihydroeugenol	ursolic acid, tulsinol, dihydroeugenol, rosmarinic acid	inhibits viral replication by binding to the spike protein of virus.	(Mansour et al., 2018)
Laurus nobilis	bay leaf (leaves, buds)	1,8-cineole, R-terpinyl acetate, sabinene, R-pinene, α-pinene, α- elemene, R-terpineol, linalool, eugenol, R-eudesmol	-	inhibits the internalization process during virus penetration	(Nivetha et al., 2021)
Aegle marmelos	Sirphal, Bela, Bel, Adhararutha, Bilva, Stone apple (root, stem, bark)	ethyl cinnamamide, halfordinol, α -phellandrene, p-cymene, marmelosin, marmesin, imperatorin, marmin, alloimperatorin, methyl ether, xanthotoxol, scopoletin, scoparone, umbelliferone, psoralen, rutin, flavone, flavan- 3-ols, seselin	seselin	active against various targets of SARS- CoV-2 such as spike protein, protease	(Pandey et al., 2018; Ahmad et al., 2021)
Anacyclus pyrethrum	Spanish chamomile, Akarkara (root)	alkaloids, tannins, triterpenes, coumarins, sterols, tannic acid, lignin, pyrethrins, cinerin, pyrethric acid, pyrethrelone, cinerolone	pyrethrin	prevents binding of the viral protein to the host receptor.	(Logesh et al., 2020; Prasad and Aggarwal, 2011)
Cocculus hirustus	Broom creeper, Patalagarudi, Jamti ki bel (Stem, root)	trilobine, isotrilobine, coclaurine, β -sitosterol, ginnol, steroids, alkaloids, glycosides, flavonoids, tannins, haiderine, hirsutine, cohirsitine, cohirsitinine, cohirsine, cohirsinine, corsutine, coclaurine	-	increases the pH of the endosome	(Babaei et al., 2020)
Curcuma longa	Turmeric, haldi, manjal, Harihar (rhizome)	curcumin demethoxycurcumin, 5'-methoxycurcumin, dihydrocurcumin, curcumin, volatile oils, d- α -phellandrene, d-sabinene, cinol, borneol, zingiberene, α - and β - termerones, β -bisabolene, bisacurone, dehydrocurdione, procurcumadiol, bis-acumol, curcumenol, isoprocurcumenol, epiprocurcumenol, procurcumenol, zedoaronediol, curlone	cyclocurcumin, curcumin	prevents the replication of the virus and also inhibit the protease	(Forouzanfar et al., 2014; Badary et al., 2021)
Nigella sativa	black cumin, black caraway seeds, kalajira (seed)	arachidonic, eicosadienoic, linoleic, linolenic, oleic, almitoleic, palmitic, stearic, myristic acid,beta- sitosterol,cycloeucalenol, cycloartenol, sterol esters, sterol glucosides, thymoquinone, thymohydroquinone, dithymoquinone, thymol, carvacrol, α - and β -pinene, d- limonene, d-citronellol, p- cymene, nigellicimine, nigellicimine n-oxide	thymoquinone	inhibits the viral replication and internalization process	(Joshi et al., 2016; Shree et al., 2020)
Withania	Ashwagandha,	withaferin A, withanolides,	withanoside	inhibits protease	(Shree et al.,

somnifera	winter cherry (root)	glycowithanolides, beta- sitesterol, polyphenols, phytosterols, withanine, withananine, withananinine,		membrane fusion	2020)
		pseudo-withanine, somnine, somniferine, somniferinine			
Allium sativum	Garlic (Bulb, stem and leave)	ajoenes (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyldithiins(2-vinyl-(4H) -1,3- dithiin, 3-vinyl-(4H)-1,2- dithiin), sulfides (diallyl disulfide, diallyl trisulfide), alliin, N-acetylcysteine, S-allyl- cysteine, S-ally-mercapto cysteine	allicin	boosts the immunity against covid 19	(Rao and Gan, 2014)
Cinnamonum verum	Cinnamon (Leave, root, fruit)	cinnamaldehyde, cinnamate, cinnamic acid, numerous essential oils	-	-	(Mao et al., 2019)
Linum usitatissimum	Flaxseed or Linseed (Seed, bark)	L-rhamnose, L-galactose, L- fructose, and D-xylose, linolenic acid, linoleic acid, oleic acid, palmitic acid, stearic acid	-	-	(Haridas et al., 2021)
Zingiber officinale	Ginger (Root, rhizome)	Gingerols, 6-gingerol, 8- gingerol, 10-gingerol, quercetin, zingerone, gingerenone-A, 6- dehydrogingerdione, terpene, β - bisabolene, α -curcumene, zingiberene, α -farnesene, β - sesquiphellandrene, essential oils, polysaccharides, lipids, organic acids.	gingerols	inhibits the binding of SARS-CoV-2 spike protein	(Alzohairy, 2016; Baildya et al., 2021)
Azadirachata indica	Neem (Leave, bark)	azadirachtin, nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, quercetin, nimbin, nimbanene, 6- desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n- hexacosanol and amino acid, 7- desacetyl-7-benzoyl- azadiradione, 7-desacetyl-7- benzoylgedunin, 17- hydroxyazadiradione, nimbiol, quercetin, ß-sitosterol, polyphenolic flavonoids	-	inhibits the protease enzyme	(Farombi and Owoeye, 2011)
Vernonia amygdalina	Bitter leaf (leave)	vernodaline, vernomygdin, vernosides A1, A2, A3, vernodalol, epivernodol, uteolin, luteolin 7-O-glucosides, luteolin 7-O-glucuronide, flavonoids	veronicoside A	binding to human SARS-CoV2 major protease	(Cinosi et al., 2015; Rehman et al., 2016)
Mitragyna speciosa	Kratom (leave)	mitragynine, speciogynine, paynantheine, speciociliatine, monoterpene, 7- hydroxymitragynine, peciociliatine	mitragynine	-	(Sytar et al., 2021)
Eurycoma longifolia	Tongk at ali or pasak (Leave, bark, root)	uassinoids, β-carboline alkaloids, canthin-6-one alkaloids, triterpene-type tirucallane, squalene, urycolactone, eurycomalactone, laurycolactone, biphenyl neolignan, bioactive steroids, β- carboline, canthin-6-one	quassinoids, alkaloids, terpenoids	-	(Bhat and Alias, 2010)
Althaea officinalis	Marshmallow, Khatma, Khatmi (Whole plant)	isoquercitrin, kaempferol, pcoumaric acid, ferulic acid, p- hydroxybenzoic acid, salicylic acid, p-hydroxyphenylacetic acid, vanillic acid, coumarins, scopoletin, phytosterols, tannins, asparagine, amino acid,	-	shows anti- inflammatory activity in upper respiratory tract diseases	(Al-Snafi, 2013; Bharati et al., 2011)

		flavonoids			
Andrographis	Kalmegh,	14-deoxy-11-oxoandro-	andrographolide	inhibits viral	(Sa-
paniculata	Kalam Egha,	grapholide, 14 deoxy-11,12-		replication	Ngiamsuntorn
	Dark cloud,	didehydroandrographolide,			et al., 2021)
	Bhui-Neem	andrographosterol,			
	(Whole plant)	andrographone, andographan,			
		stigmasterol, sitosterol,			
		andrographin, andrographolide,			
		andrograpanin			

CONCLUSION

The use of natural medicinal drugs is a potential platform for answering diverse forms of COVID-19 virus management. Herbal medicinal drugs and their bioactive fractions are probably useful in the prevention of COVID-19 and as supportive measures. Many secondary metabolites with antiviral activities had been reported from ancient and medieval medicinal plants. Various researches had been done at some point in the sector to broaden antiviral drugs as a powerful agent in opposition to SARS-CoV-2 liable for COVID-19. The nice manner of stopping COVID-19 infections might be locating the compounds liable for changing or annoying any steps of the virus replication cycle. The natural mechanism of the virus is able to inhibit or change the configuration of structural proteins (spike glycoprotein), non-structural (3-chymotrypsin-like protease, papain-like proteins protease, helicase, and RDRP) and accent proteins coded with the aid of using the SARS-CoV-2 genome are had to be explored. Usually, herbal formulations might be a safe, secure, and reliable supply to discover new drugs liable for controlling the modern-day pandemic. Protease and RNA polymerase inhibitors are recognised to be potent in opposition to SARS and MERS and also are required to be explored. Different compounds (flavonoids, polyphenols, alkaloids, proanthocyanins, and terpenoids), which might be already recognised to have antiviral activities, want to be hastily screened for the remedy of SARS-CoV-2. In the context of now no longer having verified remedy for the treatment of COVID19, sufferers rely upon supportive care and symptomatic therapy. Hence, many natural extracts and herbal formulations/plants may also assist to deal with the signs and symptoms related to SARS-CoV-2 infection.

AUTHORS' CONTRIBUTIONS

R, RS, SV, MR designed the study, R and SV performed the research method, R analysed the data, AG, and MR manage the references, R and SV wrote the paper with input from all the authors. All authors discussed the result and contributed to the final manuscript.

CONFLICTS OF INTEREST

The author(s) declare(s) no conflicts of interest.

DECLARATION

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How to cite this article?

Rishabh, Verma S, Rohilla M, Garg A, Singh R (2021). Therapeutic potential of medicinal herbs in the management of COVID-19. Current Medical and Drug Research, 5 (2), Article ID 218.
