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MEDICINAL PLANTS AS IMMUNITY BOOSTERS AND ROLE IN COMBATING DEVASTATING COVID-19 PANDEMIC

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ABSTRACT

Throughout history, mankind has faced epidemics and pandemics from infectious diseases that have raised the question of survival of life on this planet. The current scenario of COVID-19 pandemic and its rapid spread has raised the great need to identify potential natural plant sources that can help in fighting this disease either by being virucidal or by boosting the immune system. The COVID-19 infection is caused by virulent Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which belongs to a large coronavirus family. These viruses are responsible for many recent infection outbreaks, SARS in 2003, MERS (Middle East Respiratory Syndrome) in 2012 and the recent most fatal COVID-19. The mortality rate related to COVID-19 is found to be high in the case of elderly patients, children or patients with preexisting health problems, and people with weak immune systems. Medicinal plants can be potential healing agents by boosting the immune system or by posing a virucidal effect that can help people fight against this infection and thereby reduce the mortality rate related to SARS-CoV-2 infections. In this review article, we attempted to assemble and discuss many traditional medicinal plants and their bioactive phytochemical components that can help in strengthening the human immune system and also play a key role in combating devastating COVID-19 along with many other microbial and viral diseases.

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INTRODUCTION

The COVID-19 pandemic has caused devastating effects on global populations due to the rapid outbreak. The immense spread of the novel coronavirus SARS-CoV-2 has affected almost all the countries (Felsenstein et al. 2020). Most severely affected are old age persons, children and patients with clinical history of respiratory disorders, diabetes, cancer, weak immune system and other diseases (Felsenstein et al. 2020). In view of the high mortality rate with this disease and unavailability of drugs, the whole world is battling hard to discover the effective therapeutic treatment for COVID-19 either by developing novel antiviral drugs or by repurposing and remodeling the available antiviral drugs. Currently, the medical sector is using some commercially available antiviral medicines remdesivir, including ritonavir ribavirin, lopinavir individually or in combination with interferon-alpha, chloroquine, hydroxychloroquine, and are found to show some potential efficacy against SARS-CoV-2 viral infections (Khan et al. 2020). In the current scenario of non-existence of any established medicines or vaccines for the treatment of COVID-19, there may be potential antiviral herbals extracts, formulations and immune booster herbal medicines that can be the potential remedy against viral infections (Srivastava et al. 2020).

MEDICINAL PLANTS THAT Can be an effective Immunity booster Against Sars-Cov-2.

Tinospora cordifolia

Giloy (*Tinospora cordifolia*) is a medicinal herb used as a vital part of many ayurvedic medications. It has bioactive phytochemicals including alkaloids, glycosides, steroids, lactones, diterpenoid, aliphatic compounds, phenolics, polysaccharides and flavonoids with immunomodulatory activities (Singh & Saxena, 2017). It has anti-diabetic (Sharma et al. 2015). antioxidant, Anti-inflammatory (Reddi & Tetali, 2019), antiperiodic, antispasmodic, anti-arthritic, anti-allergic (Sharma et al. 2012), antimicrobial, anti-osteoporotic (Saha & Ghosh, 2012), antitoxic, anti-stress, anticancer, anti-HIV, wound healing (Sharma et al., 2019), cardio tonic, carminative, bitter tonic, and blood purifier properties that improve digestion and boost the immune system. It has been reported that methanol extract of Giloy is found to have broad spectrum antimicrobial effectiveness against various strains of bacteria (Saha & Ghosh, 2012). Due to the broad beneficial activity of its alkaloid components including tinosporin, tetrahydropalmatine, choline, palmatine and magnoflorine, it plays an important role in improving our immune system to fight against infectious diseases. Generally, the juice of Giloy can be taken orally. The following herbal formulation is getting huge acceptance and found to be helpful for preventing and curing COVID-19. Giloy + Tulsi + Ginger + Kali mirch, grind them all together and use it as herbal tea or mix it with honey and consume it. It can control cough, fever and also support immunity against SARS-CoV-2 (Srivastava et al., 2020).

Withania somnifera

Ashwagandha (Withania somnifera) is an important and valuable herb of Ayurveda. Ashwagandha's main chemical constituents are withanolides including triterpenelactones withanolides, withaferin A & D, steroidal lactones, alkaloids, tropine and cuscohygrine (Ryu et al., 2010). It is seen that the pharmacological activity of Withania somnifera is mostly due to withaferin A and withanolide D. It has been reported that Whithanone reduces the electrostatic component of binding free energies of the ACE2-RBD complex and thus blocks the SARS-CoV-2 virus entry and its

N. sativa seed oil is found to suppress the viral burden injection of black seed oil (Salem & Hossain, 2000).

Cinchona officinalis

The Cinchong bark is rich in an alkaloid chemical called quinine which has antimalarial properties. Its other biological and clinical roles include anti-parasitic, anti-arrhythmic, antispasmodic, antiprotozoal, cardiotonic as it tones, balances, strengthens the heart and as a bitter digestive aid to stimulate digestive juices. Chloroquine, which is a synthetic form of quinine sourced from cinchona bark, has been in use for centuries for malaria treatment. Antiviral properties of chloroquine were explored against SARS-CoV-1 (Keyaerts et al., 2009), which has structural similarity to the novel SARS-CoV-2. Chloroquine plays a role in raising 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 approaches to eat themselves). Treatment using chloroquine may enhance the treatment success rate, shorten the hospital stav and lower the mortality associated with COVID-19 (Gao et al., 2020: Jiehe & HuxiZazhi, 2020).

Sambucus nigra

Elderberry (Sambucus nigra) is an intense purple berry and widely present in Europe and Western Asia. It is rich in polyphenolic compounds like Anthocyanins, Flavanols, Phenolic acid, terpenes, carbohydrates mainly glucose and fructose, citric acid, malic acid and lectins and other essential nutrients. These are mainly responsible for its medicinal values and thus, it has been in use for many years due to its enormous health benefits (Sidor & Michałowska, 2014). However, their nutrient values per 100 grams are as 870 mg Vitamin A, 34.10 mg Vitamin C, 391.33 mg Potassium, 28.06 mg Calcium, 1.86 mg Iron, and 217 mg Sodium (Vulic et al., 2008) with some amount of other minerals, folic acid, amino acids, dietary fibers are also present. This fruit is enriched with flavonoids having antioxidant and anti-inflammatory properties that help protect the healthy cells from the attack of harmful free radicals, thus having implications in skin care, boosting immune system which will support the body to fight against flu, cold and other respiratory infections (Torabiana et al., 2019). The unripe elderberries, its leaves, bark and seeds contain toxic and poisonous chemicals including cyanogenic glycosides which may lead to vomiting, nausea and diarrhoea if taken in raw state (Vulic et al., 2008)). However, appropriate cooking and consuming in the form of hot syrups helps in overcoming these side effects. The flowers and fruit of the elderberry can be consumed as jam, herbal tea, syrups, juices and is an effective remedy for colds and fever.

Azadirachta indica

Neem (Azadirachta indica) is found everywhere in India. Almost every part of neem such as leaves, root, fruit, bark, oil and seed are useful and it is widely applicable to cure or control diseases that arise from parasitic, bacterial, viral or any other causes. The primary phytochemicals in neem are limonoids and terpene (Bhowmik et al., 2010). It has anti-inflammatory, antimalarial, antibacterial, antifungal, immunomodulatory (Kumar et al., 2018), wound healing effect, hepatoprotective effect, antidiabetic activity, neuroprotective effects, anti-cancerous properties (Alzohairy, 2016) and neem tree effectively works in air purifying. The chemical constituents of neem nimbidin, sodium nimbidate, gallic acid, catechin, polysaccharides are responsible for their anti-inflammatory activity while nimbidin, gedunin, cyclic trisulfide for their antifungal activity and nimbidin, nimbolide. mahmoodin, margolone, margolonone, isomargolonone for antibacterial activity (Bhowmik et al., 2010). Bioactive compounds isolated from neem seed oil possess antipyretic, antifungal and antimalarial activities. Azadirachtin, extracted from neem oil, has potential insecticidal, antifeedant properties. It is also used efficiently to inhibit the development of malarial parasites. It also has antibacterial activity on some pathogenic bacterial strains. The extract of dry neem leaf is found to be very much effective for the treatment of skin problems including scabies, eczema and ringworm. Aqueous neem leaf extract is reported to have remarkable antiviral activity and immune boosting properties (Jimenez et al., 2010; Biswas et al.,2002). Previously, many people utilized the neem extract (from leaves) for bathing to prevent viral infection.

Syzygium aromaticum

Clove (Syzygium aromaticum) is one of the valuable spices used in food preservation and medicinal applications. It has an abundance of carbohydrates, protein, dietary fibers, minerals, vitamins (A, C, E and K), thiamin, riboflavin, folate, and niacin. It has rich sources of phenolic constituents like eugenol, thymol, eugenol acetate, and gallic acid and also βcaryophyllene and has potential for cosmetic, pharmaceutical, food and agricultural applications (Gulcin et al., 2012; Kurokawa et al., 1998). It has analgesic, antioxidant, antitumor, antiviral, antifungal, anti-inflammatory and antibacterial activity. Presence of eugenol compound displayed antibacterial activity. However, the clove originated from eugenie phytochemicals and is revealed to have good antiviral properties (Lee & Shibamoto, 2001). It has been reported that Eugeniin reveals antiviral properties by inhibiting the virus polymerase enzyme and later prohibiting the DNA replication and synthesis. However, the aroma chemicals isolated from clove were responsible for their antioxidant properties (Kurokawa et al., 1995).

Panax quinquefolius L.

Ginseng (Panax quinquefolius L.) is mostly found in America and Asia and is popular for its beneficial medicinal products. Ιt has antimicrobial (Ratan et al., 2020) antioxidative, antidiabetic, anti-inflammatory and anticancer properties. It helps in enhancing the immunity, combating various cardiovascular diseases. neurological disorders and diabetes (Im et al., 2016). The major chemical compositions and bioactive chemical constituents of ginseng are triterpenoid, protopanaxatriols, protopanaxadiols, and steroidal saponins which is also known as ginsenoid which are responsible for their potential activities against pathogens that cause respiratory infections in human body. Moreover, the antimicrobial potential of ginseng and their bioactive components were also reported to be effective against various bacteria, fungi and yeast (Ratan et al., 2020). It is also found to be effective against different human viral infections such as rhinovirus, human immunodeficiency virus, influenza virus, hepatitis virus, norovirus, enterovirus, human herpes virus and rotavirus (Igbal & Rhee, 2020; Tarrega et al., 2012). It was reported for its potential benefit in treatment of health problems by boosting the immune system to enhance cognitive function in the central nervous system and it contains ginsenosides that helps in boosting immunity (Lee et al., 2014; Tarrega et al., 2012). It has virucidal properties against respiratory syncytial virus which infects the lungs and breathing passages (Ma et al., 2019). Ginseng stem and leaf saponins are found to be active in increasing the specific-antibody responses for viral infections (Leung & Wong, 2013). The antiviral activity of ginseng is due to its efficacy to block viral attachment, membrane penetration and inhibiting virus replication inside the host cell.

Glycyrrhiza glabra

subsequent infectivity. It is also reported that the host cells namely ACE 2 in the human body got entrapped by SARS-CoV-2 with the help of its spike protein (RBD) Receptor-Binding Domain (Mi-Sun et al. 2008). In response to it, the natural bioactive phytochemicals present in Withania somnifera have effects on the binding of viruses. It is also claimed that ashwagandha could be the top choice among various medicinal herbs in fight this prospective against COVID-19 infectivity. Ashwagandha roots have hiqh antiviral activities. Combinations of phytochemicals in ashwagandha, giloy, tulsi are capable of fighting coronavirus as informed by traditional healers. It inhibits the protein binding with the host cell. On the other hand, natural phytochemicals have potential to combat COVID-19 and its pathogenicity. Basically, it blocks the host protein interactions. Indirectly the triple combination helps to boost immunity against the COVID-19 infection (Keivan et al., 2012).

Piper nigrum L.

Black Pepper (Piper nigrum L.) is also known as the king of spices due to the widespread use of its dried unripe fruit (Joshi et al. 2018). This medicinal plant has different phytochemicals including lignans, alkaloids, amides, terpenes, neolignans, having many beneficial biological activities as well as medicinal properties. Antiviral, anti-bacterial, anti-inflammatory, antipyretic, anti-oxidative. anti-thyroid, antitumor, immune and vaccine bioavailability enhancing properties are among the few in list of beneficial biological functions of peppercorn and its various secondary metabolites. The biological role of black pepper has been reviewed (Ahmed et al. 2012). Its key alkaloid components, namely piperine and piperamides, are vital phytochemicals with proven antiviral properties particularly against viruses responsible for infection in the respiratory system. They may help fight against COVID-19

which is also a respiratory tract infection (Mair et al., 2016).

Ocimum sanctum

Tulsi (Ocimum sanctum), also called holy basil, is a homegrown plant in India. It is popular for its medicinal properties and therapeutic potential as antibacterial, antidiabetic, anticarcinogenic, anti-viral, anti-inflammatory, cardio-protective, and immune system booster (Jamshidi & Cohen, 2017). Healing capability of Tulsi holds promising potential in the treatment of health ailments like bronchitis, asthma, rheumatism, skin diseases, pyrexia, microbial and parasitic infections, hepatic and gastric disorders. Tulsi is readily used for curing pain, diarrhoea, cough and fever, which are common symptoms related to COVID-19 (Goothy et al., 2020). Tulsi is considered as a potential medicine to treat pneumonia. Tulsi has antiviral properties against both DNA and RNA viruses (Chiang et al., 2005). It has been reported that Apigenin and Ursolic acid are the main active antivirals found in Tulsi extract. Some studies revealed that Tulsi has a significant role in boosting the immune system that assists the human body to fight against unwanted bacteria and viruses.

Nigella sativa

Black Cumin (*Nigella sativa*) has extensive therapeutic roles and is reported to cure different health disorders and ailments including jaundice, conjunctivitis, rheumatism, diabetes, anorexia, gastrointestinal problems, asthma, cough, bronchitis, fever, bronchitis, influenza etc. (Forouzanfar & Bazzaz, 2014). Thymoquinone is the main active phytochemical responsible for most of its therapeutic properties. Regarding its implication as antiviral properties, *Nigella sativa* oil and seeds have shown ucidal properties against various deadly viruses (Molla et al., 2019). ging to the family Fabaceae. It is effectively used antifungal, antibacterial, antiviral, antias inflammatory, anti-diabetic, skin toning as well as whitening, antioxidant anti-ulcer and antiagent (Damle, diuretic 2014). The main significant constituent is lycoyrrhizin present in liquorice roots which is sweet in taste. It is also well known as glycyrrhizic acid (C42H62O16), the roots of liquorice contains phytoestrogens namely isoflavaneglabridin, isoflaveneglabrene and chalcones. The root of this plant has medicinal values and has been utilized for curing various ailments such as asthma cough, colds and Chronic obstructive pulmonary disease etc. Glycyrrhizin, a triterpene saponin, which can be a potential phytochemical against SARS-COV-2 (Damle, 2014). It is a potent medicinal herb in the form of its traditional uses as it has many bioactive constituents and holds pharmacologic activities (Ming and Yin, 2013) and also has therapeutic effects of glycyrrhizic acid (Cinatl et al., 2003). Some studies have suggested that glycyrrhizin was found to be most effective in hindering the replication of viruses. Fiore et al. (2008) studied the antiviral effects of glycyrrhiza species. Some investigations proved the antiviral properties of glycyrrhizic acid derivatives against SARS-CoV virus (Hossain et al., 2014) and found the increased activity against SARS-CoV (Anagha et al., 2014; Fiore et al., 2008; Hoever et al., 2005).

Curcuma domestica

Turmeric (Curcuma domestica) is a perennial herb and belongs to the family Zingiberaceae. The main constituents of turmeric are carbohydrates, protein, fat, dietary fiber and minerals, essential oils and curcuminoids. The phytochemicals includes vital curcumin. demehoxycurcumin and bisdemethoxycurcumin (Chaurasia, 2001) and the major group of essential oils present are germacrone, turmerone, atlantone and zingiberene. The rhizome part of the turmeric plant is majorly

used for medicinal purposes as a medicine to treat many diseases with potential immune boosting and anti-inflammatory properties and also as flavor in many cuisines. It is also used for curing various severe diseases like hematuria. hemorrhage, flatulence, jaundice, menstrual difficulties and colic or treatment of many skin diseases in the form of ointment as it has wound healing properties. Turmeric is being used in larger quantities as preventive and therapeutic measures in corona virus infected countries. Turmeric helps in the natural cleansing of the respiratory tract, fights against infection and its anti-inflammatory quality make relief in cold and flu. Curcumin is helpful in addressing low immunity issues as it helps in enhancing the immunity system. Curcumin relieves congestion, inhibits inflammation and pain thus improving the breathing process (Benzie &Wachtel-Galor, 2011). The main upper respiratory tract problems include congestion, cough, bronchial asthma, cold and shortness of breathing and thus affecting the respiratory system. Due to inflammation of the airways, the process of breathing becomes difficult. Turmeric is most commonly a rhizome which is used daily in food and sometimes as a home remedy or drugs against cough and cold, and throat infection. It has antiseptic properties with substantial antibacterial, antifungal and antiviral properties. Curcumin antiviral properties are due to its inhibitory role in viral RNA replication which leads to reduction in the viral load. It has exceptional anti-inflammatory properties and is also reported to strengthen immunity (Jinu, 2019).

Zingiber officinalis

Ginger (*Zingiber officinalis*) is a vital medicinal plant belonging to the family Zingiberaceae. It contains many bioactive chemical constituents which includes zingerone, gingerols and volatile oils responsible for its characteristic flavor and fragrance (Mao et al., 2019). These chemical constituents have antimicrobial, antiviral and antifungal activities. The antioxidant compounds present in the ginger roots have potential antiinflammatory and immune-boosting properties, fight against various toxins and infections to defend against harmful effects of bacteria, viruses and other diseases. Ginger is a powerful immune booster plant with extraordinary antiviral properties (Pradhan et al., 2013). It has been reported that the fresh ginger inhibits syncytial human respiratory virus and contributes in reducing the viral infection. Hence, it shows antiviral effectiveness against respiratory syncytial virus as reported.

nutrients, genetically engineered foods and processed cereals, beverages and soups helps in enhancing immunity (Kalra, 2003).

CONCLUSION

Immune systems in the human body hold a vital role to fight against unnatural and morbid environments, various pathogens and microbes such as virus, bacteria, fungi that cause various diseases. Due to the number of side effects of costly allopathic medicines used to boost our immune system there is a need to find alternate sources. Ayurvedic products made from medi-





Vitamins, minerals supplements, nutraceuticals supplements and probiotics along with medicinal plants can be used to enhance the immune system to defend against viral COVID-19 pandemic. Many plant based sources of vitamins are mushrooms, carrots, broccoli, almonds, citrus, guava, amla, avocados etc. play vital role of Vitamins (A, C, E and D) in combating COVID-Zinc, Copper 19. and Magnesium shows immunomodulatory responses against viral infestations (Kanika Khanna, et al., 2020). Various nutraceutical products have been isolated from herbal products, dietary supplements, isolated

cinal plants hold the potential to boost the immune system. Currently COVID-19 pandemic situation reveals that people with strong immunity have a higher recovery rate. Medicinal plants have low cost, low toxicity with the potential to enhance immunity to fight against COVID-19 and other infectious diseases and play an important role to maintain fitness.

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None.

Table 1. Vital medicinal plants used as immunity booster against COVID-19 VirusSource of table: Upreti et al., 2020

S1	Name of	Plant Part	Type of Preparations	Medicinal User
SL.	Name of Medicinal Plants	Fiant Fart	Type of Freparations	Medicinal Oses
1	Medicinal Plants	Used	Chlore from Entroyt Natural	Antipies Instigity (CARC
1	Ашит сера	Bulb	Chloroform Extract, Natural	Antiviral activity (SARS,
0		D (D)	Dut 1	HINI, cold and flu)
2	Allium sativum	Roots, Bulb	Ethanol or	Antiviral activity (SARS,
			Aqueous Extract, Natural	H1N1, cold and flu)
3	Artemisia annua	Whole plant	Extract Ethanol,	Antiviral activity
		-	_	(SARS-CoV)
4	Curcuma longa	Roots	Extract Aqueous or	Antiviral activity
			Ethanol	
5	Echinacea	Flowers,	Essential oil, Syrup, Extract,	Antiviral activity (SARS),
	purpurea	Roots, Herb	Sap	Immuno-regulatory effect
6	Glycyrrhiza glabra	Dried roots and	Powder	Antiviral, antimicrobial,
		Rhizomes		Antioxidant, antitumor
				Activity
7	Isatis indigotica	Roots	Extract	Antiviral activity
				(SARS)
8	Lycoris radiate	Stem cortex	Extract Ethanol	Antiviral activity
				(SARS-CoV)
9	Pyrrosia lingua	Leaf	Extract Chloroform	Antiviral activity
				(SARS-CoV)
10	Rhaponticum	Roots, Leaf	Essential oil, Extract	Antiviral, antimicrobial,
	carthamoides		Acetone, ethyl acetate	Antioxidant and immune-
			gr methanol	regulatory activity
11	Rhodiola rosea	Roots	Extract Aqueous	Immuno-regulatory,
				Antiviral, antioxidant.
12	Taraxacum	Whole herb	Extract Aqueous	Antiviral activity
	offcinale			(IFA—H1N1)
13	Ocimum	Whole herb	Extract, Natural	Antiviral, immune-
	basilicum			modulatory activity
14	Piper nigrum	Fruit	Natural, Extract	Antiviral, immune-
				modulatory activity
15	Citrus limon	Fruit	Natural, Extract	Reinforce body defenses
			-	and prevent numerous
				Illnesses, Antiviral,

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