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TRADITIONAL MEDICINAL PLANTS AS PROMISING SOURCE OF IMMUNOMODULATOR AGAINST COVID-19

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ABSTRACT

Outbreak of novel corona virus (Covid-19) or Severe Acute Respiratory Syndrome corona virus 2 (SARS CoV-2) was noticed in China at the end of 2019 and has now become one of the major global health threat. Although, Covid-19 virus imposes detrimental effects to all groups of persons irrespective of their age, sex, race and body physic. Immuno-compromised people are reported to be severely affected in comparison to immunocompetent persons, suggesting immunity as a major player against SARS CoV-2. Despite of great efforts and intensive researches carried all over the world, so far there are no clinically approved vaccines or specific therapeutic drugs available for Covid-19. In this regard, different traditional medicinal plants, which are vast reservoir of bioactive compounds with broad therapeutic and immunomodulatory properties, have been emerged as boon to combat with Covid-19. Along with pharmacological properties and easily availability, safety paradigm of ethnomedicinal plants makes them highly preferable immediate remedy to enhance immunity and compete with novel corona virus. Use of traditional Indian spices has been also realized as effective and safer strategy in order to boost immunity and deal with highly terrible current Covid-19 situation. Hence, there is need to boost the efficacy of the traditionally used plant based immunomodulators against Covid-19 pandemic incorporating modern biotechnological and pharmacological tools so as to enhance bioavailability and practical applicability. The present article deals with general feature of SARS CoV-2 along with recent reports on efficacy of traditional medicinal plants as well as Indian spices as an effective immunomodulator for Covid-19.

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1 Introduction

Covid-19 or novel corona virus infection which was first reported in the beginning of December, 2019 from an emerging business hub of Wuhan city of Hubei province of China (Lin et al., 2020) has currently become a major global health threat. Novel corona virus is spreading rapidly all over the world and infects people of all ages irrespective of their age, sex and community. World Health Organization (WHO) has declared Covid-19 as global pandemic which leads to create highly alarming and challenging situation to the medical practitioners, politicians and as well as scientists all over the world (Dhama et al., 2020; Malik et al., 2020). Despite of highly concerned research towards prevention measure of Covid-19, so far no effective vaccine or drug has been discovered in modern allopathic system, though efforts are being made continuously in this direction (Rodriguez-Morales et al., 2020; Rabaan et al., 2020a; Yattoo et al., 2020). It has been experienced that immunity of an individual plays a vital role to fight against SARS corona virus-2 through declining its pathogenic potency inside host (Florindo et al., 2020). Therefore, until the discovery of promising therapeutic treatment and vaccine for the virus, people are looking towards herbal formulations in order to enhance the immunity of their body system so that they can survive under this critical health emergency situation. Traditional medicinal plants or ethnomedicines have miraculous treasure to serve as immunity booster due to the presence of numerous bioactive compounds such as terpenes, tannins, flavonoids, alkaloids, saponins, phenols, glycosides and thiosulfates (Dhama et al., 2015; Dhama et al., 2018; Tiwari et al., 2018; Mahapatra et al., 2019). Besides, several phytochemicals such as silvestrol, lycorine, scutellarein, myricetin, quercetin, caffeic acid and tryptanthrin are reported to have promising antiviral potency (Mani et al., 2020). Further, Ginkgetin and tetrahydroxy flavones, biflavonoid of *Ginkgo biloba*, indole alkaloid from *Uncaria rhynchophylla*, thalimonine from *Thalictrum simplex*, polyphenolic constituent of *Geranium sanguineum* and lignans such as rhinacanthin E and F from *Rhinacanthus nasutus* along with several other phytoconstituents such as betulinic acid, agastanol, calanolide, glycyrrhizin, ursolic acid and punicalagin are also reported to have diverse array of efficacious antiviral potency (Dhama et al., 2018). Under present challenging situation of novel corona virus, different traditionally used medicinal plants have been recognized as potential candidates for developing effective and secure remedies against the devastating pandemic, thereby, inspiring scientists in formulation of effective immunity booster as an immediate preventive tool against SARS CoV-2 virus. In China nearly 60,000 confirmed corona cases are treated by traditional medicinal system (Ren et al., 2020). Chinese herbal medicines due to their therapeutic potency and practical applicability against Covid-19 have enforced Chinese health department to implement an program regarding integration of Chinese herbal medicine and western

medicine in order to boost drug efficacy against Covid-19 (Li et al., 2020). Several Chinese traditional medicinal formulations *i.e.* Jinhua Qinggan capsules and Qingfei Paidu decoction are frequently prescribed to Covid patients having effective therapeutic potency and recovery rate (Zhang et al., 2020). Another Chinese medicine *i.e.* Yupingfeng San comprising three herbs *Attractylodes*, *Astragalus* and *Fangfeng* maintained lung immunity and proved to be as effective drug against novel corona virus that mainly target lungs (Xu & Zhang, 2020). Similarly, Indian government ministry of Ayurveda, yoga and naturopathy, Unani, Sidhha and Homeopathy (AYUSH) also recommend Ayurveda as well as homeopathy and Unani as better approach to manage Covid-19 cases. Hence considering the herbal formulations as new hope in the current alarming situation of novel corona virus, the present article explores some traditional medicinal plant as an effective weapon against corona.

2 Novel corona virus: general structure and disease symptoms

Corona virus (CoVs) is small size virus of 65-125 nm diameters having single stranded RNA as their genetic material. CoV genome is reported to be the largest genome among known RNA viruses ranging between 26-32kb (Chen et al., 2020a). Virion is generally enveloped by phospholipid bilayer having genomic RNA and nucleocapsid protein (N) inside it. Different structural proteins including membrane protein (M), envelope protein (E) and spike glycoprotein (S) are also found embedded in the envelope. These proteins have different functions such as Nucleocapsid protein (N) involved in packaging of viral genome and helps in pathogenicity of virus through inhibiting interferon function (IFN), Membrane protein (M) responsible for shaping of virion, envelope protein (E) responsible for virion assembly and release while Envelope glycoprotein (S) is the key protein responsible for recognizing host cell receptor (Alanagreh et al., 2020). Corona is derived from the latin word *Coronam* means crown, which describes the presence of spike glycoproteins on the envelope of members of corona viruses giving viruses a crown like appearance (Cascella et al., 2020). CoVs belongs to the largest family of order nidovirales *i.e.* coronaviridae and sub family orthocoronaviridae. Subfamily orthoviridae basically comprised of four genera including alpha corona virus (α - CoVs), beta corona virus (β - CoVs), gamma corona virus (γ - CoVs) and delta coronavirus (δ - CoVs) among which α - CoVs and β - CoVs is associated with mammal such as bat while γ - CoVs and δ - CoVs is associated with birds and swine gene pool (Banerjee et al., 2019; Dhama et al., 2020). There are two recent outbreaks of viral pneumonia epidemics associated with β -CoVs *i.e.* severe acute respiratory syndrome (SARS CoV) and Middle East respiratory syndrome (MERS CoV) reported in year 2002 from China and in year 2012 from Saudi Arab respectively. Later on through genome sequencing it is confirmed that virus associated with Covid -19 named as novel corona virus (nCoV),

severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and 2019-novel coronavirus (2019-nCoV) also belongs to β -CoVs group (Wu et al., 2020). SARS and MERS both are originated from bats and have an intermediate host's civet and camel respectively as a human infecting intermediate. SARS CoV-2 show distinct characteristics from earlier reported SARS CoV (around 79% similarities) and MERS CoV virus (around 50% similarity) in phylogenetic analysis (Rabaan et al., 2020b). SARS CoV-2 virus shows 96.2% genetic similarity with the bat corona virus supporting its origin from bat and its transmission to human through intermediate animal hosts (Guo et al., 2020). Continuous mutation in genome of virus will also impose major challenge to researchers to discover its specific treatment. This novel corona virus has challenged the economy, medical facilities and societal health of the nations. Due to pandemic situations, affected counties are implementing lockdown to control spreading of disease but this lockdown have also negative influence on economy of nation due to dropped industrial production. Further, restrictions in traveling caused loss of millions of dollar to airlines and tourism sectors. Some countries are also facing shortage of some basic required items like mask, sanitizer and medicines due to ban on transportation. Corona virus also causes big social threat and affects mental health of persons as social gathering in form of scientific conferences, marriage parties, business meetings and sports events are suggested to avoid. Hence, Covid-19 negatively influences not only the health and economy of nation but also have negative effect on all sectors of life. This deadly disease become to be a major challenge for researchers and scientists to discover its prevention measures as the virus is fast replicating inside the host cell and have also high rate of mutagenesis and structure changing properties (Helmy et al., 2020). In addition virus has also potential to survive under wide range of environmental conditions which create major barrier in investigation of disease and therapeutic treatments (Vellingiri et al., 2020).

Covid-19 virus attaches itself to the host receptor protein i.e. angiotensin converting enzyme (ACE 2) of bronchial epithelial cells through its glycoprotein spikes which is the crucial step in pathogenesis of virus. After entering inside the host, virus replicates and leads to produce symptoms. SARS CoV-2 is having 10-20 times higher binding efficiency with ACE 2 in comparison to SARS CoV leading to enhance its infectious potential (Jin et al., 2020). Huang et al. (2020) reported that critically ill patients with SARS CoV-2 virus have enhanced concentration of cytokine and chemokines in plasma, known as cytokine storm which will leads to disease severity, multi organ failure as well as mortality. The clinical feature of Covid-19 is varied with patients ranging from asymptomatic in immunocompetent person to severe respiratory disorders and multi organ dysfunction in immunocompromised persons. The common clinical feature of Covid-19 includes fever, sore throat, coughing, fatigue and headache which remain for

several weeks (Singhal, 2020). However, in poor immunity people virus can cause severe respiratory problems such as pneumonia and bronchitis and even lead to death. People of all age groups are prone towards the Covid-19 virus although lower age group and overage people are more susceptible. Although enhanced immunity may not prevent the attack of virus, however it controls the severity of virus and also helps in fast recovery. Infection is transmitted either through inhalation of coughing and sneezing droplet from infected persons or through touching contaminated surface and then touching the nose, mouth and eyes. Subsequently, stools and contaminated water is also reported to be an important transmission source for virus.

3 Phytomedicines: as a promising warrior against Covid-19

Herbal medicines due to its miraculous antiviral potency, has been used since ancient time to treat viral diseases. Although role of modern allopathic medicines in human health management cannot be neglected but their negative consequences on health can also not be ignored. Thus, due to easy accessibility, economical benefits, less chances of toxicity, traditional medicinal system or phytomedicines are highly preferred to synthetic drugs. In allopathic systems there is always need to search for a new drug as the virus easily develop resistance against the single compound, however, in case of herbal formulations, which is comprised of several phytoconstituents virus have less chance to develop resistance and have also tremendous potency to inhibit different growth stages of virus (Akram et al., 2018). There are several ethnomedicinal plants such as *Murraya koenigii*, *Euphorbia hirta*, *Curcuma longa*, *Zingiber officinale*, *Adhatoda zeylanica*, *Acalypha indica*, *Allium sepa*, *Coriandrum sativum*, *Ocimum basilicum* *Allium sativum* etc. recommended to have effective therapeutic potential in order to treat breathing problems, cough and cold (Murthy & Vidyasagar, 2013; Dhama et al., 2018). In addition *Alstonia scholaris*, *Rubia cordifolia*, *Swertia chirata*, *Cassia occidentalis*, *Eclipta erecta*, *Achyranthes aspera*, *Piper betel*, *Azadirachta indica* and *Lantana involucrate* are some Indian herbal medicines reported to have potent antipyretic property (Umashanker & Shruti, 2011). Further, *Phyllanthus amarus*, *Withania somnifera*, *Tinospora cardifolia*, *Curcuma longa*, *Embllica officinalis*, *Glycyrrhiza glabra* and *Andrographis paniculata* are some ancient Indian medicinal plants reported to have broad antiviral and immunity bosting properties (Gangal et al., 2020). There are several plants such as *Gauzuma ulmifolia*, *Achyranthus aspera*, *Ficus religiosa*, *Carissa edulis*, *Punica granatum*, *Moringa oleifera* etc reported to have an efficacious antiviral potency (Divya et al., 2020). Several natural phytoconstituents like flavonoids, comprising variable phenolic groups are also reported to have broad bioactivity in terms of antibacterial, antiviral, anti-inflammatory, anticancerous and antioxidant potency, in this respect Bhowmik et al. (2020) explored hesperedin, quercetin, naringin and epigallocatechin gallate flavonoids as an efficient therapeutic agent to control rapid spread of

SARS CoV-2 through preventing entry of virus inside host cell. Flavonoid based phytomedicines such as equivir, caflanone, myricetin and linebacker are also reported to have promising therapeutic value against Covid-19, because it inhibits viral entry inside host through strongly binding to helicase, protease and spike proteins on ACE2 receptor and ultimately leading to change its conformation (Ngwa et al., 2020). Bailly & Vergoten (2020) reported Glycyrrhizin, triterpenoid saponin isolated from *Glycyrrhiza glabra*, *G. inflata* and *G. uralensis* as a potential phytomedicine to combat Covid-19 pandemic due to its antiviral and anti inflammatory property; further through molecular docking it is also revealed that efficiently binding of glycyrrhizin to ACE2 receptor prevent attachment of virus to host ultimately leading to prevent spread of disease. In addition, glycyrrhizin is also categorized as generally recognized as safe (GRAS) by FDA suggesting it as safe compound and is reported as potential source to reduce disease severity of covid-19 through blocking entry points of covid-19 virus through different modes such as down regulation of ACE2 receptor protein expression and cytokine storm, prevention of intracellular reactive oxygen species accumulation, and up regulation of endogenous interferon as a defense chemical (Murck, 2020; LuoLiu & Li, 2020). Sinha et al. (2020) reported glyasperin A, another phytoconstituent of *G. glabra* that inhibited viral replication after entering inside host in contrary to glycyrrhizin which prevents entry of virus inside host. Glycosides and flavonoids constituents of *Allium sativum*, *Ficus*

racemose and *Salvia officinalis* are reported to have potent DNA gyrase damaging efficacy and thus suggested being one of the possible remedy against deadly novel corona virus (Devansh, 2020). Further, Jena et al. (2020) reported polyphenolic phytoproducts such as curcumin and catechin to be a potential component in drug development against novel corona virus as these biomolecules potentially inhibit host viral interaction due to its high binding affinity with both viral S protein and host ACE2 receptor protein. Several phytocomponents of Chinese medicinal plants such as amaranthin from *Amaranthus tricolor*, calceolariside B from *Flaxinus sieboldiana*, methyl rosmarinate from *Hyptis atrorubens* Poit and licoleafol from *Glycyrrhiza uralensis* are also reported to have inhibitory role in viral replication suggesting them to be a novel natural therapeutic drug against Covid-19 (Ul Qamar et al., 2020). Notably, several ethnomedicinal plants or their therapeutic benefits are vanishes over time due to lack of proper documentation as the ethnomedicinal knowledge is transferred over generations orally. Intensive research on antiviral, anti-inflammatory and antioxidant properties of ethnomedicinal herbs strongly support them as better remedy to different disease and also as a favorable treatment of Covid-19. Moreover, standard clinical trials are strongly recommended in order to scientifically authenticate its pharmacological efficacy. Figure 1 represents the general feature of virus as well as characteristics of traditional medicinal plants as possible candidate against Covid-19.

Figure1: General feature of SARS CoV-2 and traditional medicinal plants as potent warrior against covid-19 pandemic

4 Traditional medicinal plants: as potential immunomodulators

Ayurveda is having a vast historical perspective in Indian healthcare system and supposed to be originated in India around 4500 to 1600 BC as mentioned in ancient spiritual text Rigveda (Mishra et al., 2001). Indian subcontinents are vast repository of medicinal plants where 70% of populations are still relying on Ayurvedic system of medicine for their primary health care needs (Pandey et al., 2013). At present scenario phytoproduct based formulations are highly preferred to allopathic drugs globally due to their therapeutic efficiency, cost effectiveness and safety paradigm and nearly 25% worldwide prescribed drugs are based on phytoproducts (Sen & Chakraborty, 2017). Indian traditional medicinal systems including Ayurveda, Sidhha, Unani, Yoga, Naturopathy and Homeopathy, used effectively by ancient health practitioners against different chronic diseases. Although traditional medicinal system is having historical background, due to its hidden treasure nearly 80% of world population preferred phytomedicines for their primary health care (Khan & Yadava, 2010). Importance of ancient ethnomedicinal knowledge is scientifically proved at several times one of burning example is therapeutically important *Terminalia chebula*, *Tinospora cardifolia*, *Emblica officinalis* and *Terminalia bellirica* medicinal plants which are used by ethnic tribes of chhota bhagal in ancient time based on their ethnomedicinal knowledge without having much scientific knowledge and they described importance of these plants by saying that people never get diseased if they are having these plants in their region (Uniyal et al., 2006). Ayurveda is basically plant based medicinal system having no any side effect and highly encouraged during this Covid-19 pandemic. In ancient healing system of India i.e. Ayurveda Covid-19 may be mentioned as Janapadodhwamsa vikara (epidemic disease) which is a situation in which contaminated environmental factors i.e. land, water and air may lead to manifest disease in large population leading to broad devastating situation. Although, there is no direct implementation of Ayurvedic medicine to treat coronavirus disease, however, there is evidence from New York where positive corona patient completely relieved from Covid-19 symptoms after ayurvedic treatment (Girija & Shivan, 2020). In Ayurveda there is five different ways mentioned for uptake of medicine that is either in form of decoction (kwath or kadha), kalka (in form of paste), swaras (Juice), phant (an herb infused concoction) and hima (an herb induced concoction). Decoction is an oldest form of medicine prepared from herb or spices and highly recommended by AYUSH Ministry, Government of India as an immuno booster or anti-inflammatory cure to combat crisis of Covid-19 (Ayush, 2020). *Ocimum sanctum*, *Cinnamomum verum*, *Allium sepa*, *Allium sativum*, *Glycyrrhiza glabra*, *Piper nigrum*, *Curcuma longa* and *Daucus maritimus* are some traditionally known plants having antiviral properties and their

aqueous extracts are recommended to be effective against common cold and flu (Ali & Alharbi, 2020). Under the current pandemic situation when there is lack of effective preventive and curative medicine for Covid-19, immune system of an individual is the strongest weapon to fight against the pandemic situation. Immunity has drastic effect to control pathogenesis of Covid-19 at both early non severe stage and later severe stage. At early stage strong immunity prevents further spread of virus while in later stage strong immunity grave the consequences of cytokine storm. There are several medicinal plants reported in Ayurveda as Rasayana or immunomodulator such as *Panax ginseng*, *Achillea millefolium*, *Andrographis paniculata*, *Asperagus racemosus*, *Bauhinia variegata*, *Hyptis suaveolens*, *Cleome gynandra*, *Alternanthera tenella*, *Abutilon indicum*, *Heracleum persicum*, *Lagenaria siceraria* and *Chlorophytum borivilianum* (Kumar et al., 2012). Considering importance of boosted immunity against Covid-19 situation Ayush ministry, India On march 31, 2020 has issued an advisory on variety of immunity enhancing steps and later on also recommended herbal formulation *Ayush kwath or Ayush Joshanda or Ayush kudineer* which is mixture of four medicinal herb i.e. *Ocimum sanctum*, *Cinnamomum zeylanicum*, *Zingiber officinale* and *Piper nigrum* (Gautam et al., 2020). *Ayush kwath* has both the principle properties of ayurveda, Swasthasyorjaskara i.e. immunity strengthening and roganut i.e. disease alleviation. In Ayurveda leading treatment for any epidemic condition includes Rasayana chikitsa (Immune modulating therapy), Panchakarma (five process of purification) and Sadvritta (good conduct). Immune modulatory drugs are the substances that modulate immune system. Rasyana dravyas of ayurveda such as *Tinospora cardifolia*, *Glycyrrhiza glabra*, *Andrographis paniculata*, *Boerhaavia diffusa*, *Ocimum sanctum*, *Withania somnifera* are recommended to be supportive in Covid-19 (Niraj & Varsha, 2020). Recently Yog Guru Baba Ramdev suggested an Ayurvedic drug coronil under an umbrella brand Patanjali comprised of *Tinospora cardifolia*, *Ocimum tenuiflorum* and *Withania somnifera* and is approved by AYUSH Ministry India to be sold as immuobooster against corona (Baravkar et al., 2020). Another important herbal formulation strongly suggested for deadly disease is Chawanprash which is known as ageless wonder in Ayurveda, and comprises mixture of several nutritive phytoconstituents acting singly or synergistically as immunomodulator, free radical scavenger and anti aging agent (Sharma et al., 2019). Pharmacological efficacy of herbal medicines is based on its phytoconstituents. At present time one of the highly recommended Ayurvedic immune booster for Covid-19 is Ayurvedic kadha which is basically comprised of *Ocimum sanctum*, *Piper nigrum*, *Elletaria cardamomum*, *Zingiber officinale*, *Syzygium aromaticum*, *Withania somnifera* and *Tinospora cardifolia*. Maurya & Sharma (2020) through molecular docking technique analyzed antiviral efficacy of

bioactives such as withanolide, withaferin A, withanone, quercetin, piperine, vicenin, campesterol, somniferin, isopiperine etc present in kadha and found its anti-inflammatory against virus through binding with various inflammatory mediators or nucleocapsid protein of virus. Besides, these phytochemicals also impart inhibitory effect on host viral interaction due to its high binding affinity with viral spike protein, host receptor protein and furin protein, facilitator of spike and ACE2 interaction. Similarly, Lycorine an bioactive constituent of *Locis radiata* is reported to be effective against SARS CoV as well as having anticancerous properties (Lau et al., 2008), another active component i.e. emodine found in extracts of *Polygonum multiflorum* and *Rheum officinale*, scutellarin, tetra-O-galloyl- β -D glucose (TGG) from *Galla chinensis*, Baicallin from *Scutellaria baicalensis*, luteolin from *Veronica linaria* is also reported as effective drug against SARS CoV as it inhibit binding of spike protein with host cells (Mirzaie et al., 2020). Further in view of immunomodulatory activity polynutrient based novel combination of curcumin, glycyrrhizic acid and vitamin C is also reported to prevent cytokine storm to serve as beneficial approach against novel coronavirus (Chen et al., 2020b). Thus, phytoproducts are also supposed to be a promising candidate against corona virus as it has an immunobooster property. Besides several recommended traditional medicinal plants some plant based products including fruits like orange, kiwi, guavava, papaya and vegetables like beet root, spinach and cauliflower are also recommended to be taken during this pandemic situation as these are rich source of vitamin c that enhance immunity of person (Mahim et al., 2013; Rahal et al., 2014). In addition, red onion, green tea, black tea, green leafy vegetables, apples and grapes are found to be rich source of biflavonoid i.e. quercetin which is reported to prevent viral infection including SARS CoV (Arsad et al., 2020). Further, *Panax ginseng*, *Aloe vera*, *Angelica gigas*, *Astragalus membranaceus*, *Scutellaria baicalensis*, *Lawsonia alba*, *Plumbago zeylanica* and *Cissampelos pareira* are also some other immunomodulatory herbs reported as enhancer of body stamina to fight against novel corona virus (Panyod et al., 2020). Apart from broad therapeutic values Ayurvedic herbs also have a disinfectant property which is one of highly requiring area during this pandemic, powder of *Curcuma longa*, seeds of *Trachyspermum ammi*, peel of *Allium sativum* and *Styrax benzoin* resin together used for fumigation considered to be an effective disinfectant (Rastogi et al., 2020). Some common Indian medicinal plants with their therapeutic potency that may be used as promising candidate against corona virus disease are summarized in Table -1.

5 Indian Spices as traditional immunobooster against Covid-19

Indian spices are having vast medicinal properties and are frequently used from ancient time as energy as well as immunity booster to combat common problems of cold, cough and flu.

Hence, during the worst Covid-19 situation, Indian spices appeared as gift of India's ancient wisdom for whole world which have potency to enhances immunity and prepare body to fight against SARS CoV-2 virus. Presently under situation when known remedy is lacking against onslaught of SARS CoV-2 Indian spices are best to be used, as they are easily present in every kitchen and have potent immunity boosting properties along with antiviral and several other therapeutic values. Thus, daily basis use of these miraculous therapeutic spices might be useful in mitigating risk of Covid-19. Some commonly used Indian spices which might be served as an efficacious immunomodulatory agent against Covid-19 are as follows-

5.1 *Curcuma longa* (Turmeric)

Turmeric is one of the most common Indian spices which belong to family Zingiberaceae and commonly used as household treatment against cold, sore throat and respiratory problems. Curcumin is its major active principle and reported to have several therapeutic values such as antioxidant, anti-inflammatory, antimicrobial, antiseptic, anticancerous and immunity booster (Sahoo et al., 2020). In addition, through *in silico* analyses major compounds of turmeric are also reported to have efficacious antiviral potency against novel corona virus because it effectively suppress virulence of virus by inhibiting its main protease activity (Gupta et al., 2020b). Turmeric milk along with boiled milk is also suggested as better remedy against cough, cold and respiratory problems. Therefore, turmeric might be an effective immunity booster against Covid-19

5.2 *Allium sativum* (Garlic)

Garlic, besides its quality to be used as food additive also have broad therapeutic properties as cardio-protectant, antioxidant, anti inflammatory, anti viral, anti-cancerous and as immunomodulatory substance. Allicin, an organo sulphur compound present in garlic protect body from common cold and flu through up regulating immunity of body. Garlic is reported to exhibit immunomodulatory effect through regulating cytokine and chemokines level inside body (Donma & Donma, 2020) suggesting garlic to be promising candidate in order to deal with Covid-19 mediated cytokine storm.

5.3 *Syzygium aromaticum* (Clove)

It is a dried flower bud, used widely to prepare spicy dishes due to its intense taste and fragrance. In addition, clove having eugenol as one of its phytoconstituent, reported to have wide array of therapeutic properties such as analgesic, anti inflammatory, immunomodulatory and better remedy for respiratory disorders (Dibazar et al., 2014). Besides, clove is also having an efficient antiviral and antipyretic potency.

Table 1 Some potential Indian medicinal plants used effectively against Covid-19

S. No.	Traditional Medicinal Plants	Family	Physiological effect	References
1	<i>Tinospora cardifolia</i> (Guduchi)	Menispermaceae	Berberine, tinosporin, choline, tinosponone and palmitine like phytoconstituents contributed to its antioxidant, anti-inflammatory and immunomodulatory effects. Besides molecular docking revealed it as potent inhibitor of SARS CoV-2 main protease.	Krupanidhi et al. (2020)
2	<i>Curcuma longa</i> (Haldi)	Zingiberaceae	Curcumin as an active principle have anti-inflammatory, antiviral, antioxidant and anticancerous property. Besides also used in respiratory disorders. Its efficacy against dengue, influenza, HIV and several other viral diseases access its value as effective drug against Covid-19.	Gupta et al. (2020a)
3	<i>Syzygium aromaticum</i> (clove)	Myrtaceae	Eugenol as major bioactive component and clove is reported to have anti inflammatory, anticancerous antioxidant and antipyretic property.	Mittal et al. (2014)
4	<i>Cinnamomum verum</i> (Cinnamon)	Lauraceae	Cinnamaldehyde and eugenola as active principle enhance therapeutic efficacy of herbal material in terms of antimutagenic, antiviral, immunomodulatory, and antipyretic potency.	Gulcin et al. (2019)
5	<i>Andrographis paniculata</i> (Kalmegh)	Acanthaceae	Plant is having andrographolide as its major bioactive component and reported to be effective against HIV virus, Herpes virus, and hepatitis B and C virus, Influenza A virus.	Gupta et al. (2017)
6	<i>Withania somnifera</i> (Ashwagandha)	Solanaceae	Bioactive components such as withaferin A, withanolide series and withanoside series reported to have rejuvenating, immunity boosting and antiviral efficacy against Covid-19 through inhibiting main protease deadly virusof suggesting it as efficacious possible corona drug.	Tripathi et al. (2020)
7	<i>Allium sativum</i> (Garlic)	Liliaceae	Prime organosulfur bioactive compound such as allicin, diallyltrisulfide and azoene and flavonoids such as anthocyanin and quercitins prevents entry as well as multiplication of virus inside host suggesting it as potent drug source against Covid-19.	Kaushik & Singh (2020)
8	<i>Glycyrrhiza glabra</i> (Licorice, Mulaithi)	Fabaceae	Effective in respiratory disorders, fever, stomach problems and also have anti inflammatory, antioxidant and antiviral properties.	Batiha et al. (2020)
9	<i>Ocimum sanctum</i> (Tulsi)	Lamiaceae	Known as Queen of herbs having Antiviral, antioxidant, anti-inflammatory, immunomodulatory potential and antiasthmatic property. Phytochemicals such as vincenin, ursolic acid and isorientin through molecular docking reported to suppress novel corona virus and host interaction safely and effectively.	Shree et al. (2020)
10	<i>Zingiber officinale</i> (Ginger)	Zingiberaceae	Medicinal plant widely used to treat cough, bronchitis, respiratory tract infection, have anti inflammatory, anticancerous property along with strong therapeutic potency against Chikungunya virus.	Kaushik et al. (2020)
11	<i>Boerhaavia diffusa</i> (Punarnava)	Nyctaginaceae	Plant used to ameliorate multiple diseases such as pulmonary tuberculosis, jaundice, cough, kidney disorders and gastric problems. Also have potent immune stimulatory property.	Nayak & Thirunavoukkarasu (2016)
12	<i>Vitex negundo</i> (Nirgundi)	Verbenaceae	Plant is highly important and used frequently even in allopathic drug formulations. Efficacious in cold, flu, asthma, fever, headache, dysentery and even as immunity stimulator.	Maurya & Rao (2019)
13	<i>Phyllanthus emblica</i> (Amla)	Euphorbiaceae	Vast number of medicinally important compounds present contributing it to perform hepatoprotective, nephroprotective, immune booster, anti-hepatic and anti HIV agent.	Sayed (2019)
15	<i>Piper longum</i> (Long Pepper)	Piperaceae	Piperine, a biohacer as an active ingredient of <i>Piper longum</i> enhanced its therapeutic values and used effectively to treat cough, cold, fever, jaundice and as immunity tonic.	Khushbu et al. (2011)
16	<i>Camellia sinensis</i> (Green Tea)	Theaceae	Polyphenols such as epicatechingallate, epigallocatechin gallate and galliccatechin-3 gallate are reported as a potent drug against SARS CoV-2 as it inhibits main protease of virus required for its replication. However, <i>in vivo</i> experimental results are required.	Ghosh et al. (2020)
17	<i>Withania somnifera</i> (Indian Ginseng or Ashwagandha)	Solanaceae	Bioactives such as withanolide N, ashwagandanolide, withanoside X and dihydrowithaferin A are contributed to potent anti-inflammatory, antioxidant, immunomodulatory and promising antiviral role against Covid-19.	Chikhale et al. (2020)
18	<i>Cinchona tree</i> (Quina)	Rubiaceae	Quinine, its major active compound having antiviral potency used to derive a efficacious synthetic drug chloroquine to fight with covid-19 due to its DNA intercalating property.	Jahan & Onay (2020)
19	<i>Phaseolus vulgaris</i>	Fabaceae	Phytochemicals reported to have potent antiviral activity against HIV and Drosophila C virus apart from this phytochemicals also have significant potency against novel corona virus due to its high binding affinity with main protease and ACE2 protein.	Joshi et al. (2020)
20.	<i>Petrselinum crispum</i>	Apiaceae	Apigenin as an active principle exhibited strong binding affinity towards Covid-19 virus spike protein thus having potent antiviral activity.	Subbaiyan et al. (2020)

5.4 *Zingiber officinale* (Ginger)

It is rhizomatous plant of family Zingiberaceae, commonly used as spice in Indian culture as well as an important traditional medicine comprised of antiviral, antipyretic, antibacterial, antioxidant and antihypertensive pharmacological properties. Rathinavel et al. (2020) reported 6-Gingerol, one of bioactive compound of ginger to be used as an effective candidate against Covid-19 as it binds to several target protein of virus and reduce its pathogenicity.

5.5 *Cinnamomum zeylanicum* (Cinnamon)

Cinnamon bark (Lauraceae) one of the important flavouring spices used from several centuries, having a broad pharmacological efficacy against digestive, respiratory and gynaecological ailments. Further, cinnamon is also reported to have immunity strengthening property and cinnamon taken along with honey would also lead to drastic enhancement of immunity (Niphade et al., 2009). In addition cinnamon, world's frequently consuming spice, has also been reported to have significant antioxidant, antitumor and anti-inflammatory potency due to its volatile bioactive components (Goel & Mishra, 2020).

5.6 *Elettaria cardamomum* (Cardamom)

Cardamoms are capsule of dried fruit, belongs to family Zingiberaceae having a characteristic aroma due to its bioactive components and frequently reported to be used as spice and also having medicinal importance against asthma, diarrhea digestive and kidney disorders. Further, bioactive compounds of cardamomum are also reported to have anticancer, anti-oxidant, antifungal, antiviral, anti-inflammatory and gastroprotective therapeutic qualities (Ashok kumar et al., 2020)

5.7 *Piper nigrum* (Black pepper)

Piper nigrum, belongs to family Piperaceae, known as 'king of spices' which not only enhance flavour and taste of diet as spice but can also be recommended in Ayurveda as a potent medicine for broncho-pulmonary disorders, fever, neurological disorders as well as gastrointestinal problems (Stojanovic-Radic et al., 2019). Piperine, major bioactive of *Piper nigrum* responsible for its pungency, reported to have wide array of therapeutic potencies including anticarcinogenic, hepatoprotective, anti inflammatory, antioxidant, immunomodulatory and anti asthmatic. Further, Piperine also acts as bioenhancer which boost therapeutic potency of drugs through enhancing their bioavailability (Gorgani et al., 2017). Turmeric consumed together with black pepper reported to have 2000 times enhanced absorption rate.

5.8 *Illicium verum* (Star anise)

Star shape aromatic fruit frequently being used as culinary ingredient, also reported to have diverse therapeutic applications due

to its bioactive compounds. As an important immunity booster it prepares body to resist against several viral diseases. Shikimic acid obtained from star anise is used to form drug against Influenza virus. Besides, *Illicium verum* is also having anti bacterial, antioxidant and anti inflammatory effects and widely used as remedy against cough, asthma, dysentery and arthritis (Patra et al., 2020).

5.9 *Myristica fragrans* (Nutmeg)

Myristica fragrans due to its magical sweet and spicy flavour, become one of the essential constituent in Indian kitchen since antiquity and also reported to have significant health values. Nutmeg due to having myristicine, myrcene, safrole, camphene, sabinene, linalool, 1,8-cineole and eugenol as its volatile constituent used as pain reliever, besides it is also having properties to treat stomach disorder, respiratory problems, cardiovascular problems as well as used as brain tonic, liver tonic and immunity booster (Upadhyay, 2020)

Conclusion

There are several Indian medicinal plants and their phytoconstituents that are safe and efficacious in alleviating pandemic situation as immunobooster, thereby, and preventing viral transmission. Hence, bioprospection and documentation of ethnomedicinal plants are needed in order to discover new wonder drugs against SARS CoV-2. Incorporation of nano-biotechnology and collaboration between pharmacologists, botanists, Ayurvedic practitioners and biotechnologists will boost the efficacy of the traditionally used plant based immunomodulators against Covid-19 pandemic through enhancing their efficacy, bioavailability and practical applicability.

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Conflicts of Interests

The Author declares no conflict of interests.

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