Review Article

Impact of medicinal plants on treatment of SARS-CoV, SARS-CoV-2 and influenza virus in India

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Abstract

Medicinal plants or herbs are plants used for management and treatment of specific diseases. They are used in both allopathic and traditional systems of medicine across the world, World Health Organization estimates 80% of the global population relies on traditional herbs for health care. As human needs and commercial trade for medicinal plants increases,so also its demands for a wide variety of wild species. Some herbal medicines have been used for the treatment of other coronavirus pandemic like SARS-CoV in 2013 and MERS-CoV in 2012, it is also used influenza viruses and dengue virus. Extracts from *Lycoris radiate*, *Artemisia annua* and *Lindera aggregate*, and products isolated from *Isatisindigotica*, *Torreyanucifera* and *Houttuyniacordata*, showed anti-SARS effects and also *Lycoris radiate* and *Pyrrosia lingua* exerted anti-SARS-CoV effect with 50% effective concentration. Also plants like Acanthaceae (Kalmegh), and Papilionaceae (Licorice) are reported to be effective on influenza virus.

Keywords: Medicinal plants, herbs, traditional medicine, SARS COV-2, influenza

Introduction

Medicinal plants or medicinal herbs are plants used for managing fitness or treating particular diseases, medicinal plants are used in both allopathic and conventional systems of medicine in countries across the globe. In fact public using only allopathic medicine all over their life are likely to be moderately using medicinal plant as 20-25% of allopathic drugs given are plant-derived Medicinal plant (Rates, 2001).

The World Health Organization (WHO) estimate that 80% of the global population relies largely on traditional herbs for health care (Lambert et al., 1997) and the impact of medicinal plants in health care is progressively more recognized as consultation on the function of conventional medicine in contributing to achieving the Millennium Development Goals (MDGs), three of which are health related (Ahn, 2017).

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Hundreds of chemical compounds synthesise by plants for defence against lots of human diseases. A single plant contains broadly unlike phytochemicals and the impact of using an entire plant as medicine is doubtful. Also the phytochemical content as well as the pharmacological behaviour of many plants with medicinal potential remains un-assessed by scientific study to define its potency and safety.

Medicinal plants play a vital role as traditional medicines as is used in many cultures, similarly, is used as trade product which meet the demand of often distant markets. As human needs and commercial trade for medicinal plants increases also its demands for a wide variety of wild species. Some wild species of plants are being over-exploited, and this lead to recommendation by various agencies to brought wild species into cultivation systems (Lambert et al, 1997).

Medicinal plants effective against infectious diseases of various body systems and their traditional therapeutic effects (Mahmoud Bahmani et al., 2015)

Medicinal plants and their Utility for SARS-CoV-2

Coronavirus disease 2019 or COVID-19 is the illness caused by Severe acute respiratory syndrome coronavirus-2 (SARS-

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Table 1. List of medicinal plants for infectiveness diseases

Family	Scientific name	Diseases treated	Parts used	Ways of usage
Rosaceae	*Agrimonia eupatoria* L.	Swelling and infection of stomach	Inflorescence	oiled and brewed
Malvaceae	*Altheae hirsute* L.	Pulmonary infections	Root	Boiled and brewed, fumigation
Fabaceae	*Alhagi camelorum* Fisc	Intestinal infection, bladder infection	Aerial part	Boiled and brewed
Cucurbitacea	*Bryonia dioica* L.	Kidney infection, intestinal infection	Root and fruit powder	Boiled
Brassicaceae	*Capsella bursa-pastorris* (L.) Medik.	Urinary tract infections (UTI)	Leaf	Boiled
Brassicaceae	*Cardaria draba* (L.) Desv.	Respiratory infection	Leaf, seed	Boiled and brewed, fumigation
Solanaceae	*Datura stramonium L.*	Wound disinfection	Seed	Boiled and poultice
Dipsacaceae	*Dipsacus laciniatus* L.	Anti-infection of urinary tract and genital system	Root, leaf, seed	Boiled and poultice
Equisetaceae	*Equisetum arvense* L.	Kidney infection, antipyretic	Aerial part	Boiled
Rubiaceae	*Galium humifusum* Bieb	Infectious diarrhea	Aerial part	Boiled
Fabaceae	*Glycyrrhiza glabra* L.	Stomach infection	Root, aerial par	Boiled
Amaryllidacea	*Ixillirion tataricum* (Pall.) Roem et Schult	Washing skin abscesses, disinfection of infected wounds	Gland, flowering shoot	Poultice
Lamiaceae	*Lamium album* L.	Kidney infection, UTI, vaginitis	Flowering shoot	Boiled and washed with boiled form
Lamiaceae	*Lamium purpureum* L.	Vaginitis	Flowering shoot	Boiled
Lamiaceae	*Mentha spicata*	Infectious diarrhea	Aerial part	Boiled
Lamiaceae	*Mentha longifolia* L.	Pulmonary infections	Aerial part	Boiled and brewed,fumigation
Apiaceae	*Cuminum cyminum* L.	Intestinal inflammation	Seed	Boiled
Poaceae	*Phragmites australis* (Cav.) Trin	Gastroenteritis	Rhizome	Boiled
Plantaginacea	*Plantago major* L.	Pulmonary infections and stomach ulcers	Seed, leaf, root	Boiled
Salicaceae	*Salix alba* L.	Antipyretic	Bark, leaf	Boiled
Lamiaceae	*Salvia verticillata* L.	Antipyretic, antimicrobial	Leaf, flowering shoot	Boiled
Rosaceae	*Sanguisorba minor* Scop	Disinfectant of skin wounds	Fruit	Boiled and raw
Scrophulariaceae	*Scropholaria kurdica* subsp. Glabra	Antimicrobial and antiseptic	Aerial part	Boiled
Asteraceae	*Lactuca serriola* L.	Antipyretic	Leaf	Boiled
Brassicaceae	*Sisymbrium officinale* L.	Antipyretic	Seed	Boiled
Asteraceae	*Tanacetum parthenium* (L.) Schultz.	Sinusitis, gastritis	Leaf, flower	Boiled
Lamiaceae	*Teucrium orientale* L.	Antipyretic	Aerial part	Boiled
Lamiaceae	*Teucrium polium* L.	Antimicrobial	Flowering shoot	Boiled
Lamiaceae	*Thymus kotschyanus* Boiss.	Infectious diarrhea	Flowering shoot	Brewed, fumigation
Scrophulariacea	*Verbascum agrimonifolium*	Bacterial infection of the wound	Leaf, flower	Boiled
Scrophulariacea	*Verbascum macrocarpum* Boiss.	Fungal infection of nail	Leaf, flower	Boiled
Scrophulariaceae	*Verbascum speciosum* Schord.	Bacterial infection of the wound	Leaf, flower	Poultice, boiled and concentrated
Lamiaceae	*Ziziphora tenuior* L.	Gastritis	Inflorescence	Boiled

CoV-2),a pandemic disease that is currently spreading worldwide (affecting 216 countries) with more than 4,628,903 confirmed cases and 312,009deaths (as of 19thMay, 2020)(WHO, 2020).

Several drugs are being developed rapidly some drugs undergoing clinical trialsand new targets are being identified every day (Balachandar et al., 2020). Indian medicinal plants are well recognized for handling of various diseases.

Herbal medicines have been second-hand in coronavirus outbreaks like SARS-CoV in 2013 and MERS-CoV in 2012, it is also used in epidemics caused by influenza viruses and dengue virus. Extracts from *Lycoris radiate*, *Artemisia annua* and *Lindera aggregate*, and the natural products isolated from *Isatis indigotica*, *Torreya nucifera* and *Houttuynia cordata*, showed anti-SARS effects (Lau et al., 2008, Li et al., 2005, Lin et al., 2005, and Yu et al., 2012), also *Lycoris radiate* and *Pyrrosia lingua* exerted anti-SARS-CoV effect with 50% effective concentration (Li et al., 2005).

Medicinal plants for H1N1 and influenza viruses

Swine influenza is also known as H1N1 flu, swine flu, hog flu, and pig flu. Swine influenza virus (SIV) is any strain of the influenza that is prevalent in pigs. It is a rising viral infection with thousands of cases in all over the world (Avani and Krishnamurthy, 2013). The H1N1 virus was

Table 2. List of medicinal plants which may prove useful to combat Swine flu

S. No.	Plant name	Family	Principal chemical compound	Anti-influenza Action
1.	Basil	Lamiaceae	Oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, linalool, and β-caryophyllene	Antimicrobial properties
2.	Ginger	Zingiberaceae	allicin, alliin,	Anti-nausea and anti-inflammatory properties
3.	Garlic	Alliaceae	Ajoene	Anti-inflammatory antiviral, antibacterial, and immune-boosting properties
4.	Giloy	Menispermaceae	tinosporone, tinosporic acid, syringe, alkaloid, berberine, Giloin, crude Giloininand	Anti-periodic, Anti-pyretic, Alterative, Diuretic, Anti-inflammatory properties
5.	Licorice	Papilionaceae	Glycyrrhizic acid, glycosides, coumarin, and cinnamic acid	Antiviral activity anti-inflammatory, antioxidant, and immune-modulating activities
6.	Kalmegh	Acanthaceae	Andrographolide	Anti-inflammatory, antipyretic (anti-fever), antiviral, and immunostimulatory properties
7.	Ashwagandha	Solanaceae	Anaferine, anahygrine, beta-sisterol, chlorogenic acid, cysteine, cuscohygrine, pseudotropine, scopoletin, somniferinine, withaferin α, withanine, withananine, andwithanolides	Stimulant for the immune system, also avery potent adaptogen.
8.	Turmeric	Zingiberaceae	Curcumin	Antioxidant , anti-inflammatory properties
9.	Neem	Meliaceae	Azadirachtin	Antidiabetic, antibacterial, and antiviral properties.
10.	Bael	Rutaceae	alkaloids, coumarins, and steroids	Analgesic, anti-inflammatory, antibacterial, and antiviral properties
11.	Mentha	Labiatae	Menthol, menthone, flavonoids, carotenes, tocopherols, betaine, and choline	Antimicrobial and antiviral activity

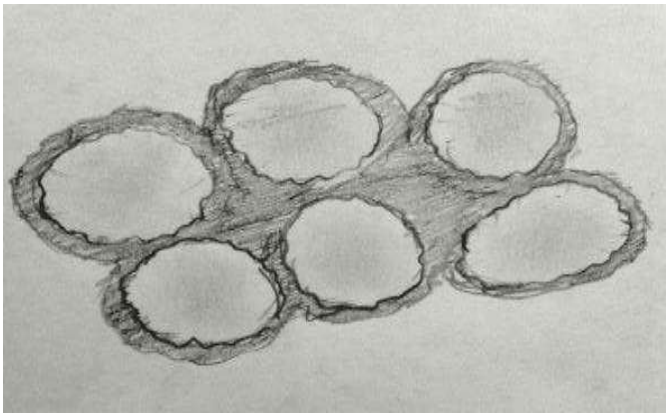

Figure 1. Electron microscopic image of H1N1 influenza virus (Wiwanitkit, 2009)

first reported in America in the year 2009. Due to the nature of respiratory virus, the transmission of this pathogenic virus is air borne transmission and its spreading rapidly, this makes the control of this infection very difficult. The known SIV strains include influenza C and the subtypes of influenza A known as H1N1, H1N2, H3N1, H3N2, and H2N3. The pandemic of the swine flu was declared over by World Health Organisation on August 2010 (The Merck Veterinary Manual. 2008).

The molecular mechanism of SARS-CoV-2

The SARS-CoV-2 belongs to the family of RNA viruses and its genome ranges from 125 nm or 0.125μm. It is a single stranded enveloped RNA virus which possess a positive-sense RNA genome also known as (+ssRNA) with a 5′-cap structure and 3′-poly-A tail (Chen et al., 2020). Viruses belonging to this class have some similar characteristics that are applicable to SARS-CoV-2. There are four essential structural proteins required to regulate the function and viral structure of the virus; which are (E) the envelope protein, (M) the membrane protein, (S) the spike protein, and (N) the nucleocapsid protein (Schoeman and Fielding, 2019). The most important proteins are S and N, where the latter helps in development of the capsid and the entire viral structure of the virus and the former helps in attachment of virus to the host cells (Siu et al., 2008; Walls et al., 2020). The three major sections of S protein are the large ectodomain, a single-pass transmembrane anchor and a short intracellular tail. These play a major role in anchoring the host cells. The ectodomain two subunits are S1 receptor-binding subunit and S2 the membrane fusion subunit. The two subunits are in crown like structure, hence the name coronavirus (corona = crown) (Zumla et al., 2016).

Many researches shows that SARS-CoV and SARS-CoV-2 have similar kind of receptors, especially the receptor binding domain (RBD) and the receptor binding motif

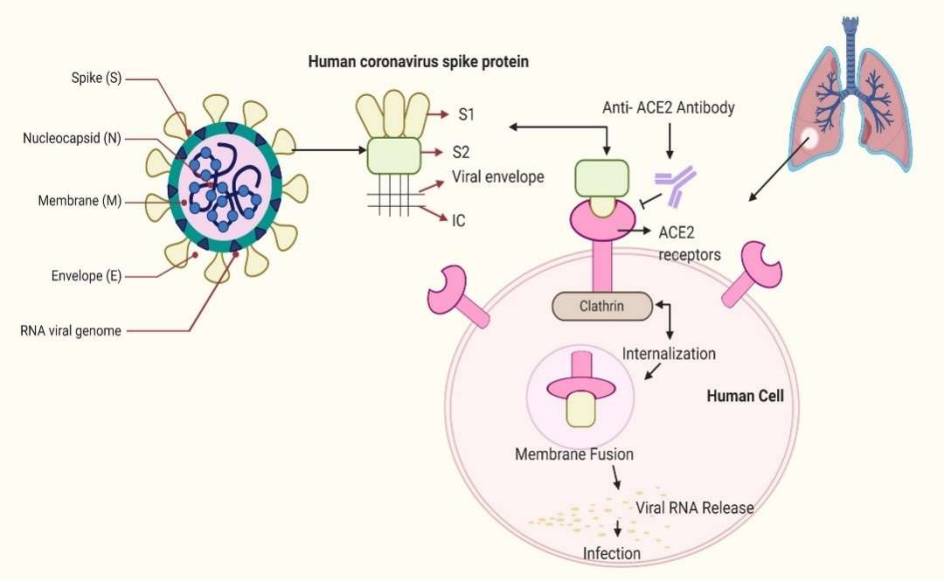

Figure 2. Structure and binding of COVID-19 virus to ACE2 (Balachandar Vellingiri et al., 2020)

Figure 3. *Allium sativum* reported to have an ability to target the viral replication of SARS-COV (Keyaerts et al., 2007)

Figure 4. *Glycyrrhiza glabra* reported to have an ability to target the viral replication of SARS-COV (Nourazarian, 2015)

(RBM) in the viral genome (Zhanget al., 2020; Tai et al., 2020; Wunderink, 2018; Yin 2018). The RBM of the S protein attached tothe Angiotension-Converting Enzyme 2 (ACE2) in the host cells during SARS infection (Phan, 2020). The ACE2 protein is expressed mainly in the lungs, kidney and intestine which are main targets of the coronavirus (Zhao et al., 2020) and SARS-CoV-2 infects host cell through ACE2 receptors leading to COVID-19 related pneumonia, acute myocardial injury and chronic damage to the cardiovascular system (Zheng et al., 2020). Researches shows that the RBM of the SARS-CoV-2 has an amino acid residue (Gln493) which help in attachment and fusion of the viral S protein of the virus into the ACE2 protein of the host cell mainly, the cells of the lungs which results in respiratory infections (Yin and Wunderink, 2018; Phan, 2020).

The simplest method to combat SARS-CoV-2 is by neutralizing the virus from entering host cells as this has been seen effective in previous viruses (Walker and Burton, 2018). Since host ACE2 protein does not change, so there is no fear about advantageous mutations that may hinder drug development (Karakus et al., 2020).

The Knowledge of the receptors and its targets and basis of viral replication will assist in finding treatment for the SARS-CoV-2 infection.

When SARS-CoV-2 virus entered in to host cells, its require RNA replication for survival. The process of replication required open reading frames (ORFs), two replicase genes (rep1a and rep1ab), a slippery sequence (5′-UUUAAAC-3′) and two polyproteins (pp1a and pp1ab). The two polyproteins contain Nsp proteins (Nsp1–11and Nsp1–16), these proteins are a common occurrence in these virus

types(Baranov et al., 2005).Current studies shows that, the Nsp 15 protein besides attacks the immune system of the host during viral duplication (Youngchang et al., 2020). These Nsp proteins assemble to form the replicase-transcriptase complex which creates a suitable environment the host cells for synthesis and replication of RNA. Also, Nsps plays a major roles in RNA replication of the virus. RNA-dependent RNA polymerase (RdRP) domain is codes by Nsp12, and Nsp13 is encrypted with RNA helicase domain and RNA 5′-triphosphase.SARS-CoV-2 have similar process of replication to SARS-CoV virus (Youngchang et al., 2020). The genomic RNA contains a 5′ end region that has the untranslated leader sequence with the transcription regulation sequence present at the descending region of the genome (Fehr and Perlman, 2015).

Medicinal plants for COVID-19

Indian herbs have been second-hand for treatment and avoidance for numerous diseases, together with respiratory viral infections (Ravishankar and Shukla, 2007) unluckily only few study were conducted in India on treatment of coronavirus with medicinal plants.

A study has shown anti-mouse coronaviral activity by some plants like *Indigo feratinctoria* (*AO*), *Vitex trifolia*, *Gymnema sylvestre*, *Abutilon indicum*, *Leucas aspera*, *Cassia alata*, *Sphaeranthus indicus*, *Clitoria ternatea*, and *Evolvulus alsinoides* in Tamil Nadu (Vimalanathan et al., 2009). Among which *Vitex trifolia and Sphaeranthus indicus* have been found to reduce inflammatory cytokines using the NF-kB pathway (Alam et al., 2002; Srivastava et al., 2015). *Clitoria ternatea* is also been reported as a metalloproteinase inhibitor (Maity et al., 20012). The plants *Glycyrrhiza glabra* and *Allium sativum* have been reported severally that they have the ability to target the viral replication of SARS-CoV, this place them as one of the most promising candidates against SARS-CoV-2. *Clerodendrum inerme* Gaertn is also another medicinal plant reported to have the potential to inactivate the viral ribosome which can be investigated further as a drug targeting SARS-CoV-2 protein translation (Nourazarian, 2015; Keyaerts et al., 2007).

Conclusion

World Health Organization (WHO) and other international as well as national health regulatory agencies should not only be emphasis on producing vaccines alone, attention should also be given to some medicinal plants that might be effective on treatment of SARS-COV, SARS-COV-2 and Influenza virus that has been reported India and other part the world.

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