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Review Article

Therapeutic potential and pharmacological properties of Indian herbs for the management of SARS-COV-2 coronavirus disease: A research based review

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ABSTRACT

Corona virus (COVs) are RNA virus that comes from the family *Coronaviridae.* COVs are pathogenic to animals as well as human beings and can cause ailment related to respiratory system such as severe acute respiratory syndrome (SARS) and COVID-19. However treatment of COVID-19 is one of the major area of concern as there are no appropriate treatment options available, however few herbal products are being used to boost the immunity of patients and in turn prevent the occurrence of infection. Historically India has always been rich with plants and is known to use herbs and plants in traditional system of healing. India has distinct traditional system of medicine called AYUSH that represents Ayurveda, Yoga, Unani, Siddha and homeopathy. This traditional system of medicine can be used to fight against COVID-19 pandemic. Present study describes about different herbs and plants of Indian origin that can be used for effective management COVID-19 and in future that can act as potential candidate for development of improved drugs for therapy of COVID-19 infection.

1. Introduction

Corona virus (COVs) are RNA virus that comes from the family *Coronaviridae.* COVs are pathogenic to animals as well as human beings and can cause ailment related to respiratory system such as severe acute respiratory syndrome (SARS). COVs primarily affects the organs of respiratory system like lungs, moreover it also affects other system such liver and gastrointestinal tract of digestive system and nerves of nervous system. First incident of corona virus infection was reported in December 2019, when the report of infection emerged from Wuhan in China. Eventually the first case led to development of pandemic when the infection spread throughout the world. The infection was termed as COVID-19 by World Health Organization (WHO). COVID-19 has an incubation period of 1 to 14 days. The symptoms associated with COVID-19 infection is fever, headache, dizziness, breathlessness and loss of sense of smell and sense of taste. In some cases patient may also suffer from diarrhea and fatigue. People of higher age group or persons having diseases like cancer, hypertension and diabetes are more prone to COVID 19 infection. Research showed that mental and neurological complication may be seen with people who are infected with COVID-19 infection. Treatment of COVID-19 is one of the major area of concern as there are no appropriate treatment options available, however few herbal products

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are being used to boost the immunity of patients and in turn prevent the occurrence of infection. The present review work focuses on the variety of herbal drugs or components that can be used for the effective management and treatment of COVID-19. Herbs and plants are used as a vital source of medicine for centuries.[1] There hasbeen evidence that traditional medicine are in use since 5000 years in the text of India, China, Rome, Egypt, Syria and Greece Around 80% of the need of medicine in the world is been fulfilled by herbs and especially in rural areas. Historically India has always been rich with plants and is known to use herbs and plants in traditional system of healing.[2] Literatures of ancient India provides evidence regarding use of medicinal plants for treatment of diseases.[3] India has distinct traditional system of medicine called AYUSH that represents Ayurveda, Yoga, Unani, Siddha and homeopathy. This system of medicine basically focuses on holistic ways to treat a disease by utilizing natural product that are obtained from plant, animal or mineral source. AYUSH has played important role in controlling different pandemics like plague, Spanish flu and cholera that had hit the mankind earlier. Therefore this traditional system of medicine can be used to fight against COVID-19 pandemic.[4] COVID-19 being a diseases which is related to weak immune system, various indigenous India plants such as *Curcuma long, Andrographis paniculata, Allium sativum, Withania somnifera and Moringa oleifera* can be used to enhance the immune property and act against viral infection.[5] Various chemical constituents present in these plants such as alkaloids, saponins, quercetin, catechins act as an inhibitor of viral entry.[6] Present review focuses on enlisting various Indian herbs that possess the potential to act against SARS-COV-2 Corona Virus.

2. Viral Invasion and Host Cell Interaction

Corona virus contains a pathogenic envelop which possess specialized surface protein called spike protein. Spike protein is responsible for invasion of virus into the host cell through angiotensin-converting enzyme 2 (ACE2) receptor.[7]

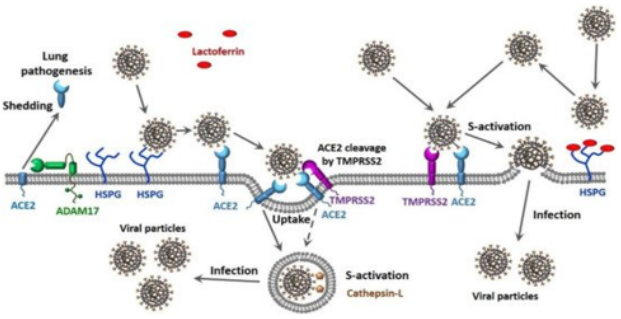

Fig. 1: SARS COV invasion and host cell interaction mechanism.

3. Plants With Antiviral Properties

Various plants shows antiviral properties against many viral diseases and are used traditionally for the protection of animals and human beings from these diseases. Therefore many medicinal plants having antiviral properties can be used as a base for developing newer approaches for the treatment and prevention of COVID-19.[8] It is believed that most of the plant with antiviral property targets an enzyme called 3-chymotrypsin-like cysteine protease which is important for the replication of coronavirus. Moreover phyto-constituent obtained from different plants such as Isoflavone obtained from *Psorothamnus arborescens,* methyl rosmarinate obtained from *Hyptis atrorubens,* licoleafol obtained from *Glycyrrhiza, myricitrin* obtained from *Myrica cerifera* are believed to be potent against corona virus. Plants and herbs displays immunomodulatory activity by producing interleukins and pro-inflammatory cytokines that in turn enhances cell mediated immunity against viruses.[9] The phyto-constituent quinine which is obtained from the bark of cinchona tree and its derivatives like chloroquine and hydroxychloroquine had shown effectiveness against SARS-CoV-2 and was beneficial in treatment of COVID-19 infection.[10]

4. Indian Medicinal Plants Effective Against Covid-19

There are numerous plants that comes under Indian traditional system of medicine which are believed to have anti-SARS-CoV-2 properties. Few plants such as *M. oleifera, Terminalia bellirica, Hippophae rhamnoides, Avicennia marina* are known to have antiviral property but their effectiveness against COVID-19 still not investigated. In-silico docking approach on few species that originated from India showed anti-SARS-CoV-2).[11] However clinical trial regarding their effectiveness against COVID-19 still to be investigated. Species like garlic, turmeric, red pepper and fenugreek are believed to affect enzyme like prioteases, envelope protein of virus and RNA binding. Moreover, many active constituent of glycyrrrhiza are investigated for their effectiveness against spike protein of virus. One constituent among the investigated compounds namely glyasperin A showed the ability to bind to spike protein and inhibit the entry of virus. Angiotensin converting enzyme-2 helps in the entry of SARS-CoV-2. Glycyrrhizin and the active metabolites glycyrrhetinic acid down regulates ACE-2 and it also reduces the expression of type 2 trans membrane serinje protease which is involved in uptake of virus.[12] According to Pan Lau et al glycyrrhizin plays an important role in therapy of COVID-19 as it binds to ACE-2, down regulates inflammatory cytokines and inhibit reactive oxygen species. The ACE-2 favors the entry of SARS-CoV-2 and also supports an anti-inflammatory pathway.

Table 1: Current herbal strategies for management of Covid-19 infections.

Herbs/herbal component	Biological Name	Common name	Parts	Major Constituents	Mechanism of action	References
Giloy	Tinospora cordifolia	Guduchi	Leaves Stem Root	Alkaloids, diterpenoidlactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphaticcompoundsand polysaccharides.	Extractsof Guduchi attenuated the brain mediated lipid level and down-regulated the blood glucose andurinaryglucose level emphasizing its anti-diabetic and lipid-lowering activity.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7484574/
Ashwagandha	Withania somnifera	Indian ginseng, Ajagandha, Winter cherry.	Stem Root Fruit	Isopelletierine, anaferine, cuseohygrine, anahygrine, withanolides, withaferins, saponins, Sitoindosides and acylsterylglucosides.	It improves the body's defense against disease by improving the cell-mediated immunity. It also possesses potent antioxidant properties that help protect against cellular damage caused by free radicals.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3252722/#:~:text=Ashwagandha%20improves%20the%20body's%20defense,damage%20caused%20by%20free%20radicals.
Tulsi	Ocimum tenuiflorum	Holy basil	leaves, stem, flower, root, seeds (whole plant).	Oleanolicacid, Ursolic acid, Rosmarinicacid, Eugenol, Carvacrol, Linalool, andβ-caryophyllene.	Extract of tulsi (has Antimicrobial mosquito repellent, anti-diarrheal, anti-oxidant, etc) help the body and mind cope with a wide range of chemical, physical, infectious and emotional stresses and restore physiological and psychological function.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4296439/#:~:text=These%20studies%20reveal%20that%20tulsi,%2C%20chemopreventive%2C%20radioprotective%2C%20hepato%2D.
Mulethi	Glycyrrhiza glabra	Jethimadhu, Licorice	Root	Glycyrrhizin/Glycyrrhetinic acid, glucuronic acid, glycyrrhetic acid, sugar, volatile oil, starch, carbenoxolone	Glycyrrhetic acid, the active metabolite in licorice, inhibits the enzyme 11-ß-hydroxysteroid dehydrogenase enzyme type 2 with a resultant cortisol-induced mineralocorticoid effect and the tendency towards the elevation of sodium and reduction of potassium levels.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3498851/#:~:text=Glycyrrhetic%20acid%2C%20the%20active%20metabolite,and%20reduction%20of%20potassium%20levels.

Table 1 Cont...

Kakdasinghi	Pistacia integerrima	Karkatshringi	Leaf Stem Bark Galls Fruit	alkaloids, flavonoids, tannins, saponins, sterols	It is beneficial for diarrhea as it prevents the loss of fluid from the body and inhibits the growth of infection-causing bacteria due to its antidiarrheal and antimicrobial properties.	https://www.1mg.com/ayurveda/karkatshringi-185
Sounth	Alpinia galanga	Lengkuas, greater galangal,blue ginger,Siamese ginger, Thai ginger, Galangal	Rhizome	Terpenoids, Diarylheptanoids, Lignans, Flavonoids, Phenolics, Steroids, Alkaloids, Stilbenes	An aqueous acetone extract of fruit of Alpinia galanga shows inhibitory effect on melanogenesis (formation of melanin).	https://innovareacademics.in/journals/index.php/ijpps/article/view/31352/19380#:~:text=An%20aqueous%20acetone%20extract%20of,for%20their%20corrosion%20inhibition%20properties.
Marich	Pipernigrum	Kalimirch, black pepper	Dried unripe fruits	Piperine, piperanine, piperyline, piperlonguminine, piperettine, piperdardine	Black pepper extracts reportedly inhibit food spoilage and food pathogenic bacteria. BPCE inhibited the tricarboxylic acid pathway of the bacteria. The extract significantly increased pyruvic acid concentration in bacterial solutions and reduced ATP level in bacterial cells.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4648884/#:~:text=Black%20pepper%20extracts%20reportedly%20inhibit%20food%20spoilage%20and%20food%20pathogenic%20bacteria.&text=BPCE%20inhibited%20the%20tricarboxylic%20acid,ATP%20level%20in%20bacterial%20cells.
Pipal	Ficus religiosa	Bodhi tree, Pippala tree, Ashvattha	Leaf Bark Shoot Seed Fruit	K, n-octacosanol, methyl oleanolate, lanosterol, stigmasterol, isoleucine, phenylalanine	Ficus religiosa has found to be potential anti-inflammatory & analgesic property. The mechanism underlying the effect is the inhibition of PG's synthesis	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3249921/
Lavang	Syzygium aromaticum	Clove, Laung	Flower buds	Eugenol, caryophyllene, acetyleugenol	It inhibits prostaglandin synthesis, thereby reducing painful symptoms and acts as a germicide to Escherichia coli, Staphylococcus aureus &Pseudomonas aeruginosa	https://go.drugbank.com/drugs/DB11338
Akarkara	Anacyclus pyrethrum	Pellitory, Spanish chamomile, Mount atlas	Roots	Pyrethrin, alkyl amides, anacyclin, inulun, sasamine, hydrocarolin	The extracts of different parts of A. pyrethrum (L) showed a significant analgesic effect against pain caused by acetic acid compared to the control lot, with an inhibition percentage that ranged from 12% to 94% ($p < 0.001$)	https://japsonline.com/admin/php/uploads/1818_pdf.pdf
Nagarmotha	Cyperus scariosus	Nut grass		Cyperene, longifolin, caryophyllene oxide, longiverbenone	It improves digestion due to its Deepan and Pachan properties, if taken in the recommended dosage. Nagarmotha oil is an effective home remedy for managing stomach disorders due to its antispasmodic and carminative properties.	https://www.1mg.com/ayurveda/nagarmotha-58
Dalchini	Cinnamomum verum	Cinnamon		Cinnamaldehyde, eugenol, benzaldehyde, cuminc aldehyde, phellandrene, pinene, cymene caryophyllene	Cinnamon extracts, essential oils, and their compounds have been reported to inhibit bacteria by damaging cell membrane; altering the lipid profile; inhibiting ATPases, cell division, membrane porins, motility, and biofilm formation; and via anti-quorum sensing effects.	https://pubmed.ncbi.nlm.nih.gov/29702210/#:~:text=Results%3A%20Cinnamon%20extracts%2C%20essential%20oils,via%20anti%2Dquorum%20sensing%20effects.

Table 1 Cont...

Daruhaldi	Berberis,aristate	Darvi, Chitra		berberine,berbamine, berbinium, berlambine, palmatine, columbamine, Jatrorrhizine, oxyberberine oxyacanthine, and magnoflorine	It has anti-pyretic, anti-bacterial, anti-microbial, anti-hepatotoxic, anti-hyperglycaemic, anti-cancer, anti-oxidant and anti-lipidemic properties.B. aristata extracts and its formulations are also useful in the treatment of diarrhoea, haemorrhoids, gynaecological disorders, HIV-AIDS, osteoporosis, diabetes, eye and ear infections, wound healing, jaundice, skin diseases and malarial fever.	https://pubmed.ncbi.nlm.nih.gov/22808523/
Anantmool	Hemidesmus indicus	Indian Sarsaparilla	Root Steam Leaves	Hexatriacontane, αamyrin, βamyrinlupeol, octacosanoate, sitosterol, coumarino-lignoid-hemidesminine, hemidesmin I and hemidesmin II50 Calogenin, acetylcalogenin-3-0-β-D-digitoxopyrannosyl-0-β-D-digitoxopyronsyl-0-β-D-digitoxopyranoside, hexadecanoic acid Tannins, flavonoids, hyperoside, rutin and coumarino, Leucoderma lignoids suchas hemidesminine, hemidesmin I and hemidesmin II	It is a depurative and tonic that is used to treat patients with chronic skin disease and other conditions such as cough, genitourinary disease, and rheumatism. Oral administration of an ethanol extract decreased activity in both cell-mediated and humoral components of the immune system Its activity is mild and may benefit patients with autoimmune disease by suppressing the Th-2 cell response.	https://www.researchgate.net/publication/353022566_hemidesmus_indicus_anantmool_a_potential_traditional_plant_with_antivenom_activity
Chandan	Santalum album	Sandalwood	Wood	sesquiterpenic alcohols(tricyclic α-santalol, β-Santalol)	The methanolic extract of wood was confirmed for antioxidant, free radical scavenging, analgesic and anti-inflammatory activities. α and β santalols present in sandal oil showed sedative effects. Its oil showed significant changes in hepatic xenobiotic metabolizing enzymes and its major constituents showed less acute oral and dermal toxicity.	https://www.koreascience.or.kr/article/JAKO201824753344011.pdf

Glycyrrhizin and its active metabolite glycyrrhetinic acid have anti-inflammatory activity through Toll-like receptor 4 antagonism, which may reduce the protection of the down-regulated ACE-2. Both are involved in reducing the expression of type 2 transmembraneserine protease, which is crucial for virus uptake.[13] Moreover the chemical constituents of *A. indica* such as nimbidin , nimbolide, nimocinol, nimbandiol, and isomeldenin possess the ability to inhibit Covid-19.[14] Furthermore *A. sativum* contain chemical constituents that possesses the potential of reducing expression of proinflammatory cytokines and prevent SARS-CoV-2 infection.[15–17] Moreover according a research the phyto-constituent found in the herbs like ginger, haldi, cloves and lemon were being assessed by the help of molecular docking about their effectiveness of against COVID-19.[18,19]Table 1 explains about the current herbal strategies that is being used for the management of COVID-19.

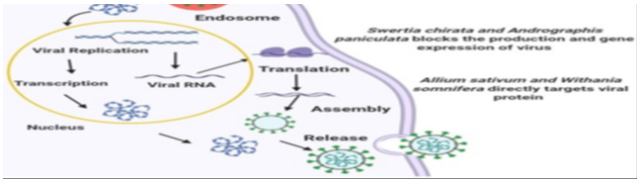

Fig. 2: Potential antiviral mechanism of Indian plants.

5. Conclusion

COVID-19 has been a major concern over the last two years and presently there are no permanent drugs for the treatment of COVID-19 is available. However few drugs are being used for the management of COVID-19but they are associated with unwanted side effects and are costly as well but if we can shift our focus to the drugs available in the form of plants and herbs we can find out more holistic approach towards the treatment of COVID-19. Present study explains about different herbs of Indian origin, having the potential to act against Covid-19 that can be investigated further for future use.

6. Source of Funding

None.

7. Conflict of Interest

None.

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