A Possible Role of Medicinal Plants in finding a Cure for Covid-19
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ABSTRACT
Since the outbreak, COVID-19 (SARS-CoV-2) has affected more than 24 million people. COVID-19 pandemic appears to lack any effective antiviral drug or vaccine therapy. Previously, it has been reported that medicinal plants are effective against pneumonia caused by coronavirus (SARS-CoV). Secondary metabolites derived from medicinal plants also play pivotal role in strengthening the immune system as well as the killing of pathogens or viruses. The present review summarized the medicinal plants and their secondary metabolites that have antiviral potentials. Further studies are required to evaluate these medicinal plants and their secondary metabolites for possible treatment of COVID-19.

Key Words: Antiviral, Covid-19, Medicinal Plants, Traditional Herbal Medicine.

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Introduction
Corona viruses (SARS-CoV) are a large family of RNA viruses that can infect a wide range of mammalian and avian hosts with a broad spectrum of diseases. Corona viruses are diversified group due to higher mutation rate and recombination during replication. Human corona viruses are pathogens which cause respiratory complications. In the past decades, Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) have placed human corona virus into the spotlight due to its higher pathogenicity. The phylogenetic analysis of corona virus disease 2019 (COVID-19) showed that this novel corona virus is from the family of severe acute respiratory syndrome coronavirus, (SARS-CoV), hence, it is named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The current pandemic has created a huge burden on the health care system of many countries. The present therapeutic conditions and disease burden has made researchers to revisit potential efficacy of medicinal plants and herbs by identifying potential phytochemicals and their derivatives in treating COVID-19. Plant-based medicines or herbal medicines are already in use for treating different viral infections. Traditionally, herbs were used as medicines to treat diseases however right dosage is important. Herbal derivatives are a variety of complex compounds, therefore it is a challenge to determine effective compounds in terms of therapeutic dose and reproducibility. Their diversified active molecular composition has the ability to identify, the specific receptors. This review aims to highlight the importance of plant-based natural products, herbs and their derivatives that shows potential antiviral activity for corona virus inhibition. It is hoped that the consolidated information presented in this review may be a guide for future research prospect.

1. Medicinal Plants and their chemical constituents with antiviral potential
Various plant-based natural products have been studied for their antiviral potential and it was reported that their main mechanism of action is inhibiting the viral replication. Although there are many but only a few have been discussed here to highlight their importance in viral therapeutics.

1.1. Nigella sativa L.
Nigella sativa L. (black cumin) has been globally acknowledged as an herbal medicine, It is effective against wide range of health problems. It belonged to the Ranunculaceae family and is a proven

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historical and religious remedy both in Islam and Christianity.\textsuperscript{10,11} Not only its seeds but the oil extracts have medicinal importance. It is reported that oil extracts can inhibit virus growth even with reduced titer of viral load in infected individual. Volatile oil from \textit{Nigella sativa} also has significant anti-inflammatory properties at various doses.\textsuperscript{12} The boiled extract of its seeds has bronchial relaxant properties and tracheal responsiveness. Some of its chemical constituents with medicinal importance are \textit{Nigellidine}, quinone, \textit{α}-hederin, thymoquinone, \textit{p}-cymene, \textit{α}-thujene, thymol, \textit{t}-anethole, \textit{β}-pinene, \textit{α}-pinene, and \textit{γ}-terpinene with anti-diabetic, anti-cancerous, antiviral, antibacterial, anti-inflammatory, anti-algesic properties.\textsuperscript{13,14} Furthermore, some other studies reported use of black cumin with honey for COVID-19 treatment.\textsuperscript{15} Honey have flavonoids that have antibacterial, anti-inflammatory, antioxidant, antifungal and antiviral potential.\textsuperscript{16}

\textbf{1.2. \textit{Curcuma longa} L.} 
Curcumin (diferuloylmethane) is a natural compound, a polyphenol extracted from turmeric (\textit{Curcuma longa} L.). It is used as a food additive and also has medicinal importance. Its mode of action against viruses is that it cut off virus adhesion to the host cell.\textsuperscript{17} It plays vital role against treating influenza, hepatitis C and HIV virus. It has the potential to integrate catalytic core of enzymes and forbid it from binding from different substrates against human respiratory syncytial virus, thus preventing the infection.\textsuperscript{18,19}

\textbf{1.3. \textit{Trigonella foenum-graecum} L.} 
\textit{Trigonella foenum-graecum} L. (Fenugreek) has pharmacological potential against inflammations, cancer, viruses and bacteria.\textsuperscript{20} They help in controlling various enzymatic activities, fever, body pain.\textsuperscript{21} So it is considered as one of the remedies to relieve some symptoms of SARS-CoV viruses.

\textbf{1.4. \textit{Olea europaea} L.} 
Olive oil extracted from \textit{Olea europaea} L. contains various polyphenolic compounds that possess antiviral, antioxidant, anti-bacterial, anti-inflammatory and anti-allergic activities.\textsuperscript{22} Olive oil derivatives like oleuropein, tyrosol, hydroxytyrosol, verboscoside, ligustroide, demethyloliveuropein are considered a potent antimicrobial and antiviral agents against herpes, hepatitis, rota, influenza type 3, bovine rhino, canine parvo, and feline leukemia virus. The olive leaf extract is also found effective in control of viral infection.\textsuperscript{23}

\textbf{1.5. \textit{Zingiber officinale} Roscoe} 
\textit{Zingiber officinale} Roscoe (Ginger) is a commonly used as a folk medicine or spice. Its chemical constituents are terpenes, phenolic compounds lipids, polysaccharides, raw fibers and organic acids. Its phenolic compounds are well known for the health benefits. Ginger has been proved to have antifungal, antibacterial, antiviral, anti-inflammatory and anticancer activities.\textsuperscript{24} It has also been noted that ginger is beneficial against human respiratory viruses like human respiratory syncytial virus. It is reported that ginger block viral attachment.\textsuperscript{25} There is potential in investigating role of ginger against coronavirus as many studies have shown its effect against other viruses.

\textbf{1.6. \textit{Aloe vera} (L) Burm.f} 
It is one of the extensively studied medicinal plants worldwide. Many reports show the pharmacological potential of this plant including antiviral activities.\textsuperscript{26,27} Mainly, anthraquinones in \textit{Aleo vera} imparts antiviral activity, however, many other bioactive molecules were also identified including catechin, emodin, quercetin, azidothymidine, kaempferol, acyclovir, acemannan, aloin. Recently, Jang-Gi et al, reported that ethanol extracts of \textit{Aleo vera} have significant anti-influenza virus activity.\textsuperscript{28} Its potential antiviral activity is also reported against COVID-19, both separately or in combination with other plant species.\textsuperscript{29} Extracts of \textit{Aloe vera} can inhibit the expression of pro-inflammatory markers and receptors involved in the induction of acute respiratory distress.\textsuperscript{30}

\textbf{1.7. \textit{Glycyrrhizae uralensis} fisch} 
\textit{Glycyrrhizae Radix et Rhizoma} is the herbaceous plant, approved as antiviral by the China food and drug administration (CFDA). Many studies documented that \textit{Glycyrrhizae} inhibits attachment of virus, entry in the cell and replication. Li and Peng reported that \textit{Glycyrrhizae} is effective plant against combating SARS.\textsuperscript{31} \textit{Glycyrrhizae Radix} has an anti-inflammatory potential and reported for the treatment of inflammatory lung condition.\textsuperscript{32} During the current pandemic this herb is used in different traditional formulas to treat the disease, regardless of disease stage.\textsuperscript{33}
1.8. Azadirachta indica A. Juss

Azadirachta indica A. Juss which is also called Neem, is an important medicinal plant and its clinical significance is mentioned in age-old medical systems like Ayurveda and Siddha. The insecticidal, antimicrobial, larvicidal, antimalarial, antibacterial, antiviral, and spermicidal effect of different parts of the plant, has been reported. Roy and Bhattacharyya reviewed different studies which documented promising antiviral potential of neem. No experimental data is available to correlate the medicinal potential of neem for the treatment of COVID-19 patients but as neem crude extract is a widely used Ayurvedic medicine to treat normal fever and malarial fever which are the common systems of Covid-19, this medicinal plant is highly recommended for treatment of patients suffering from Covid-19.

1.9. Camellia sinensis L

Different refined forms of tea especially black tea and green tea are rich sources of multi-functional bioactive molecules exhibiting antioxidative, anti-inflammatory, antitumorigenic and antiviral properties. Epigallocatechin gallate (EGCG) is a polyphenolic catechin present in Camellia sinensis (L.), especially in green tea and reported to inhibit Covid-19. Similarly, Theaflavins (TFs) are polyphenols, found abundantly in black tea, documented to have inhibition potential for Covid-19.

2. Different herbal treatment in practice

Extensive research has been done to understand the mode of action and pathogenesis of viral infection. Apart from modern medicine different traditional medicines are also in practice like Unani, Ayush, Chinese herbal, African herbal treatment. In this section, the highlighted portion will be from different herbal treatment practices around the globe. However, comprehensive studies on proper understanding of these treatments modalities are still scarce.

2.1. African herbal treatment

Herbal treatment has long history in different cultures. Patients have benefitted but for its application at global level, these traditional medicines have to go through in vitro and in vivo analysis to establish efficacy, toxicity and safety doses. Only then, effective COVID-19 treatment can be reported.
ribosomal protein replication and one of the TCM for COVID-19 treatment, Qingfei Paidu decoction (QPD, mixture of 20 herbs) consists of Scutellaria baicalensis, Magnolia officinalis, Pogostemon cablin, Glycyrrhizin, Ephedra spp., Atractylodes macrocephala, Armeniaca spp., Herbacetin, Scutellarin, Quercetin, Baicalin, Nicotianamine and Forsythia suspense. These compounds were found effective against viruses of upper respiratory tract infections.

**Conclusion**

In the treatment and prevention of COVID-19 medicinal plants and their standardized crude extracts or compounds can play vital role. The present review highlighted possible therapy, mechanism of action of medicinal plants, their standardized crude extracts and chemical constituent for the treatment of COVID-19. Further evaluation and testing, especially molecular mechanisms and simulation are required to identify the effect of medicinal plants and their chemical compounds on COVID-19.

**REFERENCES**

1. Zumla A, Chan JF, Azhar EI, Hui DS, Yuen KY. Coronaviruses—drug discovery and therapeutic options. Nature reviews Drug discovery. 2016; 15: 327-47.
2. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses. 2019; 11: 59.
3. Gorbalenya A, Baker S, Baric R, de Groot R, Drosten C, Gulyaeva A, et al. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nature microbiology. 2020; 2020: 3-4.
4. Liu Y, Gayle AA, Wilder-Smith A, Rocklov J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. Journal of travel medicine. 2020; 27: 21.
5. Tabutri J, Lye KA, Dhillion SS. Traditional herbal drugs of Bulamogi, Uganda: plants, use and administration. Journal of ethnopharmacology. 2003; 88: 19-44.
6. Diallo D, Paulsen BS. Pharmaceutical research and traditional practitioners in Mali: Experiences with benefit sharing. Responding to Bioprospecting from biodiversity in the South to medicines in the North. 2000: 133-44.
7. Etkin NL. Indigenous patterns of conserving biodiversity: pharmacologic implications. Journal of Ethnopharmacology. 1998; 63: 233-45.
8. Wu C, Liu Y, Yang Y, Zhang P, Zhong W, Wang Y, et al. Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. Acta Pharmaceutica Sinica B. 2020.
9. Begum S, Mannan A. A Review on Nigella sativa: A Marvel Herb. Journal of Drug Delivery and Therapeutics. 2020; 10: 213-9.
10. Islam MT, Khan MR, Mishra SK. An updated literature-based review: phytochemistry, pharmacology and therapeutic promises of Nigella sativa L. Oriental Pharmacy and Experimental Medicine. 2019; 19: 115-29.
11. Shrivastava RM, Agraval RC, Parveen ZE. A review on therapeutic applications of Nigella sativa. J Chem Chem Sci. 2011; 1: 241-8.
12. Salem ML, Hossain MS. Protective effect of black seed oil from Nigella sativa against murine cytomegalovirus infection. International journal of immunopharmacology. 2000; 22: 729-40.
13. Yimer EM, Tuem KB, Karim A, Ur-Rehman N, Anwar F. Nigella sativa L.(black cumin): a promising natural remedy for wide range of illnesses. Evidence-Based Complementary and Alternative Medicine. 2019; 2019: 1528635.
14. Al-Jassir MS. Chemical composition and microflora of black cumin (Nigella sativa L.) seeds growing in Saudi Arabia. Food Chemistry. 1992; 45: 239-42.
15. Patel S, Cichello S. Manuka honey: an emerging natural food with medicinal use. Natural products and bioprospecting. 2013; 3: 121-8.
16. Ahmed S, Othman NH. Honey as a potential natural anticancer agent: a review of its mechanisms. Evidence-Based Complementary and Alternative Medicine. 2013; 2013: 829070.
17. Mounce BC, Cesaro T, Carrau L, Vallet T, Vignuzzi M. Curcumin inhibits Zika and chikungunya virus infection by inhibiting cell binding. Antiviral research. 2017; 142: 148-57.
18. Chen D, Shien J, Tiley L. Curcumin inhibits influenza virus infection and haemagglutination activity. Food Chemistry. 2010; 119: 1346-51.
19. Praditya D, Kirchhoff L, Brüning K. Anti-infective Properties of the Golden Spice Curcumin. Frontiers in Microbiology.
20. Moradi N, Moradi K. Physiological and pharmaceutical effects of fenugreek (Trigonella foenum-graecum L.) as a multipurpose and valuable medicinal plant. Global journal of medicinal plant research. 2013; 1: 199-206.

21. Naidu MM, Shyamala BN, Naik JP, Sulochanamma G, Srinivas P. Chemical composition and antioxidant activity of the husk and endosperm of fenugreek seeds. LWT-Food Science and technology. 2011; 44: 451-6.

22. Fredrickson WR. F and S Group, Inc. Method and composition for antiviral therapy with olive leaves. US Patent. 2000.

23. Micol V, Caturla N, Pérez-Fons L, Más V, Pérez L, Estepa A. The olive leaf extract exhibits antiviral activity against viral haemorrhagic septicaemia rhabdovirus (VHSV). Antiviral research. 2005; 66: 129-36.

24. Mao QQ, Xu XY, Cao SY, Gan RY, Corke H, Li HB. Bioactive compounds and bioactivities of ginger (Zingiber officinale Roscoe). Foods. 2019; 8: 185.

25. San Chang J, Wang KC, Yeh CF, Shieh DE, Chiang LC. Fresh ginger (Zingiber officinale) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. Journal of ethnopharmacology. 2013; 145: 146-51.

26. Singh S, Sharma PK, Kumar N, Dudhe R. Biological activities of Aloe vera. Int. J. Pharm. Technol. 2010; 2: 259-580.

27. Sharrif MM, Sandeep KV. Aloe vera their chemicals composition and applications: A review. Int J Biol Med Res. 2011; 2: 466-71.

28. Choi JG, Lee H, Kim YS, Hwang YH, Oh YC, Lee B, et al. Aloe vera and its Components Inhibit Influenza A Virus-Induced Autophagy and Replication. The American journal of Chinese medicine. 2019; 47: 1307-24.

29. Anonymous. Accessed on 18/04/2020 Available: https://doingbuzz.com/urgentcoronavirus-un-traitement-et-uneprevention-qui-marche-aloe-vera-video/.

30. Mpiana PT, Tshibangu DS, Kilembe JT, Gbolo BZ, Mwanangombo DT, Inkoto CL, et al. Aloe vera (L.) Burm. F. as a Potential Anti-COVID-19 Plant: A Mini-review of Its Antiviral Activity. European Journal of Medicinal Plants. 2020; 31: 86-93.

31. Li T, Peng T. Traditional Chinese herbal medicine as a source of molecules with antiviral activity. Antiviral research. 2013; 97: 1-9.

32. Yang Xi, Liu D, Bian K, Zhang DD. Study on in vitro anti-inflammatory activity of total flavonoids from Glycyrrhizae Radix et Rhizoma and its ingredients. Zhongguo Zhong yao za zhi= Zhongguo zhongyao zazhi= China journal of Chinese materia medica. 2013; 38: 99-104.

33. Ang L, Lee HW, Choi JY, Zhang J, Lee MS. Herbal medicine and pattern identification for treating COVID-19: a rapid review of guidelines. Integrative Medicine Research. 2020; 29: 100407.

34. Gupta SC, Prasad S, Tyagi AK, Kunnunakkara AB, Aggarwal BB. Neem (Azadirachta indica): An indian traditional panacea with modern molecular basis. Phytomedicine. 2017; 34: 14-20.

35. Roy S, Bhattacharyya P. Possible role of traditional medicinal plant Neem (Azadirachta indica) for the management of COVID-19 infection. International Journal of Research in Pharmaceutical Sciences. 2020; 11: 122-5.

36. Sujawarso W, Keim AP, Caneva G, Toniolo C, Nicoletti M. Ethnobotanical uses of neem (Azadirachta indica A. Juss.; Meliaceae) leaves in Bali (Indonesia) and the Indian subcontinent in relation with historical background and phytochemical properties. Journal of Ethnopharmacology. 2016; 189: 186-93.

37. Chacko SM, Thambi PT, Kuttan R, Nishigaki I. Beneficial effects of green tea: a literature review. Chinese medicine. 2010; 5: 1-9.

38. Mhatre S, Srivastava T, Naik S, Patrawale V. nAntiviral Activity of Green Tea and Black Tea Polyphenols in Prophylaxis and Treatment of COVID-19: A Review. Phytomedicine. 2020; 17: 153286.

39. Sohag AA, Hannan MA, Rahman S, Hossain M, Hasan M, Khan MK, et al. Revisiting potential druggable targets against SARS-CoV-2 and repurposing therapeutics under preclinical study and clinical trials: A comprehensive review. Drug Development Research. 2020.

40. Vellingiri B, Jayaramayya K, Iyer M, Narayanasamy A, Govindasamy V, Giridharan B, et al. COVID-19: A promising cure for the global panic. Science of The Total Environment. 2020; 4: 138277.

41. Onyeji CO. Management of coronavirus disease 2019 (COVID-19)–Is there a role for complementary and herbal medicinal products?. African Journal of Traditional, Complementary and Alternative Medicines. 2020; 17: 33-8.

42. Del Rio C, Malani PN. COVID-19—new insights on a rapidly changing epidemic. Jama. 2020; 323: 1339-40.

43. Nikhat S, Fazil M. Overview of Covid-19; its prevention and management in the light of Unani medicine. Science of The Total Environment. 2020; 22: 138859.

44. Priya R. The status and role of AYUSH and local health traditions in public health. The Newsletter of the International Institute of Asian Studies. 2013; 65: 24-5.

45. COVID-19: Ministry of Ayush starts clinical trials for Ashwagandha and 4 other Ayurvedic herbs for coronavirus treatment. Science blog https://timesofindia.indiatimes.com/lifestyle/health-fitness/home-remedies/9-globally-popular-herbal-medicines/photosstory/75474449.cms?picid=75474508.

46. Ang L, Lee HW, Choi JY, Zhang J, Lee MS. Herbal medicine and pattern identification for treating COVID-19: a rapid review of guidelines. Integrative Medicine Research. 2020; 29: 100407.

47. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020.

48. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell research. 2020; 30: 269-71.