International Journal of Botany Studies
ISSN: 2455-541X; Impact Factor: RJIF 5.12
Received: 24-10-2020; Accepted: 09-11-2020: Published: 29-11-2020
www.botanyjournals.com
Volume 5; Issue 6; 2020; Page No. 310-315

Understanding the role of potent herbal drugs in management of Covid-19: A need in present scenario

Shalini[1], Aparna Singh[2], Ashutosh Pathak[3]

[1] Assistant Professor, Department of Kayachikitsa, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

[2] Assistant Professor, Department of Kriya Sharir, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

[3] Assistant Professor, Department of Rachana Sharir, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Abstract
The current situation is alarming as there is not any specific effective treatment for COVID-19. Ayurveda, the traditional Indian medicine visualizes that Covid-19 is not described in ayurvedic classical literatures but after examining the *doshas* (humour) and other indigenous factors involved in their manifestation of Covid-19 it may be considered as an *Aupasargika Roga* (contagious disease) which is pandemic in nature. Ayurveda renders to serve as preventive as well as curative effect in treatment of Covid-19. The Ayurveda doctrine relies that if *vyadhikshamatva* (immunity) of a person is strong then even after exposure to viruses, one will not be affected. During a pandemic Ayurveda emphasizes on increasing the immunity of people by promoting the intake of traditional herbs or decoctions. Hence this study was undertaken to study the role of potent herbal drugs in prevention of Covid-19.

Keywords: Covid-19, herbal drugs, ayurveda

Introduction
Corona viruses are a major group of viruses that mostly affects human beings through zoonotic transmission. In the last two decades, this is the third case of the emergence of a novel corona virus, after severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome corona virus (MERS CoV) in 2012 [1, 2]. Corona viruses (CoVs) are enveloped, single stranded RNA viruses ranging from 60 to 140 nm in diameter with spike (glycoprotein)-like projections on its surface, looks like crown appearance under the electron microscope, that's why the named CoV. There are four corona viruses namely HKU1, NL63, 229E, and OC43 have been found in circulation in humans, and generally cause mild respiratory disease [3].

The current scenario of *Covid -19* Pandemic has been derived from two words '*pan* – *"*all" + *demos* – *'*people' and originated from Greek word *pandemos "pertaining to all people"*. *So*, it is referred to as an extensive epidemic of infectious disease affecting throughout the entire country or one or more continents at the same time.

On December 2019, there was an outbreak of pneumonia of unknown cause in Wuhan, Hubei province in China, the wholesale Market of live animals. After few days, (i.e. 7th January 2020) Chinese health authorities confirmed that this outbreak was associated with a novel CoV and was named CoV disease-19 (COVID-19) by the World Health Organization (WHO) [4]. It was found that, COVID-19 is closely related with bat-derived severe acute respiratory syndrome (SARS-CoV) -like CoV (bat-SL-covzc45 and bat-SL-covzxc21) (~ 88% identity) [5]. Data as received by WHO from national authorities by 10:00 CEST, 13 August 2020, total no of Covid-19 cases 20439814 and death 744 385 were reported globally. Number of confirmed COVID-19 cases reported by India was 2396637 and death was 47033 [6].

The most common symptoms that are visualized at an initial stage were fever (99%), fatigue (70%), dry cough (60%), myalgia (44%) and dyspnoea [7, 8] whereas the less common symptoms in Covid- 19 were headache, dizziness, diarrhoea, nausea and vomiting [9]. The symptoms such as pharyngeal pain, dyspnoea, dizziness, abdominal pain and anorexia were in patients with severe illnesses [9].

Material and Methods
An extensive search on Covid-19 was undertaken as well as relevant data were searched in different ayurvedic literatures as well as the research papers published in different scholarly journals were also searched online from various scientific electronic database viz. Pubmed, Google scholar, Science direct etc.

Discussion
Role of Ayurveda in Covid-19
As this disease entity of COVID-19 is a new one and has not been mentioned as such in the classics of *Ayurveda*. Acharya Charaka encapsulates that there are so many diseases which are not described in the texts so this type of should be treated after examining the doshas (humour) and other factors involved in their manifestation. Covid-19 may be considered as an *Aupasargika Roga* (contagious disease) which is pandemic in nature. In this case virus plays a role of upasarga (infection) and develops *Aupsargika Sankramaka Roga* (Communicable disease) which affects

the subject in whom *Vyadhikshamatva* (immune strength) is compromised. Acharya Dalhana has mentioned about involvement of Kapha Dosha in *Sankramaka roga*(communicable diseases) that spreads especially through droplet infection. This looks like the *Janapododwamsa janya vikara* as described in texts of Ayurveda.

Why ayurveda is needed: The need for alternatives arises because of some of the following reasons. (Figure.1)

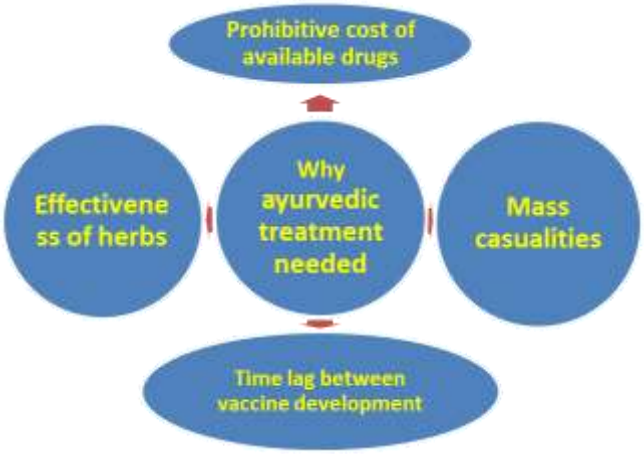

Fig 1

Solutions from Nature: Ayurveda the traditional Indian medicine is one of the world's oldest and holistic forms of medicine which lays emphasis on both preventive and curative aspects of a disease. The main purpose of Ayurveda is *Swasthasya swaasthya rakshanam* (Maintenance of wellness of a healthy person) and *Athurasya vikara prashamanam* (Curing of the ailment in a patient). According to Ayurveda principle, if *vyadhikshamatva* (immunity) is strong of the person then even after exposure to viruses, one will not be affected. During a pandemic, Ayurveda emphasizes on the immunity of people living in regions affected by viruses. This branch of medicine promotes the intake of special herbs or decoctions to increase the immunity level of the people. WHO has also suggested that we need to learn to live with the virus hence the world is now focusing in the preventive guidelines issued by the government as well focus on health in order to increase immunity? Ayurvedic medicinal herbs have safety with potential efficacy, broad-spectrum applicability, ease of availability & administration, long-term practical knowledge on clinical use, and as far as possible, affordability.

Relevance of traditional herb in Ayurveda used for the treatment of covid-19

1. ***Withania somnifera*** **(**Ashwagandha**):** Withania somnifera is a very popular herb used in ayurvedic medicines, belongs to family Solanaceae. It is used for the prevention and treatment of many diseases, such as arthritis, impotence, anxiety, cancer, neurodegenerative, cardiovascular diseases. Ashwagandha increase energy as well as stamina and strengthen immune function and help the body to overcome imbalance caused by mental or physical stress [10]. Its active compounds include like anaferine, anahygrine, beta-sisterol, chlorogenic acid, cysteine, cuscohygrine, pseudotropine, scopoletin, somniferinine, withaferin α, withanine, withananine, and withanolides. The recent studies indicate that Ashwagandha along with other ayurvedic plants stimulated the immune system and had no toxic effects. Withaferin A had a potent anti-bacterial, immuno-modulating and anti-inflammatory property in it [11].
2. ***Curcuma longa*** **(Turmeric):** Turmeric is a spice obtained from the rhizomes of Curcuma longa, belongs to the ginger family (Zingiberaceae). It is also called as 'Golden Spice of India' because of its bright yellow colour due to polyphenolic pigments known as curcuminoids. The most active constituents of turmeric are curcumin. Curcumin has antioxidant, anti-inflammatory, antiviral and antifungal property. Curcumin modulates immune system by suppressing T-cells, proliferating number of B-cells and reducing proliferation of immature B-cell lymphoma cells. Curcumin treatment inhibited the production of cytokines [12].
3. ***Alium sativum*** **(Garlic):** *Alium sativum*, also known as Lahsan belongs to family Amaryllidaceae, has been used for both cooking and medicinal purposes. Lahsun has a typical pungent, spicy flavour and has been used for hundreds of years to for the treatment of fungal, parasitic and viral infections. Garlic also has anti-inflammatory properties that show promise for prevention of cardiovascular disease. It also kills influenza virus *in vitro* [13]. *A. Sativum* extract called ajoene protects CD+ cells from attack by HIV early in the viral life cycle. Ajoene is found only in fresh *A. Sativum*. *In vitro* study, antiviral activity of *A. sativum* extract on human cytomegalovirus (HCMV) was also evaluated. A dose-dependent inhibitory effect of A. sativum extract was marked when GE was applied simultaneously with HCMV [14]. The *in vitro* antiviral effect of garlic against parainfluenza virus type 3 and human Rhinovirus type 2 has also been evaluated [15].
4. ***Zingiber officinale*** **(Ginger):** *Zingiber officinale* (Ginger), belongs to the family Zingiberaceae has pungent smell and flavor of ginger root due to mixture of zingerone, and gingerols, volatile oils and sulphur-containing compounds (allicin, and ajoene), and enzymes. The antibiotic properties of allicin are well known. The allicins have proved fibrinolytic activity, which reduces platelet aggregation by inhibiting prostaglandin E2. Compounds in ginger also increase levels of antioxidant enzymes, including superoxide dismutase and glutathione peroxidase, which may be beneficial in inflammatory reactions triggered by viral infections [16]. Anti-influenza cytokine, TNF-*α*, have been reported to be present in *Z. officinale* [17].
5. ***Ocimum sanctum*** **(Tulasi):** *O. sanctum*, (Holy Basil) also known as Tulsi is an aromatic plant belongs to the family Lamiaceae. The plant, as a whole, is a treasure house of potent compounds that's why it is very important for medicine purpose and considered as divine by the Hindus. Prakash *et al*. (1972) study indicate that *O. sanctum* act as COX-2 inhibitor, like many modern painkillers, due to its high concentration of eugenol [18]. *Tulasi* leaves contain highest percentage of essential oils, infusion of which is given in malaria. Fresh tulasi leaves cure fever and when mixed with

honey and ginger juice, it is useful in cough and bronchitis [19]. During the past few decade, antiviral activity [20] of Tulasi plant has been extensively investigated. *O. tenuiflorum* extracts in peripheral blood mononuclear cells and the active component(s) responsible for immune-modulator action were identified [21].

6. ***Tinospora cordifolia* (Giloy):** *Tinospora cordifolia*, Sanskrit name is "Guduchi", belongs to family Menispermaceae is commonly used in the treatment of various diseases in the ayurveda. The active constituents of giloya are diterpene compounds, including tinosporone, tinosporic acid, and a glucosidal bitter principle, as well as polysaccharides [22]. These active compounds had adaptogenic and immune-modulating properties.

   The study by Fortunatov MN (1952) immune-modulating activity of giloya has been studied and it was found that active constituents of giloya causes significant increases in IgG antibodies in serum, along with macrophage activation [23]. In another study by Shah A *et al*. (2013) the traditional uses suggest that mixing one foot long of the Giloy herb and seven leaves of Tulsi could effectively prevent infection of swine flu [24].

7. ***Glycyrrhiza glabra* (Yashtimadhu):** Glycyrrhiza glabra also known as Mulethee in hindi and Licorice in English belongs to the family Papilionaceae contains sweet-tasting compounds called anethole and glycyrrhizic acid. Glycyrrhizic acid is an antiviral compound significantly sweeter than sugar [25]. The powdered form of licorice root is an effective expectorant, and has been used for this purpose since ancient times. The roots of G. glabra have been used for throat and upper respiratory tract-related infections. It contains many phenolic compounds such as flavonoids and their glycosides, coumarin, and cinnamic acid derivatives. The active constituents of Licorice Triterpine, Saponins, particularly Glycyrrhizinic acid have shown antiviral activity [26]. Polysaccharide fractions obtained from *G. glabra* stimulate macrophages [27] and hence elevate and assist immune stimulation [28]. Also animal studies have revealed its efficacy against the influenza a virus that is mediated by stopping the virus replication [29]. Glycyrrhizic acid present in the plant inhibits virus growth and inactivates virus particles [30].

8. ***Alium sativum* (Lahsan):** *Alium sativum*, also known as Lahsan and Garlic, belongs to family Alliaceae. It has a characteristic pungent and spicy flavor. *A. sativum* has been used for hundreds of years to treat fungal, parasitic, and viral infections and also has anti-inflammatory properties that show promise for prevention of cardiovascular disease. *In vitro* study indicates that it kills influenza virus [31]. The recent studies are focusing on an extract of *A. sativum* called ajoene, which protect CD+ cells from attack by HIV early in the viral life cycle.

   Ajoene, the active component of A. sativum is found only in fresh form. *In vitro* antiviral activity of *A. sativum* extract (GE) on human cytomegalovirus (HCMV) was evaluated in tissue cultures, plaque reduction, and early antigen assay. A dose-dependent inhibitory effect of A. sativum extract was evident when GE was applied simultaneously with HCMV [32]. The *in vitro* antiviral effect of A. sativum against parainfluenza virus type 3 and human Rhinovirus type 2 has also been evaluated [33].

9. ***Mentha piperita* (Peepermint):** *Mentha piperita*, family Labiatae, is a herbaceous rhizomatous perennial plant widely used in Ayurved [34]. It contains volatile oil, also known as menthae piperitae aetheroleum. The major components of the oil are menthol (29%), menthone (20%–30%), and menthyl acetate (3%–10%). Other compounds found in *M. piperita* are flavonoids, polymerized polyphenols, carotenes, tocopherols, betaine, and choline [35]. *In vitro* study, Aqueous extracts of *M. piperita* leaves exhibited antiviral activity against Influenza A [36].

10. ***Azadirachta indica* (Neem):** *Azadirachta indica* (Neem) is a tree of the family Meliaceae. In neem oil, three bitter chemicals have been extracted named nimbin, nimbinin, and nimbidin [37]. The seeds of *A. indica* contain a complex secondary metabolite azadirachtin. All parts of this plant yield *β*-sitosterol. The antiviral activity of azadirachtin, nimbin, and nimbidin has been proved. *A. indica* extracts possess antidiabetic, antibacterial, and antiviral properties. There is some evidence that show neem phytoconstituents interfere with viral reproduction, thus minimizing the impact of viral infections. Effect of Azadirachtin on the replication of Dengue virus type-2 has also been reported [38].

    A recent study by Sarkar L *et al*. (2020) indicates ameliorating effect of Neem extract on propagation and pathophysiology of the coronavirus family [39]. In a computational approach study, a total of 70 compounds from *A. indica* were virtually screened against SARS-CoV-2 Membrane (M) and Envelope (E) proteins and further analyzed with molecular dynamics simulations. The compounds bind to biologically critical regions of M and E, indicating their potential to inhibit the functionality of these two components [40]. Thus, neem can serve as a source of promising future antiviral drugs.

11. ***Trachyspermum ammi* (Ajwain):** *Trachyspermum ammi*, called as Ajwain in Hindi and Bishops weed in English, belongs to the family Apiaceae. The principal constituents of the essential oil obtained from the fruit are the phenols, mainly thymol and some carvacrol. The essential oil is a strong antiseptic [41], antispasmodic, aromatic, bitter, diaphoretic, digestive, diuretic, expectorant, and tonic [42]. It is used orally in the treatment of colds, coughs, influenza, and asthma. The essential oil is also added to various cough medicines as well [43].

    In vitro assay, Hussein G *et al*. (2000) the antiviral study of Ajwain was carried out on the methanolic extract of the herb which showed significant inhibitory effects on Hepatitis C Virus (HCV) protease [44]. Another *In vitro* study done by Roy S *et al*. (2015) proved that, Ajwain oil has potent antiviral activity against Japanese encephalitis virus [45].

12. ***Andrographis paniculata* (Kalmegha):** *Andrographis paniculata* (Kalmegha) is a herbaceous plant of the family Acanthaceae, native to India and Sri Lanka. It is also known as "Indian Echinacea" because it is believed to provide much the same benefits as Echinacea.

Andrographolide, is the major constituent of the plant extract. Studies have been performed on the cellular processes and targets modulated by andrographolide treatment of immune cells. *Andrographis* was found to reduce the symptoms and shorten the duration of colds in clinical trials [46]. *Andrographis paniculata* also reduced the cold symptoms such as fatigue, sore throat, sore muscles, runny nose, headache, and lymph node swelling [47]. Unlike the Echinacea, *Andrographis* does not have any side effects

13. ***Nyctanthes arbortristis* (Parijata):** *Nyctanthes arbortristis* (Harsingara) is also called the "tree of sorrow", because the flowers lose their brightness during daytime; the scientific name arbor-tristis also means "sad tree" belongs to the family Oleaceae. Active constituents of Leaves of *Nyctanthes arbortristis* contain β-sitosterole, Flavanol glycosides, Astragaline, Nicotiflorin, Oleanolic acid, Nyctanthic acid, Methyl salicylate, Amorphous resin, Trace of volatile oil, Carotene, Iridoid glycosides, Benzoic acid [48]. Bronchodilatory effect of ethanolic extract of the *Nyctanthes arbortristis* was investigated under *in vitro* conditions [49]. Mast cell stabilizing and bronchodilatory activity of *Nyctanthes arbortristis* bark in treatment of asthma was studied by Sunil Ashokrao Nirmal. *et al*. (2012) [50]. The ethanolic extract of *Nyctanthes arbortristis* n-butanol fractions and two pure compounds, arbortristoside A and arbortristoside C, possess pronounced inhibitory activity against encephalomyocarditis virus (EMCV) and Semliki Forest Virus (SFV) [51].
14. ***Adhatoda vasica* (Vasa):** Adhatoda vasica, also known as "Malabar nut tree" belongs to Acanthaceae family. The bioactive components of the vasa are the quinazoline alkaloids vasicine, steroids carbohydrate and alkanes [52]. Vasa leaves had rich source of alkaloids of which vasicine and vasicinone are bioactive. In experimental study OP Gupta *et al*. (1977) the plant extract was evaluated for anti-tussive activity [53].

    Vasicinone and Vasicine isolated from the leaves showed bronchodilator activity in both in-vivo and in-vitro experimental studies [54]. That's why leaf extract of adhatoda has been used for the treatment of bronchitis and asthma for many centuries. In an *in vitro* study, methanolic extract of adhatoda showed antiviral effect against influenza virus by Hemagglutination (HA) reduction. Thus, results suggest that extracts of vasa have strong anti-influenza virus activity that can inhibit viral attachment and/or viral replication, and can be used as viral prophylaxis [55]. Another study suggest that the extracts of this plant, A. vasica also modulates the immunity of the host [56].
15. ***Terminalia chebula* (Haritaki):** *T. chebula* (Harad) is a medicinal plant belongs to the family Combretaceae, widely distributed throughout India. *T. chebula* is also called as King of medicine in Tibet because of its extraordinary power of healing and rejuvenating property. The phyto-costituents of *T. chebula* are tannins, flavonol glycosides & phenolic compounds, gallic acid, chebulagic acid and chebulanic acid. In an immune-modulation study, *T. chebula* has enhanced the humeral immunity. In this study, T-cells counts remained unaffected in the animals, but cell mediated immune response was stimulated by *T. chebula* [57].

    In an *in vitro* study, it was found that Tea (Camellia sinensis) and Haritaki (Terminalia chebula) has potential against SARS-COV-2. In this study, Upadhyay S et. all predict that the inhibition in protease activity may be helpful to halt the SARS-CoV-2 replication cycle and therefore, they have proposed Green Tea, Black Tea, and Haritaki plant extracts as potential therapeutic candidates for SARS-CoV-2 infection [58].

    These medicinal herbs may act *via* two basic approaches against covid-19 infection, that is enhancement of immunity of the individual or by acting against the virus by preventing viral replication or by inhibiting viral signal transduction.

Conclusion

The present study depicts that Covid-19 is a very contagious disorder which is spreading worldwide and many more people are affected and gradually increasing. This new virus pandemic has challenged the economic, medical, and public health infrastructure of not only the India but of the world also. So, it's needs of time to lower the intensity of this disease and proper treatment. Mainstream medicine currently does not have a vaccine. This study portrays an overview for the treatment of pandemic Covid -19 and covers some of the herbs that are most likely to be helpful in managing the current pandemic scenario.

References

1. Ramadan N, Shaib H. Middle East respiratory syndrome coronavirus (MERS-CoV): A review. Germs. 2019; 9:35-42.
2. Zhong NS, Zheng BJ, Li YM, Poon, Xie ZH, Chan KH, *et al*. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. Lancet. 2003; 362:1353-8.
3. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, *et al*. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health-The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis. 2020; 91:264-6.
4. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395:497-506.
5. Available from: http://www.worldometers.info. [Last accessed on 2020 Apr 1]
6. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/ [Last accessed as on 2020 Aug.14].
7. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected. Geneva: WHO, 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf, accessed on 2020 February 16.
8. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020; 395:507-13.

9. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus -infected pneumonia in Wuhan, China. JAMA, 2020. doi: 10.1001/jama.2020.1585.
10. Pompei R, Flore O, Marccialis MA. "Glycyrrhizic acid inhibits virus growth and inactivates virus particles," Nature. 1979; 281(5733):689-690.
11. Budhiraja RD, Sudhir S. Review of biological activity of withanolides. JSIR. 1987; 46:488-491.
12. Mehrotra S, Agnihotri G, Singh S, Jamal F. Immunomodulatory potential of Curcuma longa: A review. South Asian J Exp Biol. 2013; 3(6):299-307.
13. Tsai Y, Cole LL, Davis LE, Lockwood SJ, Simmons V, Wild GC, *et al*. "Antiviral properties of garlic: *in vitro* effects on influenza B, herpes simplex and Coxsackie viruses," Planta Medica. 1985; (5):460-461.
14. Guo N, Lu D, Woods GL, *et al*., "Demonstration of the anti-viral activity of garlic extract against human cytomegalovirus *in vitro*," Chinese Medical Journal. 1993; 106(2):93-96.
15. Subhose V, Srinivas P, Narayana A. "Basic principles of pharmaceutical science in Ayurveda," ˇ Bulletin of the Indian Institute of History of Medicine. 2005; 35(2):83-92.
16. Kim SO, Kundu JK, Shin YK, *et al*., "Gingerol inhibits COX-2 expression by blocking the activation of p38 MAP kinase and NF-kappaB in phorbol ester-stimulated mouse skin," American Society for Nutrition Journal of Nutrition. 2006; 136:1150-1155.
17. Wang X, Jia W, Zhao A, Wang X. "Anti-influenza agents from plants and traditional Chinese medicine," Phytotherapy Research. 2006; 20(5):335-341.
18. Prakash P, Gupta N. "Therapeutic uses of Ocimum sanctum Linn (O. sanctum) with a note on eugenol and its pharmacological actions," Indian Journal of Physiology and Pharmacology. 1972; 10(1):23-25.
19. Chopra RN, Nayer SL, Chopra IC. Glossary of Indian Medicinal Plants, Council of Scientific and Industrial Research, New Delhi, India, 1956.
20. Kumar R, Singh DP, Chaturvedi VK, Pathak RC. "A note on anti-viral property of neem (*Melia azadirachata*) and *O. sanctum* (*Ocimum sanctum*) against Newcastle disease virus," Journal of Comparative Microbiology, Immunology and Infectious Diseases, 1997, 18:192.
21. Gupta S, Sharma P, Saini BM. "Immunomodulatory potential of *Ocimum tenuiflorum* extracts in bovine peripheral blood mononuclear cells *in vitro*," Journal of Immunology and Immunopathology, 2007, 9.
22. Singh SS, Pandey SC, Srivastava S, Gupta VS, Patro B, Ghosh AC, *et al*. Chemistry and medicinal properties of *Tinospora cordifolia* (Guduchi) Indian Journal of Pharmacology. 2003; 35(2):83-91.
23. Fortunatov MN. "Experimental use of phytoncides for therapeutic and prophylactic purpose," Voprosy Pediatrii I Okhrany Materinstva. 1952; 20(2):55-58.
24. Shah A, Krishnamurthy R. Swine flu and its herbal remedies. Int. J Eng. Sci. 2013; 2(2):68e78.
25. Warrier PK. Indian 9 Medicinal Plants, vol. 4, Orient Longman, 1995.
26. Curreli F, Friedman-Kien AE, Flore O. "Glycyrrhizic acid alters Kaposi sarcoma-associated herpesvirus latency, triggering p53-mediated apoptosis in transformed B lymphocytes," Journal of Clinical Investigation. 2005; 115(3):642-652.
27. Nose M, Terawaki K, Oguri K, Ogihara Y, Yoshimatsu K, Shimomura K, *et al*. "Activation of macrophages by crude polysaccharide fractions obtained from shoots of Glycyrrhiza glabra and hairy roots of Glycyrrhiza uralensis *in vitro*," Biological and Pharmaceutical Bulletin. 1998; 21(10):1110-1112.
28. Wagner H, Jurcic K. "Immunological studies of Revitonil, a phytopharmaceutical containing Echinacea purpurea and Glycyrrhiza glabra root extract," Phytomedicine. 2002; 9(5):390-397.
29. Fiore C, Eisenhut M, Krausse R, *et al*., "Antiviral effects of Glycyrrhiza species," Phytotherapy Research. 2008; 22(2):141-148.
30. Pompei R, Flore O, Marccialis MA. "Glycyrrhizic acid inhibits virus growth and inactivates virus particles," Nature. 1979; 281(5733):689-690.
31. Tsai Y, Cole LL, Davis LE, Lockwood SJ, Simmons V, Wild GC, *et al*. "Antiviral properties of garlic: *in vitro* effects on influenza B, herpes simplex and Coxsackie viruses," Planta Medica. 1985; (5):460-461.
32. Guo N, Lu D, Woods GL, *et al*., "Demonstration of the anti-viral activity of garlic extract against human cytomegalovirus *in vitro*," Chinese Medical Journal. 1993; 106(2):93-96.
33. Subhose V, Srinivas P, Narayana A., "Basic principles of pharmaceutical science in Ayurveda," ˇ Bulletin of the Indian Institute of History of Medicine. 2005; 35(2):83-92.
34. Peirce A. The American Pharmaceutical Association Practical Guide to Natural Medicines, William Morrow, New York, NY, USA, 1999.
35. Murray MT. The Healing Power of Herbs: The Enlightened Person's Guide to the Wonders of Medicinal Plants, vol. 25, Prima, Rocklin, Calif, USA, 1995.
36. Herrmann EC, Jr. Kucera LS. "Antiviral substances in plants of the mint family (labiatae). 3. Peppermint (Mentha piperita) and other mint plants," Proceedings of the Society for Experimental Biology and Medicine. 1967; 124(3):874-878.
37. Ganguli S. "Neem: a therapeutic for all seasons," Current Science. 1994; 82(11):1304.
38. Badam L, Joshi SP, Bedekar SS. "'*In vitro*' antiviral activity of neem (*Azadirachta indica*. A. Juss) leaf extract against group B Coxsackieviruses," Journal of Communicable Diseases. 1999; 31(2):79-90.
39. Sarkar L, Putchala RK, Safiriyu AA, Sarma JD. *Azadirachta indica* A. Juss ameliorates mouse hepatitis virus-induced neuroinflammatory demyelination by modulating cell-to-cell fusion in an experimental animal model of multiple sclerosis. Frontiers in Cellular Neuroscience, 2020, 14:116. 10.3389/fncel.2020.00116 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
40. Borkotoky S, Banerjee M. A computational prediction of SARS-CoV-2 structural protein inhibitors from *Azadirachta indica* (Neem) [published online ahead of print, 2020. May 28]. J Biomol Struct Dyn. 2020;1-17. doi:10.1080/07391102.2020.1774419.
41. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants (Including the Supplement), Council

of Scientific and Industrial Research, New Delhi, India, 1986.
42. Bown D. Encyclopaedia of Herbs and Their Uses, Dorling Kindersley, London, UK, 1995.
43. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants (Including the Supplement), Council of Scientific and Industrial Research, New Delhi, India, 1986.
44. Hussein G, Miyashiro H, Nakamura N, Hattori M, Kakiuchi N, Shimotohno K, *et al*. Inhibitory effects of Sudanese medicinal plant extracts on Hepatitis C Virus (HCV) protease. Phytother Res. 2000; 14(7):510-16.
45. Roy S, Chaurvedi P, Chowdhary A. Evaluation of antiviral activity of essential oil of Trachyspermum Ammi against Japanese encephalitis virus. Phcog Res. 2015; 7:263-7.
46. Bown D. Encyclopaedia of Herbs and Their Uses, Dorling Kindersley, London, UK, 1995.
47. Melchior J, Palm S, Wikman G. "Controlled clinical study of standardized Andrographis paniculata extract in common cold: a pilot trial," Phytomedicine. 1996-1997; 34:314-318.
48. Shandhar HK, Kaur M. An update on Nyctanthes arbor-tristis Linn. Journal of Internationale Pharmaceutica Sciencia. 2011; 1:77-86.
49. Ramadan Sopi B, Muhammad Feroz Hayat Khan. Bronchodilatory effect of ethanolic extract of the leaves of *Nyctanthes arbortristis*. Pharmacognosy. Res. 2013; 5(3):169-172.
50. Sunil Ashokrao Nirmal, Subodh Chandra Pal, Subhash Chandra Mandal. Pharmacognostic evaluation of *Nyctanthes arbortristis* bark. Asian Pacific J Tropical Biomed, 2012, S494-S500.
51. Gupta P, Bajpai SK, Chandra K, Sing KL, Tandon JS. Antiviral profile of *Nyctanthes arbortristis* L. against encephalitis causing viruses. Indian J Exp Biol. 2005; 43(12):1150-1160.
52. Kumar A, Ram J, Samarth RM, Kumar M. Modulatory influence of *Adhatoda vasica* Nees leaf extract against gamma irradiation in Swiss albino mice. Phytomedicine. 2005; 12:285-293.
53. Gupta OP, Sharma ML, Ray Ghatak BJ, Atal CK. Pharmacological investigations of vasicine and vasicinonethe alkaloids of Adhatodavasica. Indian J Med Res. 1977b; 66:680-691.
54. Amin AH, Mehta DR. A bronchodilator alkaloid (vasicinone) from Adhatodavasica nees. Nature, 1959, 184:1317.
55. Chavan R, Chowdhary A. *In vitro* Inhibitory Activity of Justicia adhatoda Extracts against Influenza Virus Infection and Hemagglutination. Int. J. Pharm. Sci. Rev. Res. 2014; 25(2):231-236.
56. Apooshan PG, Sundar K. Anti-Ulcer activity of Adhatoda Vasica Leaves against Gastric Ulcer in Rats Anti-Ulcer activity. Journal of Global Pharma Technology. 2011; 3(2):7-13.
57. Sohni YR, Bhatt RM. Activity of a crude extract formulation in experimental hepatic amoebiasis and in immune-modulation studies. Journal of Ethnopharmacol. 1996; 54(2-3):5.
58. Upadhyay S, Tripathi PK, Singh M, Raghavendhar S, Bhardwaj M, Patel AK, *et al*. Evaluation of medicinal herbs as a potential therapeutic option against SARS-CoV-2 targeting its main protease. Phytotherapy Research, 2020, 1-9. https://doi.org/10.1002/ptr.6802