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Antiviral Herbs in Ayurveda

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ABSTRACT: -

Viral infections constitute a major public health concern and accounts for global socioeconomic burden, much more in developing nations. Emergence of new viral epidemics, their rapid, devastating worldwide spread and failure to develop new antiviral drugs at such pace have made it a priority to discover new antiviral agents. There is a greater need to develop antiviral drugs with better efficacy, safety, oral bioavailability, utility at both prophylaxis and treatment stages and at last which prevents drug resistance. Medicinal plants have great potential to fulfil above requirements. Several plants provide a rich source for drug discovery against both infectious and non-infectious diseases. Many plant metabolites possess broad-spectrum antiviral action. Plant kingdom is very diverse and is an unlimited source of new drugs. Plant extracts can prove to be more effective, safe and economical to areas which have limited resources. This article is an attempt to highlight the potent antiviral action of some medicinal plants; which may be beneficial in providing important lead in developing new antiviral drugs.

KEYWORDS- Viral diseases, *Yashtimadhu*, *Kalmegh*, Hepatitis, Herpes, *Nagarmotha*.



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INTRODUCTION

Viruses are the ultimate expression of obligate intracellular parasitism. They not only take nutrition from the host cells but also direct its metabolic machinery to synthesize new viral particles. There are more than 500 different types of viruses which can cause serious diseases like Influenza, Hepatitis, HIV, Herpes and Infectious mononucleosis, to name some.

Epidemiological studies show that viral diseases in developed countries don't require serious hospitalization while in developing countries like India, they cause a heavy toll on the population in the form of permanent disability and mortality. With the emergence of new viruses along with the existing ones, the need for more efficacious antiviral drugs is indisputable. The urgency to curb COVID-19 pandemic has encouraged a vast majority of researchers worldwide to recognise new drugs and also repurpose previous ones to target viral proteins and some host cells necessary for viral replication.

There are only a finite number of effective, less toxic antiviral drugs for clinical purpose. An increasing problem is the development of drug resistance against the existing drugs. New and improved antiviral drugs are in demand in the current scenario for the prophylaxis as well as treatment of a large number of viral diseases which are not adequately controlled at present. These diseases include different respiratory tract infections, hepatitis, influenza, herpes and hemorrhagic fevers.

Emerging viral diseases like SARS variant, Hantavirus Pulmonary Syndrome (HPS), H5N1, H9N2 influenza and Ebola virus have emerged as an important global health concern. As a result, exploring new antiviral agents from herbs has become more important than before. Ayurvedic literature has described numerous herbs that are said to be effective against different microorganisms. This article

is an attempt to assemble well-known as well as less widely known Ayurvedic herbs having antiviral properties.

MATERIAL & METHODS

Objective of this review is to collect the scattered information about different antiviral drugs in Ayurveda. Ayurveda classics like *brihat trayi* (Caraka Samhita, Sushrut Samhita, Ashtang Hridaya) and *laghu trayi* (Madhav Nidana, Sharangdhar Samhita and Bhavprakash Nighantu) were reviewed for *krimighna* drugs (which can be correlated to antimicrobial drugs). Various electronic databases like PubMed, ScienceDirect and Scopus; different books, newsletters available in the library of Institute of Medical Sciences, Banaras Hindu University were also searched related to topic.

REVIEW RESULT & DISCUSSION

Glycyrrhiza glabra (*Yashtimadhu*) commonly known as *licorice*, is a widely used herb in Ayurveda. In classical Ayurvedic texts, *Priyavrat Sharma* has mentioned its use chiefly in *vata pattika* diseases.^[1] *Caraka Samhita* has classified licorice as *Jeevaniya* (Nutrients), *Kanthya Varnya* (Voice & Complexion Promoters), *Sandhaniya*, *Kandungnya* (Antipruritic), *Mutravirajniya* (Corrects Urinary Pigments I.E., Color) And *Shoditasthapana* (hemostatic).^[2] Along with other important pharmacological actions like antimicrobial, hypolipidemic, hepatoprotective, antitumor; antiviral activity is most commonly reported. More than 20 triterpenoids and approximately 300 flavonoids have been identified from glycyrrhiza.^[3] Among them, Glycyrrhizin (GL), Glycyrrhetic acid (GA), Liquiritigenin (LTG), Glabridin (GLD) and Licochaleone E (LCE) are the main extracts which have antiviral action.^[3] Glycyrrhizin (GL) is one of the major components identified

from glycyrrhiza roots.^[3]

Chinese researcher Matsumoto et al. notified that GL aimed the release step in which Hepatitis C virus (HCV) particles were infecting cells.^[3] These findings suggest towards the possible new roles for GL to cure chronic hepatitis C patients. GA treatment inhibits rotavirus replication, it reduced rotavirus yields by 99% when added to infected cultures post viral adsorption. GA also possess strong action against human respiratory syncytial virus (HRSV).^[3]

Zhang's study reported that GL showed marked improvement in myocarditis caused by coxsackievirus B3 (CVB3) by significantly decreasing serological levels of cardiac markers and hence improving longevity.^[3] Several studies have proved that GL significantly inhibits influenza virus. At a concentration of 100 µg/ml, it weakened H5N1 induced production of chemokine ligand 5 (CCL5) and suppressed H5N1 induced cell death^[11]

GA, selectively promotes apoptosis in latent Kaposi Sarcoma- associated herpesvirus (KSHV) infected cells and at active concentration, it is also not toxic for uninfected cells.^[2]

Phyllanthus niruri (*Bhumyaamalaki*) is an ancient shrub with time tested medical records. In classical ayurvedic texts, it has been used as *kapha pitta shamaka* drug (as in Dravyaguna Vigyana book by Priyavrat Sharma)^[4]; *Caraka Samhita* has described it in *Kasahara* and *swashara mahakashaya* amongst 50 *mahakashaya* description.^[5] *Bhavprakasa* has specially mentioned this plant as highly effective in all types of hepatitis. It is also beneficial in productive cough and bronchial asthma.^[6] Indian medicine has utilized this shrub due to its strong pharmacological potential to be used in liver diseases and also as an antiviral agent. Perhaps, its most important effect is antiviral action.^[7]

Studies carried on sera received from chronic Hepatitis B patients and Woodchucks infected with hepatitis, which were then treated with extracts of *P. niruri* had significant reduction in viral antigen levels.^[8] Aqueous extract had marked antiviral action and assures good results especially in hepatitis B carriers. Clinical studies showed that 50-60% of hepatitis B patients experienced HBsAg seroconversion. This effect may be due to inhibitory effect on viral genetic replication. Moreover, inhibition ratios of *P. niruri* extracts (Nirtetralin and Nirtetralin B) were significant when compared with Acyclovir, highlighting that these compounds were promising as new HBV antivirals. Lignans had low cytotoxicity on uninfected cells and thus can be used at non-toxic dosages without causing any adverse drug reactions.^[9]

Aqueous extract of *P. niruri* containing repandusinic acid, shows marked inhibitory effect on HIV-1 reverse transcriptase (HIV-1-RT). It has anti dengue activity and also effective in infantile diarrheas, 90% of which are due to some Enteroviruses.

Andrographis paniculata (*Kalmegh*), commonly known as green *chiretta* is an annual nonwoody plant, indigenous to India and Sri Lanka. *Priyavrat Sharma* in his book *Dravyaguna Vigyan* has given importance to *kalmegh* as an important *pittasaraka* (cholagogue) and useful in *yakrit vikara* (liver disorders).^[10] This plant is chiefly used to cure flu, sore throat, upper respiratory tract infections and gastrointestinal disorders.

Its major chemical constituent, Andrographolide exhibits antitumor, antiviral, anti-inflammatory and antidiabetic properties. In one recent research paper, *A. paniculata* efficacy has been documented; as the molecules from this plant provides immunity and antiviral response by involving different pathways like PI3/AKT and MAP kinase pathways against COVID-19.^[11]

A clinical trial of andrographolide in HIV patients notified a significant increase in the mean CD4+ lymphocyte level.^[12] It has viricidal action against Herpes Simplex Virus 1 (HSV1) and also inhibits Epstein-Barr Virus (EBV).

Cyperus rotundus (Nagarmotha), also known as nutgrass is considered to have originated in India 2000 years back and regarded as one of the best Ayurvedic herbs. *Caraka Samhita* has classified *nagarmotha* as *lekhaniya* (weight reducing drug), *triptighna* (appetiser), *kandungnya* (antipruritic) and *stanya shodhana* (galacto purifiers).^[13] The 25th chapter of *sutra sthana* of *Caraka Samhita* has mentioned *nagarmotha* as the best among all herbs in having astringent property. *Bhavprakasa* has mentioned its therapeutic uses as- diuretic, diaphoretic, anti dysentery and in acute fevers.^[14]

It mainly possesses spasmolytic, hypotensive, anti-oxidant, hepatoprotective, anti-inflammatory and antiviral activities. Major chemical constituents are α -cyperolone, β -cyperone, iso cyperol, myristic acid and sitosterol. One research study was conducted to determine hepatoprotective, hepatitis B virus (HBV) inhibitory and hepatic CYP450 enzyme (CYP3A4) modulatory potential of *C. rotundus* rhizome fractions. The in-vitro anti-HBV activity was tested on HepG2.2.15 cells (HBsAg and HBeAg Elisa). Many fractions of *C. rotundus* had effective dose-dependent hepatoprotection.^[15]

Ethyl acetate, n-butanol and aqueous fractions had maximum inhibitory action on viral HBsAg and HBeAg secretions in both dose as well as time dependent manner. There is also mild activation of hepatic CYP3A4 potential by these fractions; highlighting towards its safe intake with respect to drug metabolism. *Nagarmotha* is one of the two ingredients of Liv.52 HB, very successful Ayurvedic drug for the treatment of Hepatitis B whose efficacy

rates are comparable to available Allopathic treatments.^[16]

Ocimum sanctum (Tulsi) is one of the highly praised Ayurvedic herb. It belongs to mint family with 150 varieties worldwide. *Caraka Samhita* has described *tulsi* in *swashara mahakashaya*^[17] while *Sushruta Samhita* has mentioned it in *shiro virechana* and *sursadi gana*.^[18] According to *Bhavprakasa*, *tulsi* reduces burning sensation and pacifies *pitta dosha*. It cures dysuria, diseases of *rakta*, pain in flank region.^[19] *Priyavrat Sharma* has mentioned its use chiefly in *vata kaphaja* diseases. *O. sanctum* is considered to be an adaptogen.

A clinical trial was done on 32 patients of viral hepatitis, using a compound preparation having *tulsi* as a constituent. Compared to 31 patients on placebo, course of illness was shortened significantly in the drug tested group, the clinical symptoms and biochemical parameters showing a beneficial change. In another clinical trial on viral encephalitis patients, *O. sanctum* leaves extract has been proved to increase longevity in patients as compared to another steroid treated group.^[20]

Several studies reveal that *O. sanctum* has a unique combination of actions which include antimicrobial including antiviral, anti-diarrheal, anti-inflammatory, cardioprotective and the list goes on. Several extracts and some purified components, like apigenin, ursolic acid and linalool exhibits broad spectrum antiviral action. Among these compounds, ursolic acid has potent action against Herpes Simplex virus (HSV1), Adenovirus (ADV-8), Coxsackievirus B1 (CVB1) and Enterovirus 71 (EV71). Apigenin has maximum action against HSV2, HBsAg and HBeAg and linalool showed marked action against AVD-II.^[21]

Mentha piperita (Pudina), is a hybrid mint from lamiaceae family. Many pharmacological studies have indicated towards its different actions like anti-oxidant, anti-allergic, antiviral

and antibacterial. The antiviral property of its leaves was assessed against Human Respiratory Syncytial Virus (HRSV) in Hep-2 cells.

M. piperita extract showed no cytotoxicity against Hep-2 cells up to a level of 200 µg/ml. Some studies have shown that leaves also have antiviral action against many viral diseases like Influenza, Herpes and HIV.^[22]

***Cinnamomum zeylanicum* (Cinnamon, Dalchini)**, an indigenous spice, is one of the most widely studied flowering plants. It belongs to the family Lauraceae and is found in almost every household. There are mainly four types of cinnamon- true cinnamon (*C. zeylanicum*), Indonesian cinnamon (*C. burmanni*), Vietnamese cinnamon (*C. loureiroi*) and cassia cinnamon. In Ayurveda, cinnamon is widely used in *kapha vata* diseases. *Bhavprakasa* has identified it as herb useful in chronic rhinitis, oil extracted from its bark is applied on tuberculous ulcers, in menorrhagia, its bark powder is given along with *asoka* to tone uterine muscles.^[23] It has antidiabetic, antioxidant and antiviral properties. Cinnamon bark is an important source as it contains a high amount of function bearing essential oil. It contains cinnamaldehyde (~ 60%) and eugenol (~18%), of which cinnamaldehyde is believed to have antiviral property.

In one study, synthesized silver nanoparticles were prepared using *C. cassia* and their action was evaluated against highly infectious Avian Influenza virus subtype H7N3. These particles increased the antiviral action and were effective in treatments before and after viral inoculation. These nanoparticles were also found to be non-toxic to vero cells. There is also a rising trend among HIV patients to use cinnamon oil as therapeutic measure in developing countries like India.^[24]

One recent study was conducted to recognise the antiviral substance from cinnamon against COVID-19 main protease enzyme and to assess

the in silico molecular basis of its action. Out of 48 compounds, seven had a higher binding affinity with the main protease enzyme and spike protein. Thus, it was anticipated that cinnamon intake likely boosts immunity against COVID-19 infection.^[25]

***Zingiber officinale* (Ginger, Shunthi)** rhizome had been long used in traditional herbal medicine. Its huge health promoting perspective is due to its rich phytochemistry. *Caraka Samhita* has classified *shunthi* amongst *triptighna* (appetiser), *deepan* (digestives), *arshoghna* (anti-hemorrhoidal), *shula prashamana* (analgesic), *trishna nighrahana* (anti-thirst) and *sheeta prashamana* (calefacients).^[26] Its synonyms *maho aushadha* and *vishwabhesaja* represent its diverse pharmacological action. *Bhavprakasa* has praised *shunthi* as a herb which improves voice, cures vomiting, spasmodic pain, gastric and heart diseases. It can pacify filariasis, oedema, haemorrhoids, upper abdominal distension and flatus.^[27]

Ginger has proven antiviral activity action human respiratory syncytial virus (HRSV). Effect of hot water extracts of fresh and dried *Z. officinale* on HRSV was tested by plaque reduction assay in respiratory tract cell lines. Fresh part inhibits plaque formation in cell lines while the dried part does not have such action. 300 µg/ml fresh ginger decreased the plaque formation to 12.9% when given prior viral incubation. It inhibited viral attachment and internalisation. It is reported that fresh part stimulates secretion of IFN- β from mucosa that possibly contributed to contain viral infection. It also has antiviral effect against Chikungunya virus (CHIKV).^[28]

***Syzygium aromaticum* (clove, lavang)** has been employed for centuries as medicinal plant due to its antioxidant and antimicrobial property. In *BhavaPrakasa*, it is described as a herb useful in vision, cold in potency, appetiser, digestant and promotes taste. It can surely cure

diseases like colic distension, dyspnoea and tuberculosis.^[29] It is a major vegetable source of many phenolic compounds. One of its main compounds, eugenin, activity was examined against herpes virus. It was found to be effective at a certain concentration. It was deduced from the study that main action of eugenin is suppressing synthesis of viral DNA.^[30]

The synergistic activity of *S. aromaticum* and acyclovir is strong against herpes simplex virus type 1 (HSV1). This action was strong in brain than in skin.^[30] In another trial, aqueous extracts of six herbs including clove and ginger; were tested for antiviral action against Feline Calicivirus (FCV) which is a surrogate for human norovirus. Pretreatment of FCV with non-diluted clove extract inactivates 6.0 log of the initial viral titre.^[31]

Urtica dioica, commonly known as stinging nettle, is widely used globally to cure different ailments. In India, it is commonly known as *bichu ghas*. It is traditionally used to palliate rheumatism and inflammatory myopathies.

In one study, extract of four herbs including *U. dioica* were investigated for their action against Dengue virus (DENV2). Methanolic extract of *U. dioica* greatly inhibits replication of dengue virus. It is a proven source of anti-dengue formulation, since the N-Acetyl-D-Glucosamine specific lectin of this plant has proved beneficial in suppressing infection due to all four dengue serotypes. It also exhibits anti-HIV action.^[32]

U. dioica has affinity for N-Acetyl-D-Glucosamine that inhibits viruses from class Nidovirales. Another trial was conducted on mouse models to examine the effect of this plant on different SARS-CoV strains replication. It was inferred from this trial that *U. dioica* reduced virus yields by 90% by targeting viral replication. Data from this study suggests that *U. dioica* likely inhibits SARS-Cov infection by inhibiting early replication

phase.^[33]

Medicinal plants have been used since ages and globally to cure different viral infections. A large number of usually used drugs contain compounds derived from plants. Above were few of the many antiviral herbs indigenous to India. Virtually, all cultures worldwide have relied historically and continue to depend on medicinal plants for initial disease management. Likewise in various other countries; many herbs having rich antiviral action have been identified which are used in several viral conditions like-

Melissa officinalis commonly known as *lemon balm*, is a perennial herbaceous plant from mint family. It is indigenous to Europe, central Asia and Iran, but is now naturalized worldwide. One study was conducted on lemon balm essential oil components in comparison with Oseltamivir against Avian Influenza virus (AIV-H9N2). The main compounds present in this oil are citral, citronellal, linalool and β -caryophyllene oxide.^[34]

Lemon balms have antioxidant, antihistamine, antitumor and antiviral properties. Its extract likely inhibits protein synthesis and exhibits antiviral activity against HSV1. Influenza virus replication was suppressed by different concentrations of lemon balm essential oil. The synergistic use of oseltamivir and essential oil also increased the former efficacy on Avian Influenza and the release of virus from pathogenic cells was also lowered by this multimodal treatment.^[34]

Taraxacum officinale, commonly known as *dandelion* is a major component in many healing methods. It is native to Mexico which is now widely used around the world for various illnesses and has compounds like taraxasterol, luteolin and caffeoylquinic acid derivatives. Like *Urtica dioica*, *T. officinale* methanolic extract also showed inhibitory effect on dengue virus (DENV2) replication.^[32] It also has inhibitory property against HIV

reverse transcriptase.^[35] Dandelion extracts can also inhibit influenza viruses by inhibiting viral nucleoprotein synthesis and polymerase activity.

Silybum marianum, also known as *milk thistle* is an annual or biennial plant of family Asteraceae. Originally, it belongs to southern Europe. Silymarin, identified from the seed of this plant is famous for its antihepatotoxicity as it reduces inflammation. It has potent antiviral action against Hepatitis C virus, making it very commonly used herbal product by HCV patients in western world. Silymarin treatment interfere with different stages of HCV life cycle like fusion, replication and virion production.^[36]

Nine phytochemicals were identified from this plant which possess anti-dengue virus activity. One important compound was silibinin, which potentially inhibits DENV viral replication. A combination of silymarin and Entecavir reduced Hepatitis B virus DNA (HBV DNA) more than either mono-treatment alone.^[37]

Thus, these medicinal plants and their derivatives can play a novel role by providing natural, non-toxic and potent therapeutic leads to treat different viral infections as these viruses are undergoing continuous mutations and hence developing resistance against current antivirals at an alarming rate.

CONCLUSION

As there are many viral diseases which doesn't have either any preventive vaccine or any effective antiviral treatments, so eradication of these viral diseases remains a huge challenge. Many natural products are observed to have antiviral properties and their discoveries can further help, develop therapeutic leads. There is also a strategy of re-purposing existing drugs with broad action which are indicated as antivirals in several similar viral diseases. One recent example is COVID-19, where drugs like

Remdesivir, Hydroxychloroquine were initially identified to have action against corona virus.

The role of several herbs possessing immunoadjuvant properties needs to be investigated for their antiviral action. Re-purposing these herbs provides a new outlook to overcome viral infections propagation. *Ayurvedic* drugs have the capacity to alleviate several serious infections, there are evidence regarding this but more research work needs to be done.

Ayurvedic herbs are composed of large number of phytochemicals like terpenoids, alkaloids, tannins, polyphenols, peptides which possess several functions against viral invasion, penetration, replication, assembly and release. There are insufficient evidences for evaluation of different herbs as antivirals. So, more studies needs to be carried out in a more elaborate way in time to come.

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