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Ayurvedic Antiviral Agents: Overview of Medicinal Plants Perspective

Choudhary R[*1], Borse L[2] and Jadhav A[3]

[1]Department of Quality Assurance, Sandip Institute of Pharmaceutical Sciences, Nashik, Maharashtra, India
[2]Department of Pharmacology, Sandip Institute of Pharmaceutical Sciences, Nashik, Maharashtra, India
[3]Department of Pharmacognosy, Sandip Institute of Pharmaceutical Sciences, Nashik, Maharashtra, India

[*]**Corresponding author:** Choudhary R, Department of Quality Assurance, Sandip Institute of Pharmaceutical Sciences, Nashik, Maharashtra, India, Tel: +91-7049433484, E-mail: rakshachoudhary26@gmail.com

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Abstract

In recent years it has been reported that many of the herbal plants contain antiviral agents which combat human disease that are caused by pathogenic viruses. The natural products which are obtained from plants as antiviral agents against viruses have gone through researches to check the efficacy and potentials of the herbal products in prevention of viral disorders. The viral diseases are challenging for the health of people around the world cause significant increase in mortality and enhance crises. There are many synthetic antiviral drugs which have large number of side effects and have narrow therapeutic window range, while in other hand herbal formulations have minimized side effects. The advantages of herbal formulation over synthetic drugs encourage us to divise and expand new herbal moieties against the emerging viral infections. The medicinal plant contains phytochemicals which have antiviral properties. In this paper the activity of antiviral agents from medicinal plants which have importance in Ayurveda are discussed along with their source.

Keywords: Medicinal Plants; Antiviral Agents; Therapeutic Window Range; Viral Infections; Phytochemicals; Ayurveda

Introduction

Viral diseases are more threatening to public health day by day. Many number of viral diseases have been reported from different regions of the world [1]. The therapeutic potentials of medicinal plants recapped by various research programs [2]. For humans the plants are the crucial source of medicine. Day by day the demand for traditional medicine is increased. To achieve the health goals it is important to use the traditional medicines as per World Health Organisation. There is about at least 35000 species of the plants which are used for the purpose of medicine. About 700 herbal products are described along with their clinical effects and properties.50 categories of the herbs have been described according to their clinical effect as antiinflammatory, antiviral, antiasthmaticantihelminthic, antipyretic, antiemetic, antipruritic, antidiarrhea, sedative, antiepileptic, haemostatic, analgesic, haemopoietic, promoter of strength, semen and sperm, voice, complexion, wound healing etc [3]. For primary health care millions of people depends on medicinal plant but it is not limited to that it is also for improvement of livelihood and generation of income [4]. Herbal formulations are the basic foundation in many traditional medicinal system worldwide [5]. The active natural ingredients of higher plants have been studied for their potency against viruses on the basis of Siddha and Ayurveda traditional system of medicine; these studies revealed the viruses e.g. feline immunodeficiency virus, coxsackie virus, herpes simplex virus, influenza virus, respiratory syncytial virus, parainfluenza virus etc. The medicinal plant contains several of the phytochemicals constituents which are responsible for their property to treat diseases. Among them some of have antiviral properties. Nowadays people demanding an alternative medicines other than conventional medicine shown by recent survey in developing countries.

What is a virus?

A virus is infectious agent or parasite of small size that itself reproduces. Viruses are called as a link between living and nonliving. The multiplication of viruses occurs only in living cells such as plant cell, animal cell and bacterial cell [6]. The genetic material of viruses is DNA or RNA. The genome is encompassed within the protein sheath called as capsid.The genetic material may be double or single stranded. Capsids of viruses are regular arrays of one or a few types of protein. Almost every ecosystem has viruses. A non-bacterial pathogen infecting tobacco plants was described by Dmitri Wanovsky 1892 article. Tobacco Mosaic virus was discovered by Martinus Beijerink in 1898 [7].

Emerging pathogenic viruses

The public threat of emerging viruses is increasing day by day. The viral diseases are very dangerous hence the scientists are continuously involved in the researches for the discoveries of antivirals for curing the new pandemics. Nowadays coronavirus is spreading increasingly which is of unknown origin.

Newly emerging viruses are given as below:

Coronavirus: Coronavirus is a single stranded RNA virus. The coronavirus is included in corona viridae family. Inhumans, it causes common cold and complications that include pneumonia and SARS can occur [8].

Ebola virus: The Ebola virus's transferal occurs from the wild animals and in the humans by human to human transmission. It is Ebola hemorrhagic fever which causes fatal illness in humans. Ebola virus is the member of filoviridae family.

West Nile Virus: It is an example of mosquito borne zoonotic virus caused by change in climate and it belongs to the family of flaviviridae and it is transmitted by mosquitoes.

Nipah virus: It was first revealed in April 1999 in Malaysia on the pigfarm. It caused the outbreak of respiratory and neurological diseases. Symptoms of encephalitis in humans and respiratory in pigs was observed the outbreak [7].

Sin Nombre virus: Sin Nombre virus is related to Hantavirus. The symptoms of the Hantavirus pulmonary syndrome (HPS) are fever, cough, headache, pulmonary edema and death at the end. SNV belongs to genus of Hantavirus of family bunyaviridae. The reservoir of SNV infection is rodent carrier (the deer mouse) the inhalation of virus contaminated deer mouse excretion is the mode of transmission of SNV. About 66.7 percent fatality rate of SNV induced HPS reported in United States.

SARS-coronavirus (SARS): It is caused by SARS-CoV. It is viral respiratory disease. In bats high probability of SARS-CoV is originated on the basis of phylogenetic analysis and in humans it spreads directly or indirectly via animals held in Chinese market.8273 cases and 775 deaths reported in china in the middle of November 2002 & July 2003.

MERS-Coronavirus: MERS-CoV is a novel coronavirus. In 2012 in Saudi Arabia it was isolated out of a patient suffered from acute Pneumonia. The fatality rate of MERS - CoV is higher than SARS-CoV upto30%.1084cases and 439 deaths was reported in March 2015.Through dromedary camel MERS-CoV spreads from bats to human.

Here is the list of major zoonotic viruses [7,8] (Table 1):

Sr. no.	Family of virus	Zoonotic virus	Reservoir host	Origin of infection in human	Disease
1.	Corona virus	SARS-CoV	Bats	Bats	Rigorous acute respiratory syndrome
		MERS-CoV	Camel	Bats	SARS-like
2.	Bunya virus	Hantavirus	Wild mouse	Mouse	Hemorrhagic fever
		Sin Nombre Virus	Wild mouse	Mouse	Hantavirus pulmonary syndrome
3.	Influenza virus	Avian influenza H5N1	Wild birds	chicken	Respiratory disease
		Avian influenza virus H7N9	Wild birds	Chicken	Respiratory disease
4.	Paramyxo virus	Hendra virus	Bats	Horse	Hemorrhage in lung
		Nipah virus	Bats	Pigs	Encephalitis
5.	Filo virus	Ebola virus	Bats	primates	Hemorrhagic fever
6.	Rhabdo virus	Rabies virus	Wild animals (bats, raccoon etc)	Animals (dog)	Paralysis and hydrophobia
7.	Flavi virus	West Nile Virus	Birds	mosquito	Encephalitis
		Dengue virus	Monkeys	mosquito	Hemorrhagic fever
		Japanese encephalitis virus (JEV)	Birds, bats	mosquito	Encephalitis

Table 1: List of major zoonotic viruses

Natural antiviral agents

Natural antiviral agents are obtained from the medicinal plants which are described in Ayurveda for along with their antiviral property. The extraction of the parts of medicinal plants gives the crude antiviral agents later these crude products can be purified by using purification techniques such as chromatography [9]. These are obtained as active phytochemicals; including polyphenols,

terpenoids, coumarins, alkaloids, phytosterols, glycosides, flavonoids, saponins, sulphides, lignans, etc [9,10]. Here are some antiviral agents from medicinal plants including their mechanism of action is explained in Table 2 [3,4,6,11].

Sr. no.	Name of plant	Active antiviral agent	Parts of plant used/extract	Common name of plant	Botanical name of plant	Mechanism of targeting the virus	Activity of antiviral
1	Lahsun	Ajoene, allicin, allyl methyl thiosulfinate and methyl allylthiosulfinate	Bulb, oil macerates &fresh garlic extract	garlic	*Allium sativa*	Interferes with virus adsorption & penetration	Common cold virus, influenza virus A, dengue virus, Herpes simplex virus1, Herpes simplex virus2, HIV, coxsackie virus, infectious bronchitis virus
2	Palandu	Quercetin	leaves	onion	*Allium sepa*	Inhibits viral entry or inhibiting components required by viral replication	Poliovirus, hepatitis. influenza A
3.	Ghritakumari	Anthraquinones: aloe emodin	flowers	Aloe vera	*Aloe barbedensis*	Partially destroys the viral envelope & inactivate them	Influenza virus, herpes simplex -1
4	Neem	N/A	Neem bark extract	Neem tree	*Azadirachtaindica*	Blocks HSV-1entry into glycoprotein D (gD) receptors expressing CHO-K1 cells	Dengue virus, pox virus (DNA), small pox virus (DNA)
5	Suryakanthisoppu	Triterpenesaponin	N/A	Scarlet pimpernel, red pimpernel	*Anagallisarvensis*	In vitro inhibits virus replication	HSV, poliovirus
6	pashanbheda	N/A	Methanolic extract	Hairy bergenia	*Bergeniaciliata*	N/A	Influenza virus A, HSV-1
7	Mulethi	Glycyrrhizic acid	roots	Liquorice root	*Glycyrrhiza radix*	GL interfere with an early step of EBV replication cycle	EBV (Epstein-Barr Virus)
8	Swarnapatri	Anthraquinones	Hot glycerine extract	Senna, indiansenna	*Cassia angustifolia*	Partially destroy the vial envelope & inactivate them	HSV
9	Asishimbi	Lectins	N/A	Sword bean	*Canavaliagladiata*	*In vitro* inhibits virus penetration	HSV, HIV, influenza virus
10	Naaranga	Tangeretin and nobiletin (polymethoxylated flavones)	pericarps	Mandarine orange	*Citrus reticulate*	Affects the intracellular replication of RSV. Teregerin down regulated the expression of RSV phosphoprotein	Respiratory Syncytial Virus(RSV)l
11	rathnagandhi	Quercetin derivatives	Aqueous extract of fruit,stem, leaf,fruit&, seed	Peacock flower, red bird of paradise	*Caesalpiniapulcherrima*	Inhibits the viral replication at early stages of cycle	HSV
12	Toona	Acid polysaccharides	Leaves fraction extracts	White cedar, cedrobatata	*Cedrelatubiflora*	Inhibits virus replication	HSV, Vesicular Stomatitis virus
13	ustukhudus	Lignin-carbohydrate complex	Fruit spikes	woundwort, carpenter's herb	*Prunella vulgaris*	Inhibits penetration of HSV-1 & blocks binding to vero cells	HSV-1, HSV-2
14	Guanandi	Apetalicacid, calanolide band C	Hexane extracts of leaves	Brazil beauty leaf	*Calophyllumbrasiliense*	Inhibitory effect on reverse transcriptase	HIV
15	Chanaka	Phenolic compound	Seed, fruit skin ,aerial parts	Chick pea	*Cicerarietium*	N/A	HSV
16	Narikela	Catechin, epicatechine & B type procyanidins	Husk fiber's water extract	Coconut	*Cocosnucifera*	N/A	HSV
17	Mahinimba	Meliacarpin	Ethyl acetate extracts of leaves	Indian lilac,china berry tree	*Meliaazedarach*	Inhibits the virus replication	HSV

Sr. no.	Name of plant	Active antiviral agent	Parts of plant used/extract	Common name of plant	Botanical name of plant	Mechanism of targeting the virus	Activity of antiviral
18	kumkum	Crocin, picrocrocin	N/A	kesar	*Crocus sativus*	Inhibition of viral replication at beginning & later when virions incorporated into vero cells, inhibit viral entry & replication	HSV-1 HIV-1
19	Kataphala	Tannin (prodelphinidin B-2,3,3'-di-O-gallate)	Bark	Red bayberry	*Myricarubra*	Inhibits the viral attachment with cell	HSV
20	Bililotan	N/A	Volatile oils	Lemon balm, balm mint	*Melissa officinalis*	Inhibits virus replication	HSV
21	Punnaga	Inophyllum, calanolide A coumarins	N/A	Alexandrian laurel, balltree	*Calophyllum inophyllum*	Inhibitory effects on reverse transcriptase	HIV
22	Rajamasha	Unguilin	seed protein	Cow pea	*Vignaunguiculata*	inhibiting effect on reverse transcriptase and the glycohydrolases alpha and beta glucosidase	HIV
23	Simdalu	Quercetin 3rhamnoside(Q3R)	Aerial parts	chameleon plant	*Houttuyniacordata*	Inhibit replication in initial stage of viral infection by direct interaction with virus particle	Ant-influenza
24	asmagnhni	Scopadulcic acid B	Whole plant	Broom weed	*Scopariadulcis L.*	Inhibit the viral replication	HSV-1
25	Bhora	Polysaccharide	Alkaline extract	Asiastic mangrove	*Rhizophoramucronata*	Inhibited the viral binding to cell	HIV
26	Amla	N/A	Solvent extract of dried fruits	Indian gooseberry	*Phyllanthusemblica*	Inhibits HIV reverse transcriptase	HIV
27	Tulsi	Apigenin, ursolic acid	Methanolic holy basil extract	holy basil	*Ocimumtenuiflorum*	Viral adsorption & penetration	HSV, hepatitis, enterovirus
28	Kalmegha	Diterpeneandrographolide, neoandrographolide&14-deoxy-2911-1230didehydroandrographolide	N/A	Green chireta	*Andrographispaniculata*	N/A	HSV
29	Adrak	Beta-sesquiphellandrene	Fresh rhizomes	ginger	*Zingiberofficinalis*	Blocks viral attachment & internalization	Respiratory syncytial virus(RSV)
30	Yashtimdhu	Glycyrrhizin, licorice	N/A	liquorice	*Glycyrrhizaglabra*	N/A	Japanese Encephalitis Virus
31	Haritaki	Chebulagic acid, chebulinic acid	Chebula extract	Chebulicmyrobalan	*Terminaliachebula*	Inhibits viral attachment & penetration	HSV-2,HIV
32	Sarifa	N/A	Peel extract	Custard apple	*Annonareticulata*	Inhibition of HIV-1 reverse transcriptase	HIV
33	Syamapatri	Epigallocatechine 3-gallate	leaves	Green tea	*Camellia sinensis*	Inhibition of primitive stages of infection such as attachment and entry & inhibit membrane fusion by interfering with viral membrane protein	Dengue, Hepatitis B Virus, hepatitis C virus, HIV, HSV, EBV
34	Eranda	Lectin	N/A	Castor oil plant	*Ricinuscommunis*	Inhibits reverse transcriptase &N-glycohydrolases	HIV

Sr. no.	Name of plant	Active antiviral agent	Parts of plant used/extract	Common name of plant	Botanical name of plant	Mechanism of targeting the virus	Activity of antiviral
35	Haridra	Curcumin	root	turmeric	*Curcuma longa*	Reduction of RNA expression, protein synthesis &virus titer	coxsacievirus
36	Lavanga	Eugenol	Flower bud extract	clove	*Eugenia caryophyllus*	Direct inactivation of virus	HSV
37	Vasa	Vasicine	Leaf/justiciaadhatoda crude extract	adusa	*Adhatodavasica*	Inhibits viral replication	Influenza, HSV-1
38	Ashwagandha	Withaferin A		ashwagandha	*Withaniasomnifera*	Inhibits neuraminase of H1N1 influenza virus and inhibits viral release from host cell	Influenza virus
39	Chandana	Beta- santalol	Stem	sandalwood	*Santalum album*	Inhibition of viral mRNA synthesis of influenza A/HK (H_3N_2)	Influenza A
40	Aaavartaki	N/A	Leaves/bark extract	Babul tree	*Acacia nilotica*	In vitro inhibit viral attachment & replication, Inhibit influenza A virus infection by interacting with viral hemagglutinin	Influenza, hepatitis C virus

N/A: Not Available; HIV: Human Immunodeficiency Virus; HSV: Herpes Simplex Virus; EBR: Epstein Barr Virus; RSV: Respiratory Syncytial Virus

Table 2: Antiviral agents from medicinal plants including their mechanism of action on the virus

Mechanism of action of the antivirals obtained from plants

The natural antiviral agents obtain from plants as phytochemicals [9]. This phytochemicals acts on the virus during the infection of host cell by virus & inhibits the further viral infection.

The infection of host cell by virus involves following steps [3] (Figure 1):

- The first step is adsorption of virus on the surface of host cell. This occurs due to interaction of glycoprotein present on the surface of virus with trans membrane receptor on host cell surface.
- After adsorption penetration of virus through cell wall occurs.
- Then the uncoating of virus involves deliverance of genetic material.
- This delivered genetic material integrates or it may remain exists in the nucleus with the host's genetic material and this interfere with replication, transcription and translation processes and protein synthesis occurs.
- These proteins assembles and forms virions and release by the process of exocytosis [3].

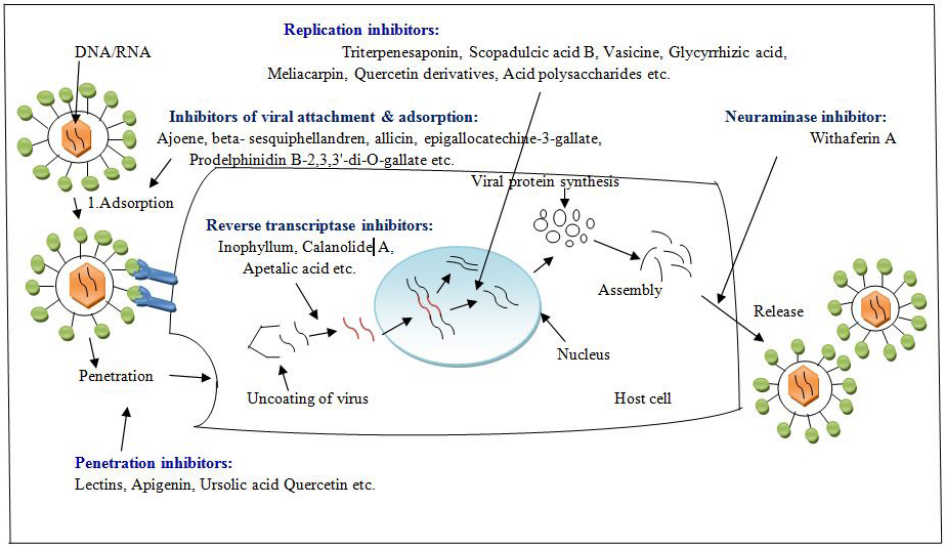

Figure 1: Mechanism of action of antivirals obtained from plant source

The natural antiviral drugs can act on different steps as given above and inhibit viral replication in viral synthesis. The adsorption of virus on the surface of host cell in first step. Inhibition of these step occurs by natural agents such as Quercetin, epigallocatechine-3-gallate, Ajoene, allicin tannin such as prodelphinidin B-2,3,3'-di-O-gallate etc [6,12]. The penetration through cell wall is inhibited by apigenin, ursolicacid, lectins, lignin-carbohydrate complex etc [4]. After uncoating the early enzymes and gene products are formed for control of nucleic acid synthesis. This step is inhibited by antiviral agents such as calanolide A, inophyllum, etc [4,13] which inhibit the reverse transcriptase enzyme. The inhibition of transcription, translation, DNA replication process can be done by Triterpenesaponin, glycyrrhizic acid, meliacarpin, vasicine, scopadulcic acid, acid polysaccharides, quercetin and its derivatives, meliacarpin, scopadulcic acid B etc [10,12]. The viral neuraminase responsible for release of virus from host cell, this neuraminase is inhibited by withaferin A. One more recognized mechanism of action of opposing viruses carrying DNA as genome is the demolition of coating of virus facilitated by natural antivirus such as anthraquinones like aloe emodin [14-19].

Conclusion

Keeping in view it has been concluded that in Ayurveda many of the medicinal plants contain similar phytochemicals that are responsible for their antiviral property. The enzymes which are essential for viral replication are targeted by phytochemicals procured from plants and acts on different stages of viral replication. The mechanism to target virus of many phyto constituents have not been discovered yet. The discoveries & researches on these phytochemicals for their mechanisms to target the viruses are in the progress throughout the globe. In this era of emerging viral infections new bio active moieties should be discovered. The medicinal plants are taken as source for finding of new antiviral agents with potent antiviral activity then conventional antiviral compounds.

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