



Plants of Ethnoveterinary Medicine Importance with Antiviral Activity

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Abstract

Indian heritage is rich in diversified flora due to its diversified geographical locations. Amongst these flora, several of them have been in traditional use for the treatment of ailments and several of them are yet to be explored. Out of all, antiviral plants and their activity seeks attention as during past one decade several emerging viral diseases came into existence. RNA viruses are capable of mutating at a faster rate than the DNA viruses, show antiviral resistance and their vaccine development requires quite a lot time. In such a scenario antiviral plant and their pure compounds/extracts can open newer insights for combating the antiviral resistance. Thus, in this chapter antiviral activity of plants against human and animal viruses have been discussed.

Keywords: Plants; Antiviral Activity; Viruses; DNA; RNA

Introduction

Livestock and poultry industry contribute a major source of income to Indian economy. The animal husbandry is a major contributor to the Indian economy and overall contribution is 28-32% in agricultural GDP and 4 to 6% of the national GDP. Total export earnings from livestock, poultry and related products is approximately Rs. 2,54,088.6 million. However, it has been reported that the viral diseases in poultry and livestock species causes heavy losses to Indian economy. The viral diseases causing heavy losses in livestock and poultry are Foot-and-mouth disease, Peste des petits ruminants, Blue tongue, Infectious bovine rhinotracheitis, Ranikhet disease, Mareks disease, Fowl pox, etc. Moreover, there are losses incurred to livestock Industry due to vaccine failure in animals.

The antiviral drugs to treat the viral disease are accompanied with other complications like virus resistance to drugs, viral latency and side effects. Thus the present condition demands development of alternate therapies which can rule out the above issues. While exploring new horizons related to above domain, ethnopharmacology may provide an alternate resource for discovering novel antiviral agents. It involves study of medicinal plants with a known history of its traditional use as a medicine with specific pharmacological activity.

Several antiviral compounds derived from plants have been studied earlier and have been found to have inhibiting viral replication and viral genome synthesis. In the past, there are reports that some plant extracts have been found to have antiviral activities [1-3]. However, the work needs to be validated in a broader perspective by testing more effective antiviral and immunomodulatory drugs. These novel drugs should be cheap, effective and reachable at village level so that the poor farmers can use it at their own level. Also, there are several Himalayan plants that are known for their various activities but still need to be tested for those activities.

A wide variety of natural compounds derived from medicinal plants (herbs) have been extensively studied in terms of their antiviral activity. Several hundred natural active compounds have been identified worldwide. Hence, keeping in mind the above points use of ethnopharmacology along with application of in-vitro assays can be used to exploit these novel antimicrobials for the treatment of viral diseases. Alternatively, certain herbal drugs can act as immunomodulatory drugs that can boost up the immune system of the animals to combat the infection.

Methodology to Explore Plants with Antiviral Activity

Indian heritage of Uttarakhand is rich in such novel plants and their activity can be further explored in cell based assays followed by

their in-vivo testing in lab animals. Earlier, several scientists have worked in this domain to test the antiviral activity of the medicinal plants [1-3]. However, the work needs to be validated in a broader perspective by testing more effective antiviral and immunomodulatory drugs. These novel drugs should be cheap, effective and reachable at village level so that the poor farmers can use it at their own level.

Plants having antiviral activities

Plants of ethnomedical use endowed with antiviral property, have been used for treatment of veterinary and medical viral diseases [4-6]. For the first time scientists were lured for the development of antiviral agents after second world war in Europe. Inspired by this idea, 288 plants were tested for their activity against influenza virus in embryonated chicken eggs, out of which 12 extracts were found active to inhibit viral activity [7]. Canadian scientists further explored that juices from grape, strawberry and apple were active against poliovirus, coxsackie virus and Herpes simplex virus [8-10]. Following this study, British Columbian medicinal plants were tested [11] and several plants were explored to have antiviral activity. It was found that extract of *Ipomopsis aggregata* was active against parainfluenza virus type 3, *Lomatium dissectum* root extract against rotavirus, *Rosa nutkana*, *Amelanchier alnifolia* were active against enteric corona virus, root extract of *Potentilla arguta* and a branch tip extract of *Sambucus racemosa* was active against respiratory syncytial virus (RSV) [11]. In a study by Semple and colleagues [12], forty plants were tested for antiviral activity against Ross River virus (RRV), human cytomegalovirus (HCMV), and poliovirus type 1. The active extracts against poliovirus were the aerial parts of *Pterocaulon sphacelatum* (Asteraceae) and roots of *Dianella longifolia* var. *grandis* (Liliaceae). Extracts active against HCMV were extracts of *Euphorbia australis* (Euphorbiaceae) and *Scaevola spinescens* (family-*Goodeniaceae*). Extracts of *Eremophila latrobei* subsp. *glabra* (family-*Myoporaceae*) and *Pittosporum phylliraeoides* var. *microcarpa* (family-*Pittosporaceae*) exhibited antiviral activity against RRV.

Crude extract of *Sanicula europea* has been found to inhibit the activity of human parainfluenza virus type 2 [13]. Other medicinal plants *Nepeta coerulea*, *Nepeta nepetella*, *Nepeta tuberosa*, *Sanguisorba minor magnolii* and *Dittrichia viscosa* have been found to have antiviral activity against DNA (HSV-1) and RNA viruses (VSV). *Dittrichia viscosa* have been found to have activity against Polio virus-1 [14] (Abad, et al. 2000). Leaf extract of *Azadirachta indica*

has been found to be active against chicken pox (DNA), smallpox (DNA), poxvirus (DNA), poliomyelitis (RNA) and herpes viruses (DNA) [15]. Extract from *Opuntia streptacantha* (cactus plant) has been shown to have antiviral activity against HSV, equine herpes virus, pseudorabies virus and influenza virus [16]. Plants like *Bergenia ligulata*, *Nerium indicum* and *Holoptelia integrifolia* have been found to have antiviral activities against influenza virus (RNA virus) and Herpes simplex virus type 1 (HSV-1) (DNA virus) [17]. Extract of tuber from *Dioscorea batatas*, *D. ecne*, *D. alata*, *D. pseudo-japonica* have been found to show antiviral activity against adenovirus, a herpesvirus (e.g., HSV-1), a poxvirus (e.g., an orthopoxvirus such as variola or vaccinia, or molluscum contagiosum), a picornavirus (e.g., rhinovirus or enterovirus), an orthomyxovirus (e.g., influenzavirus), a paramyxovirus [e.g., parainfluenzavirus, mumps virus, measles virus, and respiratory syncytial virus (RSV)], a coronavirus (e.g., SARS), a papovavirus (e.g., papillomaviruses).

The herb mixtures prepared using various Chinese medicinal plants namely *Aeginetiae herba*, *Blechni rhizoma*, *Lespedezae herba*, *Polygoni cuspidati rhizoma*, *Forsythiae fructus*, and *Ligustri fructus*, or contain the herbal ingredients namely *Aeginetiae herba*, *Lonicerae flos*, *Prunellae spica*, and *Lespedezae herba* in varying proportion of weights have been found to have antiviral activity against Murine Leukemia virus (MuLV) and Human immunodeficiency syndrome virus (HIV). It has been found that Milk Thistle Fruit dry extract, Chinese Sage Root dry extract, Schisandra Fruit dry extract and Astragalus Root dry extract has activity against viruses of Flaviviridae. In a recent study, four herbs *Terminalia belirica*, *Salacia chinensis*, *Zingiber montanum* and *Peltophorum pterocarpum* have been found effective against highly pathogenic avian influenza (H5N1) [3]. In another study, plants from Himalayan region have been reported to be effective against Bronchitis caused by influenza virus, rhinovirus, adenovirus, coronavirus and respiratory syncytial virus [18]. It was concluded that plants from Himalayan region of India having ethnoveterinary importance are active against respiratory disease, however, few studies have been related with their in-vitro validation. Herbs found active against influenza viruses (H1N1, H3N2, H5N2 and H3N8) are *Wrightia tinctoria*, *Strychnos minor*, *Hypecoum erectum*, *Momordica cochinchinensis*, *Terminalia chebula* and *Alchemilla mollis* (aqueous extract) [19-21]. Two herbal compound dipotassium glycyrrhizinate (DG) and sodium tanshinone IIA sulfonate (STS) which are Triterpenoids and Diterpenoids, respectively were found to be effective in-vitro against Marek's Disease virus [19]. Methanolic extracts of several

Cholistani plants *Achyranthes aspera*, *Haloxylon recurvum*, *Haloxylon salicornicum*, *Panicum antidotale*, *Salsola baryosma*, *Sporobolus icolados* were shown to have the optimal antiviral potential in Pakistan [22]. On investigating in-vitro antiviral activity of *Hibiscus sabdarifa* on Hep-2 cells against Measles virus it was found that at 5, 10 and 15 mg/ml concentrations, *H. sabdariffa* had antiviral activities [2]. Turmeric (Curcumin, phenolic constituent) has been found to inhibit replication of bovine herpes virus type-1 (BHV-1) [23].

National status

In Indian scenario, animals are reared for the purpose of getting milk and meat. As a by product dung is also obtained from them and utilised as a source of fertiliser and fuel. However, India being a sub-tropical country, the animals are vulnerable to various infectious diseases. This is further aggravated by lack of proper veterinary facilities and higher price of drugs which leads to increased mortality of animals. India is rich in medicinal plants and these can be exploited for the treatment of ailments in a cost effective way. Various plant parts fruit, rhizome, stem, seed have been used for the treatment of veterinary ailments. The route of administration used is primarily oral followed by topical applications. Three plant extracts *Hypericum mysorensense*, *Hypericum hookerianum* and *Usnea complanta* exhibited significant antiviral activity against Herpes simplex virus (HSV) [19]. Similarly, *Acacia arabica* and *Eugenia jambolana* showed antiviral activity against goat pox virus (Bhanuprakash., *et al.* 2008). Another variety of *Acacia*, *Acacia Nilotica* was found to have antibacterial, antifungal, antiviral, and immunomodulatory action. In a study by Pant and colleagues hydroalcoholic extract of *Withania somnifera* roots have found to have antiviral activity against Infectious Bursal Disease virus (IBDV). This extract was able to inhibit cytopathic effect of IBDV upto 99.9% [19].

Why it is important to develop ethopharmacological antiviral approach

Ethnopharmacology forms an alternative approach for the discovery of novel antiviral agents. It is one of the most intriguing field as it involves application of traditional methods using substances known to have a particular biological activity. With increasing resistance of microorganisms (bacteria, viruses and parasites) to standard antimicrobial therapy, alternative treatments especially from herbal sources are being re-explored at gaining speed. In the past few years due to increase in antimicrobial resistance there has been heightened interest to find alternate effective methods for the treatment of diseases. Herbal plant's extracts and their pure

compounds are the alternate sources for the treatment of those ailments. Several medicinal plants have been tested and have been found effective against lethal viral infections. However, their activity was not found sufficient to suppress the viral activity effectively.

In most cases the pharmacological mechanisms of the combinations are not well-studied and exaggerated adverse effects or therapeutic failures have been observed, although successful treatments using combination of medicinal plant products with orthodox drugs were also reported. In a clinical study Corina., *et al.* (1999) examined the effect of extracts of Romanian medicinal plants in combination with acyclovir in the treatment of 52 patients suffering herpetic keratitis [24]. Better results and faster healing of ulceration were obtained using *Actium lappa*, *Calendula officinalis* and *Geranium robertianum* extracts then with the usual acyclovir treatment only. Amantadine hydrochloride is an accepted and well-studied selective inhibitor of influenza virus reproduction.

Link with religious sentiments

In folklores of Ramayana, Sanjeevani booti has been illustrated which saved Laxman's life. Scientist claim that they have discovered this wonder herb Sanjeevani. It's botanical name is *Rhodiola rosea*. This herb is found in high altitudes of Himalaya mountains of Uttarakhand. This herb is being investigated by the DRDO lab for its adaptogenic properties that can be used by the soldiers to adjust the low pressure, low oxygen environment and anti-depressant properties. However, other properties like antiviral, antibacterial and antioxidant properties needs to be further explored. Similarly, several other plants are there in high altitudes of Uttarakhand which are used by the local people and have not been reported in any literature/article. These plants need to be explored by local communication to villagers, its identification and testing for the desired property.

Conclusion

The Indian land is blessed with rich and diverse culture and plant resources. Detailed description of these plants in curing local ailments and their ethnopharmacological value can lead to development of novel herbal drugs or isolation of pure compounds. Pure compounds from various plant species are shown to have antiviral activity. Some of the pure compounds like tanins, flavones and alkaloids are found to have antiviral activity. Also, it has been found that selection of plants on basis of ethnomedical uses have a higher chance of getting a plant of desired activity than the screening programs.

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