



A PRIMITIVE APPROACH ON REVIEW OF SIDDHA HERBS, HERBO-MINERAL FORMULATION EXHIBITING ANTIVIRAL ACTIVITY

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ABSTRACT

Viral disease is an issue of global and public health concern in this modern era. The traditional use of Siddha medicines serve as a milestone even in this scientific world in which a number of chemical combinative medicines are used. Several thousands of plant and herb species that are powerful antiviral agents have been studied. A wide variety of active phytochemicals, such as the flavanoids, terpenoids, lignans, sulphides, polyphenolics, coumarins, saponins, furyl compounds, alkaloids, polyenes, thiophenes, proteins and peptides are identified in herbs. Volatile oils of some commonly used kitchen herbs, tea of herbs and spices do possess antiviral activity. But it is still questionable about the pharmacopoeia of compounds in medicinal plants. These phytochemicals either inhibit viral DNA or RNA formation or viral replication. Antiviral drugs are said to be those drugs which effectively counteract the causative viruses. The present review is an initial step to consolidate the Siddha antiviral drugs present in the literature. This review illustrates that, there are countless potentially useful medicinal herbs for evaluation, exploitation and validation for therapeutic applications against morphologically, genetically and functionally different viral families such as Retroviridae, Hepadnaviridae and Herpesviridae. Several potential works have been done to list out the active principles, lateral research of selective viral diseases. The present review covered all the Siddha literatures from time immemorial till now.

KEY WORDS : Antiviral Drugs, Phytochemicals, Siddha Medicine, Viral Diseases.



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INTRODUCTION

Viral diseases are still a life threatening diseases with high degree of complication to the human population because of its rapid outbreak as a pandemic throughout the world. The causative agents of the most fatal diseases are viruses, such as cancer, anti-acquired immune deficiency syndrome (AIDS), herpes simplex¹. To control the viral diseases, is a great challenge even today because of its metabolic properties. Only to a limited number of viral infections are currently protected for preventive vaccinations possible. Antiviral drugs cannot act effectively due to its easy adaptability and development of resistance as well as the emergence of new hybrid viruses. Only few Antiviral drugs are available and show a variety of side effects². So in the past decade, a search for safe natural remedies came into centre of interest. Viral diseases, the most common cause of human illness caused by a small infectious agent consists of a nucleic acid genomic composition either single stranded or double stranded, RNA or DNA³. Virology, the study of virus has become a sub-speciality of microbiology now. The word virus referring to poison in Latin has

been named as virion since 1959⁴. Viruses are inert and cannot live in a free state and infect host cells to survive. So they have been described as intracellular parasites. Hence virion can be effectively defined as a single stable infecting particle released from the cell and fully capable of infecting other cells of the same type⁵. By using the host material, they synthesize protein and reproduce genetic material. Hence, the viral infections from mild fever to threatening diseases like AIDS, originate from direct or vector mediated spread. The clinical characteristics of viruses may differ from species to species even though belonging to the same family.

Classification of Viruses

The International Committee on Taxonomy of Viruses (ICTV) operated on authoritative database containing taxonomic information for 1,950 virus species⁶. Viruses can be classified as DNA viruses and RNA viruses based on genotypic characters and the classification of DNA and RNA viruses are listed in Table 1 and Table 2 respectively.

Table 1
Classification of DNA Viruses

Virus (DNA)	Clinical Manifestation
Adenoviruses	Upper RTI/pharyngitis, Acute Diarrhoea
Herpes Viruses	Vesicular Rash-(HSV I & II), Chicken pox (Varicella zoster), Hepato-renal infection, Roseola infantum (HSV 6,7), Infectious Mononucleosis, Burkit's lymphoma (EB viruses), Nasopharyngeal Ca (HSV 8), Kaposis Sarcoma
Human Papilloma Virus	Common Wart
Pox Viruses	Small pox

Table 2
Classification of RNA Viruses

Viruses (RNA)	Clinical Manifestation
Picornavirus	Gut and Neurological illness, Upper Respiratory tract infection
Rheo viruses	Mild Upper Respiratory tract infection, gut disease, Gastro enteritis (Rotavirus)
Toga viruses	German measles(Rubella), Haemorrhagic/Yellow fever, Chronic hepatitis (Hepatitis C)

The species of the above said families manifest in various symptoms from mild to severe. Symptoms of such viral diseases include fever with chills (Influenza), swelling of the parotid gland (Mumps), headache, retro-

orbital pain (Dengue), diarrhea, nausea, vomiting, jaundice (Hepatitis), abdominal pain, vesicular rashes (small pox) and loss of weight (HIV), body pain, myalgia (Glandular Fever)⁷. For these clinical syndromes,

which spread through droplet or blood or fecal-oral contact, many chemical compounds possessing antiviral activity like famciclovir, valciclovir, acyclovir have been seriously

questioned owing to various health hazards⁸. Some of the adverse effects of viral drugs have been listed below in Table 3.

Table 3
Side effects of Antiviral Drugs

Antiviral Drugs	Side Effects
Acyclovir	Burning sensation, Hypotension
Famciclovir	Diarrhoea, Pruritus
Zidovudine	Insomnia, Anaemia, Neutropenia
Nevirapine	Rashes, Nausea, Hepatotoxic
Sagurinavir	Photosensitivity
Amantadine	Insomnia, Dizziness, Decreased Mental Concentration

Several potential approaches and searches have been made towards the discovery of safe and effective phytomedicines from traditional practices. In Siddha system of medicine many viral diseases have been described by a variety of terminologies along with effective remedies⁹.

Siddha Review of Measles

Measles is described by the terminologies like "KuruNoi, Maari, Vichbodagam, Vaisuri, Thattammai" in Siddha system of medicine. Due to the derangement of humours especially pitham, fever followed by maculopapular rashes sets in. According to a saint, Yugimuni, measles is classified into 14 types and Thattammai can be clinically correlated with measles in which symptoms like fever, rashes with centripetal distribution symptoms of upper respiratory tract infection like running nose, can be seen.

Cause for Provocation of Measles

During the summer, intensive scorching sun increases body heat and leads to the sudden eruption of rashes all over the body.

Siddha review of Mumps

Mumps is called by terms like "Puttalammai and Pootuthalammai". After three to four days of mild fever, slight swelling of the parotid gland on one side or both sides can be seen. But this is a non-suppurative disease. In some cases mastitis and orchitis can also be seen.

Siddha review of the disease Chikungunya

Described by the term 'Senkaraisuram' it is manifested by the symptoms like intense fever, immobility of joints, pain in the body.

Antiviral substances in plants

Medicinal plants of Tamil Nadu (Southern India) are a rich source of antiviral activities which contain different phytochemicals, such as alkaloids, terpenoids, lignans, coumarins, tannins, flavanoids, and saponins¹⁰. The mode of action of alkaloids is not extensively explored. The focus of this present review is particularly on antiviral agents of herbs used in traditional medicines and it is listed below in Table 4.

Table 4
Mode of action of alkaloids

No	Botanical name	Synonym	Alkaloids	Action
1	<i>Glycyrrhiza glabra</i>	Licorice	Glycyrrhizin	Induction of interferon production via effects of T-cell function ¹¹
2	<i>Allium sativum</i>	Garlic	Alliin	Inhibit replication of influenza B virus, Herpes simplex virus ¹²
3	<i>Ocimum sanctum</i>	Tulsi	Eugenol	Inhibition of nucleic acid synthesis ¹³
4	<i>Mentha piperita</i>	Peppermint	Menthol	Inhibit activity against HSV-1&2 ¹⁴
5	<i>Melia dubia</i>	Common bead tree	Ethyl acetate extract	Inhibit activity against HSV-1&2 ¹⁵
6	<i>Cissus quadrangularis</i>	Veldt Grape	Methanolic extract	Inhibit activity against HSV-1&2 ¹⁶

7	<i>Phyllanthus urinaria</i>	Indian Phyllanthus	Ellagic acid	Inhibit immunotolerance against Hepatitis B virus e-antigen ¹⁷
8	<i>Indigofera tinctoria</i>	Indigo plant	Indigoferin	Inhibitors of HIV-1&2 replication ¹⁸
9	<i>Zingiber officinale</i>	Ginger	Nucleoside	Exert activity against HSV and Hep-B Virus ¹⁹
10	<i>Azadirachta indica</i>	Neem	Azadirachtin	Effective against Chikungunya virus, Dengue virus Type 2 and HSV-1 ²⁰
11	<i>Thuja occidentalis</i>	White cedar	Thujyl alcohol	Increase secretion of cytokine and inhibit replication of HIV-1 ²¹
12	<i>Echinaceae purpurea</i>	Cone Flower	Extract	Causes migration of neutrophils from bone marrow into circulation ²²
13	<i>Opuntia streptacantha</i>	Cactus	Cell wall extract	Inhibits intracellular DNA and RNA virus replication ²³
14	<i>Olea europoeae</i>	Olive	Olein	Interfere with amino acid production and stop viral replication ²⁴
15	<i>Gossypium arboreum</i>	Cotton seed	Gossypol	Exhibit antiviral activity against HSV-2 ²⁵
16	<i>Artemisia annua</i>	Sweet worm wood	Artemisin	Exhibit antiviral action against CMV, HSV-1&2, Hep –B&C virus, EB virus ²⁶
17	<i>Calophyllum inophyllum</i>	Doomba oil tree	Calanolide A	Inhibit against HIV-1 ²⁷
18	<i>Tamarindus indica</i>	Tamarind	Glyoid	Inhibits Rubella virus antigen synthesis ²⁸
19	<i>Curcuma longa</i>	Turmeric	Curcumin	Inhibit growth of HPV and interfere with replication process of HSV ²⁹
20	<i>Cryptostegia grandiflora</i>	Rubber Vine	Extract	Inhibit against HIV-1 ³⁰
21	<i>Usnea complanta</i>	Beard of Koa	Extract	Inhibit against HIV-1 ³¹
22	<i>Calophyllum lanigerum</i>	Poon Tree	CalanolideA,B	Effective against HIV-1 ³²
23	<i>Hypericum perforatum</i>	Tipton's weed	Hypericin, Anthraquinone	Inhibit HIV-1 reverse transcriptase ³³
24	<i>Hypericum mysorense</i>	St.John's wort	Hypericin	Inhibit against HIV-1 ³⁴
25	<i>Hypericum hookerianum</i>	St.John's wort	Hypericin	Inhibit against HIV-1 ³⁵

Antiviral herbal and mineral preparations³⁶⁻³⁸

1. *Argemone mexicana*

Latex of the plant is applied over the warty lesions.

2. *Withania somnifera*

Root of the above plant is mixed with powder of licorice and lemon juice and applied over the warts.

3. *Hygrophilus auriculata*

Whole plant is burnt and ash is mixed with castor oil and applied for warts.

4. *Azadirachta indica*

Paste of neem leaves is applied over the swelling of mumps.

5. *Caesalpinia crista*

Paste of seeds of the above plant is mixed with egg white and applied for orchitis and mastitis in case of mumps.

6. *Cyanadon dactylon*

Oil of the plant is applied over bumps caused by pox virus.

7. *Shorea robusta*

Paste is applied over papular lesions of bumps.

8. *Corollocarpus epigaeus*

Paste is applied over vesicles of Shingles.

9. *Carica papaya*

Unripened juice of the plant is consumed to reduce biliousness caused by hepatitis.

10. *Datura metel*

1-3 drops of the plant along with sugarcane candy is given for rabies.

Table 5
Metallic antiviral agents

S.no	Name of the mineral preparation	Effect on the disease
1	Galena sulphide	Warts
2	Pearl oxide	Measles
3	Gold sulphide	Mumps
4	Hydrargyrum per chloride	Molluscum contagiosum
5	Red ochre sulphide	Herpes zoster
6	Coral oxide	Measles
7	Vermilion	Measles
9	Borax powder	Herpes zoster
10	Zinc oxide	Hepatitis
11	Ruby oxide	Measles
12	Copper oxide	Hepatitis
13	Lead oxide	Hepatitis
14	Red ochre sulphide	Measles
15	Silver oxide	Hepatitis

Compound herbal preparations for some of the viral diseases

For Treatment of Hepatitis

1. Adhimathura nei(ghee)

The main ingredients are *Azadirachta indica*, *Michelia champaca*, iron dust and the drugs given in the form of ghee in 2-3 drops.

2. Kadukkai nei

Consists of *Terminalia chebula* and *Phyllanthus amarus* in the preparation and it is consumed in ghee form in 2-3 drops.

3. Thanneervittan kizhangu nei

Drugs like *Strychnos potatorum* seeds, *Hemidesmus indicus* along with *Asparagus racemosus* are included and the ghee is given 2-3 drops.

4. Kittathychooranam

Drugs including three myrobalans and iron dust are included in the preparation and it is given in chooranam(powder) at a dosage of 1 gm thrice a day.

5. Aridhradhi chooranam

Three myrobalans along with turmeric are included and the chooranam is given at a dosage of about 1 gm a day.

6. Kodiveliathy kudineer

Main ingredients are root bark of *Plumbago zeylanica*, *Zingiber officinale*, *Piper nigrum*, *Piper longum*, *Tinospora cordifolia* and it is given in the form of kudineer(Decoction) at a dosage of 30 ml.

7. Gowri Chinthamani Chenduram

Main ingredients are Purified Sulphur, Purified Mercury, Purified Borax, *Zingiber officinale*, *Piper nigrum* and the sulphide form of the drug is given at a dosage of 488mg.

8. Sathilinga kuligai

Main ingredients like *Piper nigrum*, *Piper longum*, *Zingiber officinale*, Mercuric sulphide, Rock salt are included in the preparation and it is given in the form of tablet.

9. Natthai nei

Flesh of snail, *Plumbago zeylanica*, *Withania somnifera* and three myrobalans are included in this preparation and the nei is given at a dosage of 2-3 drops.

Preparations for curing Measles

Vaeppa Eerku kudineer

Azadirachta indica, Root of *Citrus medica*, *Allium sativum*, Young leaves of *Mangifera indica*, *Murraya koenigii* are the main ingredients included in this kudineer and the dosage is 30 ml.

Herbal preparation for curing Rabies

Leaves of *Moringa oleifera*, *Allium sativum*, piece of *Curcuma longa*, salt, *Brassica alba* are mixed together, grounded and applied on the sore externally.

Some of the medicinally important herbs are described below⁴¹

1) Glycyrrhiza glabra

Common name: Licorice

Family name: Fabaceae

It is a perennial herb plant with aromatic roots, sweet and bitter in taste. It measures between 1 m and 1.5 meters high, with pinnate leaves and purple to pale whitish flowers of 0.8-1.2 cm with oblong fruit pods containing several seeds. It possesses expectorant, mild laxative and expectorant properties. It is used for treating coughs and catarrhal effects. The extract is efficient in the treatment of gastric ulcer and Addison's disease. Poultice of leaves of licorice heals head scalds and armpit perspiration. The main ingredients are Glycyrrhizic acid, Anthocyanin, Isoliquiritin, Coumarin Isoliquiritoside from the root of licorice which has an antiviral activity against Kaposi's sarcoma associated virus and also against DNA and RNA viruses like Hepatitis A virus, Hepatitis B virus, Corona virus, Influenza A virus, HIV-1 etc. Glycyrrhizin and glycyrrhizic acid slows the development of the virus. Glycyrrhizic acid is also effective in the replication in SARS associated corona virus in vivo and also exerts antiviral activity against Herpes virus 1&2, Japanese encephalitis, Varicella zoster virus, Ebstein Barr virus, Influenza A virus, CMV¹¹.

2. Azadirachta indica

Common name: Neem

Family name: Meliaceae

It is found abundantly in tropical countries and has enormous potential to withstand drought. The leaves and seeds of neem has been used a treatment for thousands of years in India

and now being practiced in many parts of the world. It is a large tree of 12-18m height with imparipinnate leaves and white or pale yellow flowers. Bark has numerous furrows and tubercles with grey, dark grey or reddish brown in colour. It is rich in alkaloids like Nimbin, Nimbidin, Nimbinin. Aqueous extract of tender leaves exhibit antiviral activity against Foul pox, Vaccinia, Variola, Chickungunya virus, Measles virus, Dengue type 2 virus. Methanolic extract of neem has an effective action against group B Cocksackie virus. Aqueous extract of bark of neem has an effective action against HSV- 1. Aqueous extract of neem bark serves as a powerful inhibitor of entrance against HSV-1 infection. The rich chemical constitution of flavanoids, triterpenoids and glycosides of neem are the reason behind its antiviral activities. Leaf of neem has proven to be an effective antiviral activity against dengue virus type 2.

3. Phyllanthus urinaria

Common name: Phyllanthus

Family name: Euphorbiaceae

It is an annual herb with glabrous, erect stem of about 30 cm in height. The stem is purple in colour, with oblong compound leaves, obtuse apex, glabrous short petiole, 2-3 male flowers in the clustered leaf axils and with acrid and sour taste. It contains Gallic acid, Ellagic acid, Daucosterol, Ferulic acid, Lignans, Heamatoxylin acid, Corilagin, Flavanoids, Rutin. According to folklore, the entire plant is used as a medicine has analgesic activity, treats hepatitis-B, diarrhoea, sore throat, appendicitis. It is effective in treating biliousness, anuria and a diuretic in dropsical infections. The flavanoid ellagic acid found in this plant inhibits immunotolerance against HBV e-antigen¹⁶.

4. Curcuma longa

Common name: Turmeric

Family name: Zingiberaceae

It is an underground rhizome with 5% oil, 5% Curcumin, a polyphenol form of the active ingredient. It is very stable in the presence of light and its stability can be improved by adding citrus juices. Curcumin, the active principle present in turmeric interferes with the replication of HSV. Researchers from the

Institute of cytology & preventive oncology in New Delhi found out that curcumin in turmeric bound on the same receptor sites as that of Human papilloma virus, thereby preventing the chances of cervical cancer in future⁴². Curcumin inhibits Herpes simplex virus by a mechanism independent of p300/CBP histone acetyl transferase activity. The active principle also activates transcription factor AP-1 in cervical cancer and suppression and AP-1 activity in HeLa cells²⁸.

5. *Allium sativum*

Common name: Garlic

Family name: Liliaceae

It is a large perennial herb with long, acute, flat leaves with solid bulbils. Garlic, the main culinary herb in the kitchen contains active ingredients like Allicin and Allisatin. Garlic cloves are said to have properties of antibiotics and increase prevention of cancer. Garlic cloves have significant on viruses causing flu, colds. The main ingredients are Allicin, Liallylsulphide, Ajoene, diallyltrisulfide. Allicin has been used commonly in lab experiments to arrest cancerous growth in mice in immune compromised individuals, garlic extract is found to be useful in the prophylaxis of Human Cytomegalo virus infection⁴³. Garlic with a good selectivity index has an inhibitory effect on influenza virus proliferation and penetration in cell culture⁴⁴. Ajoene found in oil macerates of garlic exert antiviral activity against HSV-1, HSV-2, parainfluenza virus type 2, human rhino virus type -2.

6). *Zingiber officinale*

Common name: Ginger

Family name: Zingiberaceae

It is a herbaceous, thick lobed, rhizomatous, pale yellowish differing in size and shape. It is a carminative and serves as an important ingredient in some narcotic preparations. The sesquiterpene alcohol, Zingerol, Zingiberine are the main active ingredients present. Fresh ginger blocks viral attachment and internalization and acts against HRSV-induced plaque formation on airway epithelium⁴⁵.

Recent researches in antiviral activity of plants

The antimicrobial activities of plant extracts and oils have been recognized and explored for many years. The antiviral action of essential oils of *Myristica eucalyptus*⁴⁶ exhibited a high level of antiviral activity against HSV-1 & HSV-2 in viral suspension tests. Sandal wood oil, an essential oil of *Santalum album* showed a dose dependent effect against HSV-1 with no reported cytotoxicity⁴⁷. Black seed oil from *Nigella sativa* exhibited a striking antiviral activity against murine Cytomegalovirus infection⁴⁸. Aloe polymannose, a mannose purified from *Aloe barbadensis* enhance antibody concentrations against enteroviruses and polio virus strains⁴⁹. The Ellagitannin extracted from *Syzygium aromaticum* exerts its antiviral activity against Herpes simplex virus⁵⁰. Eugeniiin exerts inhibitory action on DNA synthesis. Anthraquinones from extracts of *Aloe barbadensis* and *Rheum officinale* is found to be active against HSV-1⁵¹.

CONCLUSION

It is estimated that there are 250,000 to 500,000 species of plants on Earth⁵². The bio-active principles of most of them have been identified with plenty of antiviral agents. People nowadays pay a greater attention towards herbal remedies since they do suffer from side effects, cost, undesirable effects they experienced. So a greater expectancy towards herbal standardization and evaluating pharmacological activities is the need of the hour. Hence it is an urge need to explore the scientific evaluation of bioactive medicinal plants. Hence open, placebo controlled, double blind clinical trials are to be done to prove effectively the therapeutic value of medicinal plants, thereby providing the way for safe, effective, cheap phytotherapies.

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