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A REVIEW ON SIDDHA HERBAL FORMULATION DEVA CHOORANAM FOR IMPROVING THE QOL IN ACQUIRED IMMUNO DEFICIENCY SYNDROME (AIDS)

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ABSTRACT

The ancient *Siddha* system of medicine has its origin right from the genesis of mankind. According to this medical system, herbs and human have proved their inseparable unification time and again all through the ages. Either of the two is inevitably reliable on each other based on the concept of Mukkutram (humoural theory) and Arusuvai (taste theory). Scientifically the existence of multitudinous variety of plants on the earth has always exhibited their incalculable efficacy to dreadful diseases such as HIV infection. Hence this article aims to explore the therapeutic efficacy and scientific facts behind the *Siddha* drug *Deva Chooranam*. *Deva Chooranam* is a combination of three medicinal herbs, *Cedrus deodara* (Devadaru), *Alpinia galanga* (Arathai), *Cinnamomum tamala* (Lavanga pathiri). Each of these herbs has promulgated their hundred-proof medicinal properties by redressing man from some of the ailments and diseases which have proved to deadweight burden to mankind for ages. The rhizome of *Alpinia galanga* (Arathai) has exhibited its property owing to HIV infection and all the three plants significantly showcased the Immunomodulatory property.

KEY WORDS: *Siddha*, *Siddha medicine*, Deva Chooranam, HIV, AIDS, Antiviral activity, Immunomodulatory activity.

INTRODUCTION

The therapeutic efficacy of the plant kingdom has been known to mankind since ages. Even before the discovery of synthetic drugs, various floral families have been in the aid of treating various ailments. The ancient man was treating numerous diseases using the seeds, fruits, gums, barks, roots and other parts of the plants. Now even after the evolution of the 'synthetic drug era' the usefulness and credibility of the therapeutic plants are being discerned scientifically. In the past few decades, Human Immune deficiency virus, the causative agent of AIDS has become the recent foeman of public health throughout the globe.

HIV is one of the alarming deadly diseases with various co morbid conditions leading to debilitating illness and death. The prevalence of HIV is increasing worldwide although new infections decreased from 3·3 million in 2002, to 2·3 million in 2012. Global AIDS-related deaths peaked at 2·3 million in 2005, and decreased to 1·6 million by 2012[1]. India, with a population of almost 1 billion people and 4 million people have been estimated to be infected with HIV, and it is thought to be the country with the largest number of HIV-infected people. According to UNAIDS, HIV is decisively set in India's general population and rapidly spreading into rural areas. [2,3] Almost 500,000 people are infected in Tamil Nadu and the infection rate is 3 times higher in villages than in cities.[4]

Since antiretroviral therapy is too expensive for most Indians, vaccine research must be accelerated in India. HIV infection in India is mainly of HIV-1. HIV-2 has been reported sporadically. HAART (highly active antiretroviral therapy) is the most recent treatment strategy which targets the viral entrance and the reverse transcriptase and protease enzymes.[5,6] But unfortunately like in any synthetic drug, this approach also succumbs numerous side effects.[7] Therefore an alternate therapy is best appreciated which can overcome the drawbacks of the currently available synthetic drugs.

Deva Chooranam is a combination of three herbs namely *Cedrus deodara* (Devadaru), *Alpinia galanga* (Arathai) and *Cinnamomum tamala* (Lavanga pathiri*)*. The choice of these three herbs mentioned in Agathiyar gunavagadam of classical *Siddha* literature is based on the indications mentioned such as Chronic fever, diarrhea, dysentery, oral ulcers, respiratory

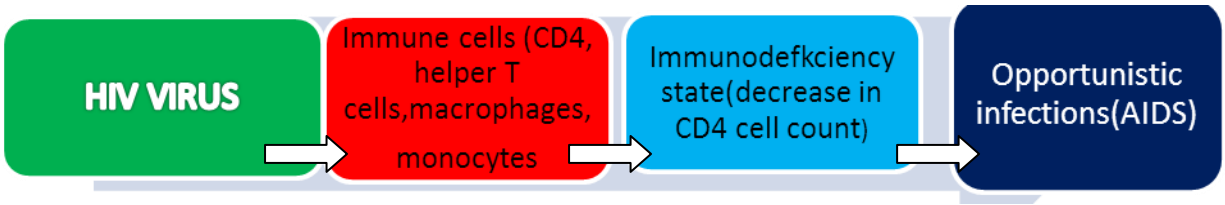
ailments, skin diseases and tumours that can be found in the co existing clinical conditions of HIV infected individuals.[8]

Preparation of trial drug

All the ingredients *Cedrus deodara* (Devadaru), *Alpinia galanga* (Arathai),*Cinnamomum tamala* (Lavanga pathiri)*)* are taken in equal amounts and ground into fine powder and filtered using a mesh cloth and stored in a sterile container.[8]

Dosage: 5-10 gms twice daily in Milk.

HIV and Immunodeficiency



HIV excels in having greater affinity towards the immune cells specifically those carrying the receptors of CD4 cell surface receptor molecule. It takes advantage of cellular pathways while neutralising and hiding from the different components of the immune system. Thus the helper T cells are more profoundly affected resulting in immunodeficiency state and opportunistic infections.Moreover defective killing of intracellular microorganism, impaired antigen presentation and production of TNF alpha results in other infections such as wasting, dementia and unexplained fever. Hence drug targets for HIV infection should aim to combine several potent antiretroviral agents, to suppress the viral replication and also to focus on drugs having immunomodulatory activity. So that, the CD4+ T-lymphocyte numbers would increase, and may lead to immune reconstitution that is sufficient to reverse clinically apparent immunodeficiency.[9]

Role of *Siddha* system in the treatment of HIV

The Concepts of traditional *Siddha* system of medicine are about several thousand years old. Judicious combinations of modern science and traditional medicine have the potential to cure a number of diseases and can provide new leads for drug discovery. Currently, more that 1.5 million traditional medical practitioners in India are using medicinal plants for prophylactic and curative purposes. Acquired Immuno deficiency disease can be correlated broadly with Mega Noigal mentioned in *Siddha* texts. The etiologic factor of *Mega Noigal* has been

describe as "*Kanni mayakathaal kandidu megamey*" indicating that this is a sexually transmitted disease.[10]

The humoural theory of *Siddha* system

According to *Siddha* concept,the physiological function in the body is mediated by three Humours- *Vatham, Pitham, and Kabam* which are said to maintain the integrity and function of our body. *Vatham* is formed by the basic elements space and air. *Pitham* is formed by fire and *Kabam* is formed by earth and water. If these three functions normally, health is maintained. These humours also called as *Uyir Thathukkal* that govern the 96 fundamental principles operating in human body and the seven physical constituents viz. *Saaram* (Plasma), *Senneer* (Blood), *Oon* (Muscle), *Konzhuppu* (Adipose tissue), *Enbu* (Bone), *Moolai* (Marrow) and *Sukkilam* (Reproductive tissue) called as *Udal Thathukkal*.

All these three humours are constituted by means of Arusuvai (six tastes) that are presented in all universal substances and in our daily diet. The *Siddha* philosophy relies on the concept that any alteration in these humours caused by diet and lifestyle can result in *dosham* or diseases. Therefore the way out for diseases caused due to altered humours are dealt upon by means of six taste theory which can be manifested in substances such as herbs, metals, minerals and animal species that are used as medicines. Each taste is also a combination of any two components of *panchabootham* (air, water, fire, earth and space). Hence by means of this combination the *Siddha* medicine tends to alter the derranged humours and helps in the restoration of ill health.[11]

Pathologic basis of *Mega Noigal*(Sexually transmitted diseases)

According to *Siddha* pathology *Mega noigal* are mainly caused due to increased sexual activity and also due to exposure to excessive heat and spicy foods which in turn vitiates the *pitha* humour followed by alteration in *kapha* humour resulting in the detoriation of the seven *Udal thathus* resulting in symptoms of *Mega Noigal* such as genital discharge and ulcerations, urinary disorders, fever, diarrhoea, emaciation, weight loss, Oral thrush, arthralgia, dyspepsia, skin diseases and tumours.[12]

Analysis of humoral theory of Deva Chooranam

S.no	Botanical Name	Tamil Name	Suvai (Taste)	Action on humours
1	*Alpinia galanga*	Sitrarathai	Karpu (Acrid)	Pacifies vitiated **kabam**
2.	*Cedrus deodara*	Thevathaaru	Kaippu (Bitter)	Pacifies vitiated **pitham** and **kapham**
3.	*Cinnamomum tamala*	Lavanga pathiri	Karpu (Acrid)	Pacifies vitiated **kabam**

PHARMACOLOGICAL REVIEW OF INGREDIENTS OF DEVA CHOORANAM

1. *Alpinia galanga*

Alpinia galanga belongs to the ginger family Zingberaceae. It is known as *arathai* in Tamil, Kulinjan in Hindi, Dumparastramu in Telugu and Cittaratta in Malayalam. It has a bitter taste and is used in the treatment of arthritis, renal calculi, inflammations, bloating, cough, hiccups, dyspepsia, hyperglycemia, obesity, and pyrexia of unknown origin. The plant is well known in ayurveda for its various therapeutic actions like thermogenic, aphrodiasic, anti-inflammatory, carminative, nerve stimulant, antifungal, antiulcer and antiallergic Properties.[13,14] The flower and rhizome are used in the preparation of Indian cuisines.[15]

The plant A. galanga has a rich treasury of therapeutic phytochemicals. It has an abundance of phenolic compounds like phenolic acids and flavonoids[16] .Jahu et al., first reported the isolation of new phenolic glycoside galangogalloside from the rhizomes of A. galangal [17]. It also contains flavones like galangin, alpinin, kampferide and 3-dioxy-4-methoxy flavones[18,19].

Twelve phenyl propanoids were isolated from this plant namely p- caumaryl, methyleugenol, trans-3,4-dimethoxycinnamyl alcohol, p-hydroxybenzaldehyde, p-hydroxycinnamaldehyde, trans-p-coumaryl alcohol, galangin, trans-p-coumaric acid and galanganol B, p-coumaryl diacetate, 1'-acetoxychavicol acetate, 1'-acetoxyeugenol acetate, trans-p-acetoxycinnamyl alcohol, from hexane, chloroform and ethyl acetate extracts.[20]

Antioxidant activity of *Alpinia galanga*

The antioxidant activity of the plant was first reported by Padma S. Vankar et al., in which the methanolic extract of *Alpinia galanga* showed better activity compared to other Zingiberaceae counterparts.[21]

Anti HIV activity of *A. galanga*

Ying and Baoan isolated the 19S-19- Acetoxychavicol acetate and first reported that the compound inhibited the replication of Human immune deficiency virus by blocking the transport of the Regulatory HIV-I protein (Rev).[6]

The antimicrobial activity of the plant also have been well studied by different researchers Sawangjaroen et al and Phongpaichit et al. [22,23] In addition extensive research have been made on the efficacy of the rhizome against *Mycobacterium tuberculosis* which demonstrated the efficacy of plant extracts in treating tuberculosis among the AIDS patients in Thailand.[24,25]

Antifungal activity

Khodavandi et al., demonstrated the antifungal activity of *A. galanga* against Candida species *in vitro*. Since oral candidiasis is a common medical manifestation in immune compromised patients, the anti fungal activity of A. galanga makes the plant, a promising candidate in the treatment of various clinical manifestations in AIDS patients. [26]

Immuno modulatory effects

Bendjeddon et al., demonstrated the immunostimulating activity of polysaccharide extracts of *Alpinia galanga* on the reticulo-endothelial system (RES) and peritoneal exudate cells (PEC) and spleen cells of mice. Matsuda et al., isolated anti-allergic phenyl propanoids from the aqueous acetone extracts of *Alpinia galanga* rhizomes which inhibited degranulation and release of TNF-alpha and Interleukin 4 in RBC-2H3 cells of mice. [27,28]

2. Cedrus deodara

Commonly known as Deodar or Himalaya cedar, this tree is a common resident of the temperate forests where rainfall ranges from 1000mm to 3000mm per year[29]. It is now a member species of the IUCN Red List of Threatened Species.

The principle constituent of the cedar wood oil is sequisterpen. The pine needles contain chemical constituents like 9- hydroxyl-dodecamoic acid,ethyl laurate, ethyl stearate, beta

sitosterol, shikimic acid, ferulic acid, beta sitosterol which were identified under spectroscopic analysis. [30].

The lead acetate purified butanol fraction of the wood yielded two lignans which were reported by Agrawal and Rastogi in 1982.[31] The leaves of C.deodara contain major class of phytochemicals like flavonoids, alkaloids, tannins and saponins.[32]

Pharmacological activity

Many researchers have demonstrated the efficacy of the tree and its oil. Literature have revealed the various pharmacological activities of the tree and its oil like antibacterial, insecticidal activity, Molluscidal activity, antitubercular activity, anxiolytic and anticonvulsant activity, neuroleptic activity, antidiabetic activity, antioxidant activity, antimalarial activity and cytotoxic activity [33-47].

Immunomodulatory activity

Shinde et al., studied the immunomodulatory activity of C. deodara wood oil. They demonstrated that the oil significantly inhibited neutrophil adhesion to nylon fibers when administrated orally at doses 50 and 100mg/kg.[48] The oil also inhibited Type III and type IV hypersensitivity reaction induced by sheep erythrocytes and oxazolone. Further immunomodulatory efficacy of the cedar wood oil was tested in rats[49] (neutrophil adhesion) and mice[50,51] (athrus reaction, SRBC induced delayed type hypersensitivity DTH) hemagglutination antibody titer calculation, oxazolone induced contact hypersensitivity. [52,53]

3. *Cinnamomum tamala*

Cinnamomum tamala is an Indian plant and since it is a native plant to India it is usually called as Indian Bark or Indian bay leaf. It is also called mostly in India by other vernacular names depending upon the region it grows such as Tejpatta (Hindi); Tejpat (Manipuri); Talishappattiri (Tamil); Tamalapatram (Malayalam);Talisapatri, Talisha, Patta akulu (Telugu);Patraka (Kannada); Tejpat (Bengali); Tezpat (Urdu);Mahpat, Tejpat (Assamese); Tamaal patra (Gujarati); tamalapattra (Sanskrit).

Pharmacological properties

Right from the genesis of mankind, plant and man have proved their inseparable unification time and again all through the ages. Either of the two is inevitably reliable on each other. The existence of multitudinous variety of plants on the earth have always exhibited their

incalculable efficacy to mankind. One such efficacious plant is *Cinnamomum tamala* and this plant besides being popularly used as a spicy and flavouring ingredient in various food preparations it also posses and showcases some of its outstanding medicinal properties.

The various medicinal properties of *Cinnamomum tamala* leaves such as hypoglycemic, stimulant, carminative have been reported in some studies.[54,55] Some studies have even reported that *Cinnamomum tamala* are still being used in the treatment process for curing variety of ailments like cough, diarrhoea, boils,irritations,itchings and diseases like gonorrhea, rheumatisms, etc.[56]

Essential oils of *Cinnamomum tamala*

An investigational study was conducted by Baruah *et al* to perform a detailed study about the compounds and their properties present in the stem bark oil and leaf oil of *Cinnamomum tamala*.[57] In this study GC-MS analysis was performed comparatively alongside with the reference compound using a Finnigan Matt INCOS 50 GC-MS/DC equipped with library search data of 42222 spectra using a DB-5 fused silica capillary column 0.25m film thickness.

The outcome of the study was quite interesting to find that the leaf oil was golden yellow mobile liquid and gave a yield of 1.4% with a refractive index of 1.5253, whereas the stem bark oil was a pale yellow mobile liquid with a refractive index of 1.4233 and rendered a yield of 0.5%. Nearly, 24 components were detected representing the total leaf oil compounds of which chief among them were the Eugenol comprising of 70.63% followed by Phellandrene 14.93%.In the case of stem bark oil, 25 components were identified showcasing the total stem bark oil components and the major of the compounds were a-terpeniol (47.16%) followed by p-cymene (9.66%)..[58]

The immunomodulatory property of Cinnamomum tamala

The immunomodulatory property of *Cinnamomum tamala* Linn leaves was explored in a study performed by Chaurasia et al in 2010. In the study, *Cinnamomum tamala* leaves were collected and the leaves were allowed for shade drying. After the leaves were dried, they were powdered. The dried powder of *Cinnamomum tamala* leaves were extracted with hexane and solvent free extract (CTH).Then for 10 days, the extract was given orally to rats in different doses. Its effect was studied on peritoneal macrophage functions, and was compared with ascorbic acid (1,000 mg/kg, immune-stimulant) and cyclophosphamide (10

mg/kg, immune-suppressant). The prominently the extract exhibited a significant activity that suppressed the phagocytosis (EC(50) 2,355 +/- 52.45 mg/kg), reduced production of superoxide (EC(50) 275.91 +/- 10.21 microg/ml) and cellular NADPH (EC(50) 384.959 +/- 4.85 microg/ml) content in concentration dependent manner. It also inhibited Lipopolysaccharide induced production of nitric oxide (EC(50) 143.75 +/- 3.40 microg/ml) and iNOS protein expression (EC(50) 183.132 microg/ml). In conclusion this study clearly portrays that non-polar hexane fraction of leaves of *Cinnamomum tamala* possesses immunosuppressive property, which is mediated through modulation of innate immunity.[59]`

DISCUSSION

Upon considering the traditional literature evidences of the ingredients of *Deva Chooranam* and analysing them in the light of scientific researches, it can be found that the bitter taste of *Cedrus deodara* pacifies both the vitiated humours (*pitham and Kapham*)of *Mega Noigal* and also has immunomodulatory property. The plant Alpinia galangal is scientifically reported to inhibit the replication of Human Immunodeficiency Virus. Both *Alpinia galanga* and *Cinnamomum tamala* possess acrid taste (Pacifying kabam) has been found to have potent immunomodulatory activity. Therefore the drug Deva Chooranam can be expected to have an effective therapeutic potential against AIDS associated opportunistic infections.

The long term adverse effects of synthetic drugs cannot be evaded. The chronic use of synthetic drugs builds up unusual chemical load in the human system which manifests in several ways. On the other hand, the plant kingdom is stuffed up with beneficial phytochemicals which confer health and overall well being. Since all the three plant candidates are rich in phytochemicals which enhance immunomodulatory action and one among the ingredient (*Alpinia galanga*) inhibits viral replication of HIV, they can offer further preclinical studies invitro and invivo and clinical studies may be essential to prove the potential of this herbal combination. These three medicinal plants are efficient candidates for the long awaited anti-HIV drug. The pre clinical pharmacological studies and human studies are yet to be done to support scientific evidence.

CONCLUSION

The *Siddha* Herbal formulation Deva Chooram with the three ingredients of interest *A. galanga, C.deodara, Cinnamomum tamala* possess diverse pharmacological properties which were briefly discussed. The anti-HIV and immunomodulatory activities further need more scientific backup. Hence preclinical pharmacological (*in vitro* and *in vivo*) and

toxicological studies may be essential to prove the potentiality of this herbal combination. After successful *in vitro and in vivo* studies these medicinal plants will prove to be efficient candidates for the long awaited anti- HIV drug.

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