A REVIEW OF THE INDIVIDUAL CONTENTS OF *JEEVANIYA MAHAKASHAY* AND ITS ROLE AS IMMUNOMODULATOR

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ABSTRACT

India has the third largest HIV epidemic in the world. In 2016, HIV prevalence in India was an estimated 0.3%. This equates to 2.1 million people living with. HIV infection affects multisystem, chiefly the Immune System which can be correlated to Oja Kshaya. Rasayana Chikitsa is the frontline therapy employed to treat Ojas disorders. For the process of rejuvenation, Ayurveda has described a unique therapy-Rasayana therapy. Drugs described under Rasayana act on Agni, Dhatu and Srotas level and help in formation of prashasta dhatus maintaining a perfect equilibrium of all the doshas *and dhatus. Jeevaniya gana is mentioned in Charak Samhita sutrasthana chapter fourth Shad virechana shatashritiya adhyay. Charakokta Jeevaniya Mahakashay-Jeevak, Rsabhaka, Meda, Mahameda, Kakoli, Ksheerakakoli, Mudgaparni, Mashaparni, Jeevanti, Madhuk. Detail usage of the individual drugs of Jeevaniya gana has been mentioned in the article and its role as immunomodulator has been* discussed. *Jeevaniya gana nowadays used is-Shatavari, Vidari, Ashwagandha, Mudgaparni, Mashaparni, Jeevanti, and Madhuk*

Keywords - Shatavari, Vidarikanda, Ashwagandha, Mudgaparni, Mashaparni, Jeevanti, Yashtimadhu, HIV, Immunomodulator.

INTRODUCTION

Jeevaniya gana mentioned in *Charak Samhita sutrasthana* chapter fourth *Shad virechana shatashritiya adhyay. Charakokta Jeevaniya Mahakashay-Jeevak, Rsabhaka, Meda, Mahameda, Kakoli, Ksheerakakoli, Mudgaparni, Mashaparni, Jeevanti, Madhuk.* Of the above mentioned dravyas, the first six, i.e. *Jeevak, Rsabhaka, Meda, Mahameda, Kakoli*, and *Ksheerakakoli* are extinct. According to *Acharya Bhavamishra*, author *of Bhavaprakash Nighantu,the* the use of following *dravyas* can be used instead of the extinct ones-[1]

Following *dravyas* to be used in place of extinct ones-Table number-1

Dravya	Substituted with
Meda and *Mahameda*	*Shatavari*
Jeevak and *Rsabhaka*	*Vidari*
Kakoli and *Ksheerakakoli*	*Ashwagandha*

Jeevaniya gana is-

Shatavari, Vidari, Ashwagandha, Mudgaparni, Mashaparni, Jeevanti, Madhuk

According to our classical texts *Jeevaniya gana* bestows long life.

NEED OF TOPIC

There is no vaccination availability for HIV-AIDS which has prompted for research of various herbal drugs which are potent to a certain extent in patients having HIV. Hence only option is use of Anti Retroviral therapy (ART).There is a high prevalence of the disease and an even higher mortality .The cost of medicine is expensive. Compromised immunity and reduced quality of life has prompted for further research in this field in order to improve the immunity of the HIV infected population. This particular disease can be easily transmitted thereby increasing the HIV infected population. Mass awareness needs to be created.

Some of the common side effects seen after starting of ART are-Loss of appetite, Lipodystrophy, Fatigue ,higher than normal levels of cholesterol and triglycerides, mood changes, depression, anxiety, nausea, vomiting, rash, difficulty in sleeping, hypersensitivity or allergic reactions, with symptoms such as fever, nausea, and vomiting, bleeding, bone loss, heart disease, high blood sugar and diabetes, lactic acidosis (high lactic acid levels in the blood),kidney, liver, or pancreas damage, numbness, burning, or pain in the hands or feet due to nerve problems. Hence it is the need of time to find minimize these side effects caused due to ART and to find better, more effective options of herbal medicines in the management of HIV.

AIM AND OBJECTIVES

Aim-

To do a literary study of the individual contents of *Jeevaniya Mahakashay* and its role as immunomodulator.

Objectives-

1) To do a literary review of the karma of individual contents of *Jeevaniya Mahakashay.*

2) To do a literary review of the pharmacological activity of individual contents of *Jeevaniya Mahakashay* especially immunomodulatory activity.

MATERIAL AND METHODS

Review work done and all literary references related to *Jeevaniya gana dravyas* has been collected from *Ayurveda* classical texts, pharmacological activity of *Jeevaniya gana dravyas* has been collected from recent modern studies done on the subject and research papers for the same have been collected through the source of internet.

1) *Shatavari-*

Shatavari is generally used as a general tonic and a tonic for female reproductive system. *Asparagus racemosus* (Fam. -Asparagaceae) is commonly known as *Shatavari* .It is highly effective and potent. It has *Madhur Rasa, Madhur Vipaka*, and *Sheeta Veerya*. It is used in the management of *soma roga*, chronic fever and internal heat[2, 3].

This herb is beneficial in diseases of female reproductive system. *Acharya Charak* and *Acharya Vagbhat* have enlisted *Shatavari* as part of the many formulae in management female health disorders [4,5,6,7]

Shatavari is a commonly used effective *Ayurvedic rasayana* which helps in preventing ageing, improves longevity, impart and develop immunity, helps the improve mental functions, restores vigor and adds vitality to the body and is also used in nervous disorders, dyspepsia, tumors,hepatopathy,neuropathy inflammation. Studies have proved the pharmacological activities of *Asparagus racemosus* extracts of root like antioxidant, antiulcer, antidiabetic, antidiarrhoeal, and immunomodulatory activities. A study based on classical *Ayurveda* literature claimed multiple therapeutic attributes to the roots of *A. racemosus* and has been specially used as a galactogouge and cases of threatened abortion. Roots of *A. racemosus* are having a bitter-sweet taste, cooling, emollient, nervine tonic, and aphrodisiac, galactogouge, diuretic, antiseptic, carminative and as tonic. Efficacy of the root of *A. racemosus* can be seen in nervous disorders, bronchitis, hyperacidity ,dyspepsia, diarrhoea, dysentery, cough, neuropathy, hepatopathy tumors, inflammations, hyper dypsia, , and certain infectious diseases[8,9].

The major active constituents present in of Asparagus racemosus are steroidal saponins that are found to be present in the roots. Shatavarin IV has shown to significant activity as an inhibitor of core Golgi enzymes transferase in cell free assays and recently has exhibited immuno-modulation activity against specific T-dependent antigens in immuno compromised animals[10]

Immunomodulatory activity-. Immunomodulating property of *A. racemosus* has been shown to protect the rat and mice against experimental induced abdominal sepsis in cases where intra-abdominal sepsis is major causes of mortality following trauma and bowel surgery .In a study where the survival rate was compared to the group treated with a combination of gentamicin and metronidazole the percentage rate of mortality in animals treated with A.Racemosus was found to be significantly reduced. Oral administration of decoction of powdered root of *A. racemosus* has been reported to produce enhanced phagocytic activity of the macrophages and polymorphs alongwith leucocytosis and predominant neutrophilia. *A. racemosus* has shown to be devoid of antibacterial action and hence protection is provided by *A. racemosus* against sepsis indicating its possible immunomodulatory property by altering f unction of macrophages [11, 12]

2) *Vidari-*

Vidarikanda pacifies vata, pitta and rakta dosha and is having *Bruhaniya, Jeevaniya, Vrushya, Stanya, Shukral, Balya, Rasayan Dahahar, Mutral, Kanthya, Varnya* properties. . *Vidarikanda* is highly beneficial in *Rajyakshma, Jwara, Kshtaksheena, Kasa, Raktapitta, Vatarakta* and *Vatavyadhi*. The *Vidarikanda* tubers are sweet, cooling potency, aphrodisiac, galactogouge, diuretic, cardio tonic, expectorant, emetic and hence useful in various ailments [13] .Tubers have rich content of in isoflavanoids.Its *Bruhan* effect is seen prominently in *Karshya vyadhi*[14]. In STZ- induced diabetes in rats it showed to have an effective anti-diabetic potential.[15]

Immunomodulatory activity-It holds an enterprising importance as a therapeutic potential due to the immunomodulator activity the effects mostly being due to the rich content of isoflavnoids. [16] The major isoflavnoids present in *Vidarikanda* is Puerarin and it has proven as an antioxidant activity.[17] Puerarin possesses cardio protective activity and gives protection against stress induced myocardial ischemia [18] .P.tuberosa may be

added to the list of thrombolytic agents of plant origin due to its fibrinolytic activity in patients of coronary artery disease. It has negligible side effects and is cost effective. It has shown and proved its aphrodisiac effect which is mentioned in *Ayurveda* classical texts.[19]. P. tuberosa increases the hormonal levels of testosterone, LH, FSH, and gonadotropin release hormone GnRH. The role of phytoestrogenic compounds from P.tuberosa in the improvement of sexual function and testosterone production in male rats can be attributed to the role of phytoestrogenic compound of P.tuberosa. Hence it is evident that it helps in improvement of sexual performance and fertility because of its ethnopharmacological utilization. [20] Nootrropic effect i.e. memory enhancer, cognitive enhancer, neuro enhancer and intelligence enhancer effect has been proven with study [21]. Studies have shown that there is an improvement in activity of red blood cell anti-oxidant enzymes and hence is an useful anti-inflammatory agent[22]

3) *Ashwagandha-*

The roots of the *Ashwagandha* plant are having *rasayana* property by augmenting the defense against disease, helps in arresting the process of ageing, revitalization of the body in debilitated conditions, increasing the individual's capacity to resist the adverse environmental factors and thereby creating a sense of mental wellbeing in the individual [23]. It can be used for a very long time in all age groups and in both sexes, even during pregnancy, without having any side effects [24]The pharmacological activity of the roots was attributed to the presence a group of steroidal lactones known as withanolides. [25] Its leaves are beneficial in *Ayurveda* for treatment and management of tumors and tubercular glands [26].

W. somnifera exhibits antibacterial, anti-fungal and antitumor properties wherein a number of withanolide steroidal lactones from the leaves have been isolated[27, 28] *Ashwagandha* is beneficial to help calm the mind, relieve body weakness and nervous exhaustion, build high sexual energy and promote a healthy sleep according to *Ayurveda* i.e. It acts as a booster for vitality and longevity. It is also an adaptogen.

Immunomodulatory activity -*Ashwagandha* has shown a significant immunomodulatory activity in immune reactivity in animal models. Ashwagandha helps prevent myelo-suppression in mice treated with the three immunosuppressive drugs which are Cyclophosphamide, Azathioprin, and Prednisolone. On treatment with *Ashwagandha* it was found that there was a significant increase Haemoglobin concentration, platelet count, RBC count, and body weight in mice [30.]

Ashwagandha extract has been proven to significantly reduce the leucopenia which is induced by Cyclophosphamide (CTX) treatment. Also, another study showed that administration of *Ashwagandha* extract was found to significantly reduce the leucopenia which is induced by the sub-lethal dose of gamma radiation [31]. Withaferin A and Withanolide E have exhibited the specific immunosuppressive effect on mice thymocytes and human B and T lymphocytes. Withanolide E had specific effect on T lymphocytes whereas Withaferin A affected both B and T lymphocytes [32.]

4) *Mudgaparni* –

Phaseolus trilobus is also commonly known as *Mudgaparni* or *Ranmoong*.It is highly useful in diseases like jaundice, haemorrhoids, dyspepsia, diarrhoea, coolant, and sedative, good for eyes and anti helminthic. The plant is also having beneficial effects as a tonic, hepatoprotective diuretic, antimicrobial and antioxidant. It is also proved that it induces defence mechanisms when against the exposure of UV-B radiations. The plant contains a vast range of active components like flavonoids, isoflavnoids, stigmasterol, tannins, vitamin C, vitamin K and proteins which have been isolated from the plant[33, 34.]

Immunomodulatory activity- In the *Prakara Yoga* the 35th chapter of the *Ayurvedic* pediatric classic text book in *Ayurveda* known as "*Arogyakalpadruma*" written by *Vaidya Kaikkulangara Rama Varrier*.[35] *Mudgaparni* has been mentioned in the *prakar yogas* as one of the useful herbal drug as immunomodulator.

5) *Mashaparni*-

The fruit is bitter, sweet in taste, cooling in potency , aphrodisiac, acts as an astringent to the bowels,tonic,galactogouge, antipyretic, it helps in the conditions of biliousness, inflammation, gout, blood diseases, fevers , bronchitis, thirst, burning sensation; consumption, useful in paralysis, rheumatism and diseases of the nervous system according to *Ayurveda*. It is considered to be very useful in haemoptysis and catarrh [36]

Teramnus labialis is one of the Life Promoting vis-à-vis Jeevaniya medicines as mentioned in Charak Samhita. It increases kapha and decreases Vata, Pitta and. It is also one of the important Rasayana drug in Charak Samhita[37].

Immunomodulatory activity- In the *Prakara Yoga* the 35th chapter of the *Ayurvedic* pediatric classic text book in *Ayurveda* known as "*Arogyakalpadruma*" written by *Vaidya Kaikkulangara Rama Varrier*.[35] *Mudgaparni* has been mentioned in the *prakar yogas* as one of the useful herbal drug as immunomodulator.

6) *Jeevanti*-

L. reticulata is considered as *Rasayana* drug and is helps to nourish, vitalize, and rejuvenate the body. [38] It is mainly administered to persons suffering from weakness, lack of energy, general debility. It has good efficacy in involuntary seminal discharge, general debility[39]. It is a restorative, tonic, wound healer and is useful in mouth ulcer.Also, *L. reticulata* has exhibited antiepileptic activity [40] ,hepatoprotective and anti-anaphylactic [41] activity and antibacterial activity [42] in animal models.

Immunomodulatory Activity-In a study conducted by Girish Kumar et al. 43 the whole plant aqueous extract of L. reticulata had proved to offer superior protection against immunosuppression which was induced by chromate (VI). Thereby confirming the possibilities of therapeutic using L. reticulata for modulating and alleviating the chromate (VI)-induced immunosuppression. Similarly, the immunomodulatory and antioxidant activity of the ethanolic leaf extract of L. reticulata was studied and evaluated by Pravansha et al. [44]. The study revealed and proved that L. reticulata extract (100 and 200 mg/kg) significantly induced a delayed type of hypersensitivity reaction, increased Neutrophil adhesion (%) to nylon fibers, increased antibody titer values- dose-dependent manner, and the rate of phagocytosis.Also, there was found to be a significant increase in the hematological profile, superoxide dismutase ,reduced glutathione and catalase activities. This thus proves the potential immunomodulatory and antioxidant properties of L. reticulata.

7) *Yashtimadhu* -

The sweetness in liquorice is attributed to glycyrrhizin, which is having a sweet taste.[45, 46]

Glycyrrhizin has also antimicrobial, antiviral, anti-inflammatory, blood pressure increasing effects, hepatoprotective in vitro and in vivo, as this is supported and proved by the finding that administration of intravenous glycyrrhizin slows the progression of viral and autoimmune hepatitis.[47, 48]

The laxative, anti inflammatory, antiulcer, antidiabetic, immunomodulatory, expectorant, anti tumor properties of liquorice has been studied.

Licorice is beneficial in a range of ailments including ulcers, irritation, cholesterol, fever, heart burn, hepatitis and liver problems, menstrual problems, asthama, psoriasis, body odour, depression, colds, pain, stress, coughs, gingivitis, arthritis, sore throat, prostate enlargement.[49]
It has been stated in the classics that it possesses *Guru, Snigdha Guna, Madhur Rasa, Madhur Vipaka* and *Sheeta Veerya*.

Jeevaniya Mahakashay dravyas –Table 2-

Sr. No.	Drug	Latin Name	Family	*Rasa*	*Veerya*	*Vipaka*	*Karma*
1	*Shatavari*	Asparagus Racemosus	Liliaceae	*Madhur, Tikta*	*Sheeta*	*Madhur*	*Rasayana Balya Shukravardhak Stanyavardhak Medhya*
2	*Vidari*	Pueraria tuberosa	Leguminosae	*Madhur, Tikta*	*Sheeta*	*Madhur*	*Balya Shukravardhak Rasayana*
3	*Ashwagandha*	Withania somnifera	Solanaceae	*Tikta, Kashay*	*Ushna*	*Katu*	*Mamsavardhak Shukravardhak Vrushya Balya Kshayanashak*
4	*Mudga parni*	Phaseolus trilobus	Leguminosae	*Madhur, Tikta*	*Sheeta*	*Madhur*	*Balya Shukravardhak Jwaraghna*
5	*Masha parni*	Terannus labials	Leguminosae	*Madhur, Tikta*	*Sheeta*	*Madhur*	*Mamsavardhak Shukravardhak Balya Jwaraghna*
6	*Jeevanti*	Laptadenia reticulata	Asclepiadaceae	*Madhur*	*Sheeta*	*Madhur*	*Shukravardhak Kshayanashak*
7	*Madhuk (Yashtimadhu)*	Glycyrrhiza glabra	Leguminosae	*Madhur, Tikta*	*Sheeta*	*Madhur*	*Balya Shukravardhak Kshayanashak.Rasayan*

DISCUSSION

A healthy immune system is vital for individuals. Immunity is the ability of the body to resist attack of harmful microbes from entering the body. Immunity can be classified as specific and non-specific. Other factors of the immune system can adapt themselves to each new disease which is encountered and are hence are able to generate a pathogen-specific immunity. Nonspecific or innate immunity is the natural resistance which a person is born with. It provides the body's resistance through most of the chemical, physical and cellular approaches [50]

Immunomodulators- An immunomodulator may be defined as a substance, which may influence any of the constituents or functions of the immune system in a nonspecific or specific manner including either of the innate or adaptive arms of the body's immune response.[51] These immunomodulators are a vast and diverse array of recombinants that maybe synthetic and natural preparations, usually cytokines. Some of these substances for example the granulocyte colony-stimulating factor (G-CSF), imiquimod , interferons and the cellular membrane fractions from the bacteria these are already licensed to be used in patients. Others which include IL-2, IL-7, and IL-12, various synthetic cytosine phosphate-guanosines (CpG), chemokines, glucans and oligodeoxynucleotides are currently under investigation and studied extensively in the clinical and preclinical studies. Immunomodulatory regimens provide a promising approach as they mostly have fewer side effects than the existing drugs being used, including the less potential ones used for creating the resistance in microbial diseases [52]

Concept of immunomodulation according to *Ayurveda-Ayurveda* has laid the foundations of the concept of immunity as "*Vyadhikshamatva*" [53.] *Acharya Chakrapanidatta* has postulated and interpreted the term *Vyadhikshamatva* a as *Vyadhi bala Virodhitva* which literally means one which is antagonistic to the virulence and strength of the disease and the *Vyadhyutpada Pratibandhakatva* which means the capacity to bind and inhibit the factors and causes of the disease [54] .One of the therapeutic management strategies in *Ayurvedic* medicines is to enhance and improve the body's overall natural resistance to the disease causing agent rather than directly neutralizing the agent itself. The guiding principle of *Ayurveda* has been the use of herbs and herbal sources for improving and enhancing the overall resistance of body against pathogens and common infections [55.] Such herbs possessing immunomodulatory effects are referred to as *Rasayana* in *Ayurvedic* classics. They are supposed to have the ability of protecting the body against external factors that induce disease. This implied resistance against disease may represent the modern concept of immunity.[56]

CONCLUSION

It may be concluded that *Jeevaniya Mahakashay* is a potent group of *Rasayan Dravyas* as stated in *Ayurveda* classics. Due to its *Rasayan* effect and the various pharmacological studies conducted in vitro and in vivo have shown and proved the efficacy and pharmacological action of these drugs as "immunomodulators" and hence this group of drugs may be classified as "immunomodulators".

SCOPE FOR FURTHER STUDY

More in vivo studies need to be conducted and clinical trials in immuno compromised patients must be undertaken wherein the trial drug of Ayurvedic immunomodulators may be administered in single drug form or in a combination of drugs together to understand the overall efficacy of the drugs especially in immuno compromised patients for example in patients of HIV/AIDS, cancer and transplant patients who are taking certain immunosuppressive drugs, and those who are inherited with diseases that affect the immune system for example congenital agammaglobulinemia,congenital IgA deficiency.

The role, scope, mode of action and extent of efficacy of herbal immunomodulators needs to be studied which is the need of time.

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