



(REVIEW ARTICLE)



Kayakalpam (Rejuvenative) herbs: An immunomodulators in Siddha system of medicine: A scientific review

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Abstract

Background: *Kayakalpam* (Rejuvenative) medicine is one of the prime treatment technique in the Siddha system of medicine. *Kayakalpam* has potential to heal, rejuvenate and balance the vatham, pitham and kapam (tri-dhosas) which make the body and mind to attain its stability. Several studies have been done on *Kayakalpam* medicines, but, this review article states about few *Kayakalpam* herbs, their chemical constituents, pharmacological activities and its immunomodulatory mechanism towards the prevention and management of non-communicable diseases and several other diseases.

Methods: A literature review was conducted using the following scientific databases: PubMed, Research gate, Science Direct, Google scholar, Ayurvedic Pharmacopoeia of India and Siddha Pharmacopoeia of India. The aim was to identify published data on traditionally used medicinal plant for rejuvenation and immuno-modulatory effect. From that, few *Kayakalpam* herbs have been chosen which has been mentioned in the Siddha literature and reviewed its nature.

Conclusion: This literature review reveals the potential effect of *Kayakalpam* herbs and its nature. Beyond any doubt it will help in prevention and management of non-communicable diseases and several other diseases.

Keywords: Kayakalpam; Siddha System of Medicine; Rejuvenation; Immuno-modulator; Kayakalpam herbs; non-communicable diseases

1. Introduction

According to the World Health Organization (WHO), about three-quarters of the world population rely upon traditional remedies (mainly herbs) for the health care of its people. In fact, herbs and/or plants are the oldest friends of mankind. They not only provided food and shelter, but also served to cure different ailments. Traditional medicine all over the world is currently being revalued through extensive research activity on various plant species and their therapeutic properties [1]. Non-Communicable Diseases (NCDs) are the leading cause for morbidity and mortality worldwide, with three-fourth of deaths occurring in the low and middle-income countries like India [2]. Between the years 1990 and 2016, disease burden in India due to NCDs increased from 48% to 75%. Currently, three out of the top five causes for morbidity and mortality in the country are NCDs [3]. Rising burden of NCDs is due to rapid urbanization and social development occurring in the country over the past two decades. The change occurring in social structures transforms lifestyles of populations that are mainly characterized by increased adaptation of unhealthy diet, physical inactivity and tobacco use [2]. These modifiable risk factors precede the development of metabolic risk factors and then progress to NCDs in populations [4]. *Kayakalpam* is one of the unique therapeutic formulations in Siddha system advocated for rejuvenation, longevity and elimination of disease causing factors. The Siddhars had primly focused on their spiritual well-being through this *Kayakalpam*. In recent years lifestyle modification is one of the main causes of many diseases

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including cancer. So it necessitates to turn towards *Kayakalpam* herbs which are rich in natural source of antioxidants [5]. Production of free radicals results in oxidative stress due to damage of Deoxyribonucleic acid (DNA), proteins, lipids and has been suggested to be the cause of most of the serious human diseases [6]. This article is a review of *Kayakalpam* herbs as mentioned in Siddha literature and scientific exploration of its potential immuno-modulatory activity towards the prevention and management of non-communicable diseases and several other diseases.

2. Material and methods

A literature search was conducted using the scientific databases including PubMed, Research gate, Science Direct, Google Scholar, Ayurvedic Pharmacopoeia of India and Siddha Pharmacopoeia of India. The aim was to identify published data on traditionally used medicinal plant for rejuvenation and immuno-modulatory effect. The search terms used were “rejuvenation and plants”, “traditional plants”, “medicinal plants and immuno-modulatory effect” and “mechanism of anti-oxidant action” and many herbs have been described and their possible mechanism of anti-diabetic, anti-cancerous, anti-oxidant, anti-inflammatory, anti-microbial, hepato-protective, and immuno-modulator action has been mentioned. From that, few *Kayakalpam* herbs have been chosen which has been mentioned in the Siddha literature.

2.1. Brief history of Siddha System of Medicine (SSM)

An ancient system of medicine prevalent in Tamil Nadu, South India. The word Siddha comes from the Tamil word for perfection. Those who attained an intellectual level of perfection were called Siddhars. Siddha drugs arrest the degeneration of cells in the body. The Siddha system advocates control of breathing and diet. Meditation and yoga are part of the system [7]. The sages of south India, who practiced tantrism contributed and established a medical system to serve the humanity in general and their own society in particular. Those sages were called as Siddhars and the medical system used by them is called as SSM. Though the creation of this system is ascribed to Lord Siva, the creator of the universe, the sage Agasthiyar is considered as a father figure of the Siddha medical system. He is also considered to be the father figure of the Tamil language and culture [8]. SSM has been closely identified with Tamil civilization too [9].

2.2. KayaKalpam

The word *Kayakalpam* means (*kayam*-body, *kalpam*-able, competent) to make our body competent and youthful. It is a unique discipline of Siddha system of medicine that addresses the methods and drugs for longevity and enhancement of innate health. They can be divided into *kalpa* medicines, *kalpa* practices of life style and *kalpa* diet. In this science 108 herbs and herbo-mineral combinations are recommended for normal individuals to boost immunity, to promote general health, for prevention of diseases (*pothu karpam*) and also for restoration of health from specific type diseases (*sirappu karpam*). Current science confirms the health benefits of many *Kayakalpam* drugs are due to their anti-oxidant property [10].

2.3. Immuno-modulation by Medicinal Plants

Plant extracts used in traditional therapy are being reviewed for their chemo protective and Immuno-modulatory activities. Immuno-modulators are biological response modifiers; exert their antitumor effects by improving host defense mechanisms against the tumor. They have a direct anti-proliferative effect on tumor cells and also enhance the ability of the host to tolerate damage by toxic chemicals that may be used to destroy cancer [11]. Immuno-modulatory therapy could provide an alternative to conventional chemotherapy for a variety of diseased conditions, especially when host's defense mechanisms have to be activated under the conditions of impaired immune responsiveness or when a selective immunosuppression has to be induced in a situation, like inflammatory diseases, auto-immune disorders and organ/bone marrow transplantation [12]. Anti-oxidants are molecules that interact with free radicals, neutralize the electrical charge and terminate the chain reaction. Anti-oxidants also fight against ROS (Reactive oxygen species) and protect the cells from their damaging effects. Therefore the production of ROS during cellular metabolism is balanced through their removal by anti-oxidants. Any condition leading to increased levels of ROS results in oxidative stress, which promotes a large number of human diseases including cancer. Therefore, anti-oxidants may be regarded as potential anti-carcinogens and they are classified according to their mechanism of action as anti-oxidants which break or interrupt the steps involved in the production of free radicals and also as anti-oxidants which prevent the formation of oxygen free radicals by several actions. Since Synthetic anti-oxidants have possibility of promoting carcinogenesis natural anti-oxidants from herbal sources are considered as superior preferably [10]. A number of Indian medicinal plants and various *Kayakalpam* herbs have been claimed to possess immuno-modulatory activity. Therefore, this article comprises some of the common *Kayakalpam* herbs and their immunomodulatory actions which is reconfirmed by scientific parameters.

2.4. Kayakalpam Herbs as Immuno-modulator

2.4.1. *Aloe barbadensis* Mill

Aloe barbadensis Mill (Siddha/Tamil name – *Katrashai*) is a very well-known medicinal plant and it belongs to the family Asphodelaceae. It grows in arid climates and widely distributed in Africa and other arid areas. It is claimed that *Aloe barbadensis* has wound and burn healing properties and also possess a strong anti-inflammatory and immunomodulatory effects. The bioactive components of *Aloe barbadensis* have aid the treatment of gastrointestinal diseases, i.e., inflammations, gastric, duodenal and intestinal ulcers. It also aids lipid and carbohydrate metabolism, which helps to maintain normal blood sugar and cholesterol levels as well as normal body weight. Due to aloin, the daily intake of aloe juice should not exceed 30–40 ml, because excessive consumption may not only have a strong laxative effect but also toxic effects. [13-16].

Chemical Constituents

Flavonoids, terpenoids, lectins [17,18], fatty acids, anthraquinones [19], mono- and polysaccharides (pectins, hemicelluloses, glucomannan), tannins, sterols (campesterol, β -sitosterol), enzymes, salicylic acid, minerals (calcium, chromium, copper, iron, magnesium, manganese, potassium, phosphorus, sodium and zinc) and vitamins (A, C, E, β -carotene, B1, B2, B3, B6, choline, B12, folic acid) [20–23].

Immunomodulatory Mechanism

The effects of *Aloe barbadensis* on microcirculation and levels of TNF- α and IL-6 were investigated in rats after inducing burn. It was found that the amount of leukocyte adhesion was significantly reduced in the *Aloe barbadensis* treated burn wound rats compared to rats in the control group. It was also observed that the levels of TNF- α and IL-6 reduce significantly [24]. Dihydrocoumarin derivatives (1, 2) were isolated from *Aloe barbadensis* which exhibited immunomodulatory activity in relation to increasing the phagocytic activity and stimulating the production of superoxide anions in the oxygen respiratory burst of rat peritoneal macrophages [25].

2.4.2. *Asparagus racemosus* Willd

Asparagus racemosus Willd (Siddha/Tamil name – *Thanneervittan*) is a widely occurring medicinal plant belonging to the family of Liliaceae. This species is found abundantly in subtropical and tropical zones such as India, Asia, Australia and Africa. *Asparagus racemosus* is frequently used in siddha drug preparations as it is known to treat conditions such as ageing, to boost immunity, improve longevity, vigor, mental function. *Asparagus racemosus* also finds its application in curing neurological disorders, hepatopathy, tumors and dyspepsia [26]. Various therapeutic properties of root of *Asparagus racemosus* is well documented in ancient siddha literature. The therapeutic property is owing to the presence of various pharmacological properties such as antioxidant property, anti-inflammatory property antiseptic and antimicrobial property [27, 28]. *Asparagus racemosus* is recommended for prevention and treatment of gastric ulcers, dyspepsia and as a galactagogue. The *Asparagus* genus is considered to be of medicinal importance because of the presence of steroid saponins and sapogenins in various parts of the plant. Immunomodulating property of *Asparagus racemosus* has been shown to protect the rat and mice against experimental induced abdominal sepsis [30].

Chemical Constituents

Saponins (Shatavarin I-V), alkaloids, polyphenols, flavonoids, vitamin C [29].

Immunomodulatory mechanism

It shows antioxidant activity through the free radical scavenging, superoxide anion radical scavenging, hydrogen peroxide scavenging, nitric oxide scavenging, metal chelation, reduction power and inhibition of lipid peroxidation in rats [29]. *Asparagus racemosus* showed anti-sepsis activity by altering the function of macrophages, indicates its possible immunomodulatory property. Alcoholic extract of *Asparagus racemosus* has been found to enhance both, humoral and cell mediated immunity of albino mice injected with sheep red blood cells as particulate antigen. Oral administration of decoction of powdered root of *Asparagus racemosus* has been reported to produce leucocytosis and predominant neutrophilia along with the enhanced phagocytic activity of the macrophages and polymorphs [30]. Studies have proved the role of aqueous *Asparagus racemosus* root extract in protecting the gamma radiation induced damage in the liver. The antioxidant potential was well characterized against lipid peroxidation [31].

2.4.3. *Solanum trilobatum* Linn

Solanum trilobatum Linn (Siddha/Tamil name – *Thoothuvalai*) belongs to the family Solanaceae with genus *Solanum* native to India and is found everywhere in Tamil Nadu. It is widely used as an Indian alternative system of medicines like siddha, ayurveda, herbal medicines and natural home remedy for various conditions like stomach pain, asthma, respiratory problems, cough and cold etc., and is also used for various recipes. *Solanum trilobatum* is reported to cure numerous diseases viz., respiratory problems and bronchial asthma [32]. *Solanum trilobatum* was reported to harbour hepatoprotective activity, antimicrobial activity, larvicidal activity, antidiabetic activity, cytotoxic activity and anticancer activity. The leaves and stem of *Solanum trilobatum* are reported to possess anti-mitotic, anti-inflammatory and anti-ulcerogenic properties. The leaf extracts are used to increase male fertility and to cure snake poison [33]. The major alkaloids identified in the alcoholic extract from leaves and stem part of *Solanum trilobatum* has been shown to possess anti-mitotic and anti-microbial activity against bacteria and fungi. Biological screening of the alkaloid mixture of this plant revealed anticancer activity against certain type of cancer and its effectiveness as an adjuvant in cancer chemotherapy [34].

Chemical Constituents

Steroids, triterpenoids, sugars, reducing sugars, phenolic compounds, tannins, anthroquinone, amino acids, saponins [35]. Carbohydrates, phytosterols, flavonoids and cardiac glycosides. Alkaloides such as soladunalinidine and tomatidine(4) chemical compounds like Sobatum(1), β -solamarine, solasodine(2), solaine(3), glycoalkaloid and diosogenin(5) [36].

Immunomodulatory mechanism

Aqueous extract of leaves of *Solanum trilobatum* was pharmacologically validated for its immuno-modulatory properties in experimental animals. Oral administration of the extract at a dose of 100, 200 & 400 mg/kg significantly increased in percentage neutrophil adhesion ($P < 0.001$). The Delayed Type Hypersensitivity also showed a dose dependent activity ($P < 0.001$). Further, a dose related increase in haemagglutination antibody titer was observed with different doses as compared to control group. Phagocytic index was significantly increased after the administration of *Solanum trilobatum* compared to control group ($P < 0.001$). These findings suggested that the immuno-stimulatory activity of *Solanum trilobatum* influences by potentiating humoral as well as cellular immunity [37].

2.4.4. *Tinospora cordifolia* Willd

Tinospora cordifolia Willd (Siddha/Tamil name – *Seenthil*) belonging to the family of Menispermaceae. This is a perennial climber distributed throughout the tropical Indian subcontinent. It is categorized well known for its adaptogenic and immuno-modulatory activity in fighting infection. The activity of this drug appears to be due to alkaloid. It is shown to effective against various types of experimental induce infection [38]. The plant has several therapeutic properties such as jaundice, rheumatism, urinary disorder, skin diseases, diabetes, anemia, inflammation, allergic condition, anti-periodic, radioprotective properties, etc [39-41]. The root of *Tinospora cordifolia* is used as potent emetic and for bowel obstruction. The starch (*Seenthil Sarkarai*) of this plant serves a beneficial household remedy for chronic fever, relieves burning sensation, increases energy and appetite. *Tinospora cordifolia* is useful in the treatment of helminthiasis, heart diseases, leprosy, and rheumatoid arthritis, support the immune system, the body's resistance to infections, supports standard white blood cell structure, function, and levels [42].

Chemical Constituents

Diterpenoid furanolactone, 3- (α 4 - dihydroxy-3-methoxy benzyl) 4-(4-hydroxy-3- medoxybenzy1) tetra-hydrofuran, tinosporaside. tinosporide, magnoflorium, giloin, gilosterol, gilenin, columbin, chasmanthin, palmaria, tinosporin, tinosporic acid, tinosporal and amritoside A,B,C and D [43].

Immunomodulatory mechanism

Increase the total white blood cell count, bone marrow cellularity and α -esterase positive cells enhance the macrophage activation [44]. The compounds rise to significant increases in IgG antibodies in guinea pig serum. Cordioside (TC-2), cordiofolioside A (TC-5) and cordiol (TC-7) activated macrophase with increasing incubation times [45].

3. Conclusion

Amongst 108 herbs in the Siddha system, examined only 4 herbs for this article. Based on their therapeutic properties, pharmacological activities, chemical constituents and immunomodulatory mechanism, this *Kayakalpam (Rejuvenative)*

Herbs certainly useful in aspects of the prevention, treatment and management of NCDs. Many other questions have yet to be explored and offer the possibility of further investigation.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

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