

Kadukkai- *Terminalia chebula* Retz.

(Elixir of Rejuvenation) –

A Gift of Siddha Medicine

ABSTRACT

Natural products with are gradually gaining importance because of its medicinal value in clinical research due to their well-known property of fewer or no side effects as compared to synthetic drugs. World Health Organization also advised the general public to focus on enhancing their immune system to prevent getting affected by pandemic diseases. In the traditional Siddha system of Medicine, there is a concept known as, 'Yegha Mooligai Prayogam' (Yega – single, Mooligai – herb, and Prayogam – application) which deals with single herb and their clinical application. Polyherbal formulation were consisting of herbs, metals, and minerals but, single herb therapy is safe, convenient and economical. The concept of Single herb as a therapeutic agent is widely recognized nowadays. Kadukkai (*Terminalia chebula* Retz., Family: Combretaceae) possesses a great therapeutic value and it is widely distributed in all over the India. Siddha Kayakarpam (rejuvenation) therapy has been traditionally used in India for its immunomodulatory and adaptogenic effects, and more recently has been included as a therapeutic adjuvant for several maladies. Amongst several other herbs, Kadukkai plays an important role in Kayakarpam therapy which balances the three bodily humors (*Vatham, Pitham, and Kabam*) or doshas that are the main reasons for illness. Kadukkai properties are known to support healthy bowel movements and gut health. Nowadays modern science also recognizes the gut as "the second brain" -perhaps the ancients recognized the relationship between a healthy gastrointestinal (GI) tract and clarity of mind. Thereby, the single herb Kadukkai finds a special place, which has been compared as superior to the nursing mother. This study concluded that the consumption of Kadukkai in a certain way with various adjuvant in respective seasons will boost our immunity and helps to prevent diseases.

Keywords: Chebulic myrobalan, Gut health, Immunity, Kadukkai, *Kayakarpam*, Rejuvenation, *Terminalia chebula*

I. INTRODUCTION

Daily variations in the environment have constrained life on Earth, with circadian cycles identified in most living organisms, including in human physiology and cognition. [1] Our changing demographic profile, changing climate, and a lot of stress work all cause many harmful diseases. A changing climate threatens the quality and continuity of care provided at health care facilities due to more frequent, severe extreme weather events and increased health risks from a range of other climate hazards. Health care facilities will become increasingly vulnerable to the impacts of climate change without adaptation. To prevent all these hazards effects on the health of human beings' traditional way of life showed by Siddha Medicine is the only choice. Siddha system of medicine is probably the first which efforts to protect life from diseases and aging. Siddha system of medicine is not merely a materialistic science but a philosophical and fact full truth which is put forward by our great ancestral sages through their experience logic and power of wisdom. The science of Siddha is not only holding within the measures for alleviation of discomforts but its foremost aim is maintenance of homeostasis and a better approach toward a healthy and happy life. The fundamental principle of the Siddha system of medicine is to protect the health of individual health before the occurrence of the disease.

II. INFLUENCE OF SEASONAL VARIATION IN HEALTH

Siddha medicine also considers the human body as the direct replica of nature. It was explained in the quote "*andathil ullathey pindam, pindathil ullathey andam*" stated by siddhar sattaaimuni . As a fact of substitution any ailments pertaining to human body there is a healing part in nature [2]. Seasonal variations in the environment have triggered the annual adaptations that are observed in majority of the species. However, seasonal variations may seem more limited in our species (human beings). Seasonal variation has been reported

for several physiological aspects including blood pressure, cholesterol or calorie intake, with higher levels seen in winter or fall for food intake. Recently, seasonal variation in expression levels of a large set of genes has been reported for human white blood cells and adipose tissue

It was found that the seasonal variations have been observed in several behavioural dimensions with peaks occurring at different time of year depending on the variable considered i.e. conception (winter/spring peak) and death [winter peak or violent suicide [spring/summer peak].[1]

Periodic seasonal changes have influenced in all life forms, as exemplified by seasonal physiology and behaviours, especially in humans, many complex polygenic diseases, including cardiovascular, autoimmune and psychiatric illnesses, have established seasonal patterns of incidence and disease activity.

Infectious disease seasonality is well established in humans, and it has been proposed that an inborn physiological rhythm underlies the seasonality of diagnoses of infectious diseases and their pathologies like COVID-19, but direct evidence of such a system is lacking.

The numbers of all seasonal cell types (leukocytes)	Peaked during the rainy season (June through October), during which time the immune system faces different pathogenic challenges, such as an increased infectious disease burden, including malaria.
Total monocyte numbers in blood	Increased during winter
The circulating level of the acute-phase complement activator, C-reactive protein,	Increased during winter months

The seasonal human immune system contributes to host-mediated pathology and morbidity after infection and it plays a significant impact on immunity. [3]

Table 1- Seasonal variation influences in gene expression [3]

MARKERS	SEASONAL INFLUENCE
Anti-inflammatory circadian ARNTL (Aryl Hydrocarbon Receptor Nuclear Translocator Like) mRNA	Peaking in the summer months of June, July and August. With lowest expression in the winter
Receptors for the prostaglandins (<i>PTGDR</i> - Prostaglandin D2 Receptor, <i>PTGIR</i> - Prostaglandin I2 Receptor and <i>PTGER4</i> - Prostaglandin E Receptor 4), leukotrienes (<i>CYSLTR1</i> - Cysteinyl Leukotriene Receptor 1) and oxoeicosanoids (<i>OXER1</i> - Oxoeicosanoid receptor 1)	Highly expressed in the winter
Receptors for adiponectin (<i>ADIPOR1</i> - Adiponectin Receptor 1), estradiol (<i>ESR2</i> - Estrogen Receptor 2) and antidiuretic hormone	Highly expressed in the summer

III. IMMUNITY

Immunity can be defined as a complex biological system endowed with the capacity to recognize and tolerate whatever belongs to the self, and to recognize and reject non-self. [4] WHO advised the general public to focus on enhancing their immune system to prevent getting affected by this pandemic disease.

IV. BASIC CONCEPTS AND DISEASES IN SIDDHA SYSTEM

As per Siddha system of medicine *Udal vanmai* (Immunity) was described by Siddhargal thousands of years ago. Now-a-days, the same is known as immunity in the modern science. It also depends upon nutritional, environmental and individual factors – both physical and mental. The *Udal vanmai* (Immunity) is stated to be of three types:

(1) *Iyarkkai vanmai* (Natural strength)– These are three physiques formed with *Sathuva gunam*, *Rajo gunam* and *Thamo gunam*. It is genetic and inborn resistance to disease, which exists since birth. It is said to increase with the growth of tissues and does not depend upon any other cause, both mental and physical strength present naturally by birth.

(2) *Seyarkkai vanmai* (Strength according to age and season) – This type of immunity is said to be influenced by seasonal traits and the age of the person.

(3) *Kaala vanmai* (Strength acquired artificially)– This strength is acquired by keeping the Seven *thathus* (*Saaram-Chyle* essence of the food, *Senneer*-Blood, *Oon*-Muscles, *Kozhuppu*-Fat, *Elumbu*-Bones, *Moolai*-Marrow, *Venneer*-Semen) intact by proper diets and activities suitable for the

physique composed of the three gunas. This type of *udal vanmai* briefly refers to modulation of body's resistance against diseases by resort to appropriate diet, physical exercise, restorative rest and therapies in keeping with seasonal needs. [5]

V. RELATIONSHIP BETWEEN SEASONAL VARIATION AND DOSHAS

The body consists of 3 types of *Doshas* (*Vatham*, *Pitham* & *Kabam*) and 3 types of *Gunangal* (*Sathvam*, *Rajo* and *Thamo Gunam*) in different quantity. These components are very important & have so much effect in our body.

The three humours – *Vatham*, *Pitham*, and *Kabam* are responsible for the occurrence of a disease.

- Basically, in a human body these three humours which are known as *Vatham*, *Pitham* and *Kapham* and they are in a normal ratio that is 1: ½ : ¼ respectively. This is called *Thannilai* the state of normalcy.
- During the onset of a disease, a single humour gets vitiated from its normal state is called the *Thannilai valarchi*.
- Then it slowly affects any of the other two humours along with it and results into a more aggravated state with signs and symptoms. This state is called *Vetrinilai valarchi*.

As per Siddha system of medicine, the day is divided into six parts (*Sirupozhuthugal*) and there are Viz. *Maalai* (Evening), *Yamam* (Mid night), *Vaikarai* (Dawn), *Kaalai* (Morning), *Nannpakal* (Noon) and *Erpaadu* (Afternoon).

There are totally six seasons (*Perumpozhuthugal*) according to the Siddha system of medicine in one year and the body needs to adapt itself according to the seasonal variation to remain healthy and disease-free life. It is because the body of every person is unique according to Siddha in terms of their *Thegi* and *Thrithodam* effects.

TABLE 2- DERANGEMENT STAGES OF *UYIR THATHUKKAL* IN RESPECTIVE SEASON [5,6]

DERANGEMENT STAGES	VATHAM	PITHAM	KABAM
Thannilai	<i>Mudhuvanri kaalam</i> (Jun 15 - Aug 14)	<i>Kaar kaalam</i> (Aug 15 - Oct 14)	<i>Munpani kalam</i> (Dec 15 - Feb 14)
Thannilai valarchi	<i>Kaar kaalam</i> (Aug 15 - Oct 14)	<i>Koothir kalam</i> (Oct 15 - Dec 14)	<i>Pinpani kalam</i> (Feb 15 - Apr 14)

Vetru nilai valarchi	<i>Koothir kalam</i> (Oct 15 - Dec 14)	<i>Munpani kalam</i> (Dec 15 - Feb 14)	<i>Ilavenil kalam</i> (Apr 15 - Jun 14)
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So, the above table shows how minutely a season can affect our body. *Kadukkai* (*Terminalia chebula Retz*) is the only herb mentioned in Siddha classical literature that describes its varieties along with their sources, identifying features, therapeutic uses and its method of consumption in a certain way with proper adjuvant in respective seasons.

VI. KADUKKAI – A POTENTIAL SIDDHA HERB FOR REJUVENATION

In the Siddha system of medicine, a lot of immune-boosting formulations, therapies like *Kayakarpam* (rejuvenation), *Pranayama* (breathing exercise), and health drinks are available. *Kayakarpam* procedures and techniques are of great current value in preventive and curative aspects of geriatric health care. The context of *Kayakarpam* therapy and *Attanga yogam* [*Iyamam* (Pureness of Mind), *Niyamam* (Good conduct), *Aadhanam* (Postures), *Praanayamam* (Breathing exercises), *Pratyaakaaram* (Abstraction), *Dhaaranai* (Concentration), *Dhyaanam* (Meditation), *Samaadhi* (Liberation)] and *karpa avizhtham* components are largely unexplored part of ancient wisdom.[7]

Kadukkai (*Terminalia chebula Retz*) is held in high esteem in Siddha for its properties to prevent and cure diseases. It has enjoyed the prime place among medicinal herbs mentioned in Siddha literature since ancient times. *Kadukkai* is called the 'King of Medicines' and is always listed first in Siddha because of its extraordinary therapeutic benefits.

Kadukkai is considered a rejuvenator with its acclaimed antioxidant property. *Terminalia chebula* possesses more phytoconstituents like tannins, anthraquinones, chebulinic acid, chebulic acid, ellagic acid and gallic acid.

Kadukkai properties are known to support healthy bowel movements and gut health. Now the science also recognizes that the gut as "the second brain" perhaps the ancients recognized the relationship between a healthy GI tract and clarity of mind few thousand years back.[8]

Kadukkai is a very ancient herb used for various health problems, individually enriched with numerous health benefits, pacify three doshas and has rejuvenating effects. It helps to regulate *Vatham* (strengthening the nervous system), *Pitham* (providing healthy metabolic process), and *Kabam* (improves structural integrity). *Kadukkai* also plays an important role in increasing the vitality of our prana. Purified *Kadukkai* powder consumed with water would give disease-free life to a person.[9]

VII. OTHER NAME MENTIONED IN SIDDHA LITERATURE

Other name for Kadukkai- *Paranatha, Iresaki*
Pranadha --- is another name for Kadukkai (When eaten as kaya karpam, it prevents the death of cells in the body and prolongs life) *Pranadha* - offering life

Resaki- Pulling the life force inside - Inhale - *Purakam*;
Disposal of waste products - Exhalation - *Resagam*. As it removes the unwanted substances from our body it was called *Resaki*. Kadukkai - Not only from faeces, but also from respiration it removes waste products from our body.[10]

Synonyms with definitions

Amalai- Goddess/ A woman who is pure

Amutham-Sweetness/ Offerings made to the gods in a sacrificial fire

Ammai- Mother/Goddess of virtue/Beauty

Amrutha- nectar

Haritaki -Born in the abode of Hara (Lord Shiva) in Himalayas

Resagi-(Yoga) let out-breath

Aiyavi- A weight/ Upright bar for the gate of a fort/Bundle of arrows

Siva- Hindu god of destruction and reproduction

Divya - divine in nature

Devi- Goddess/ heavenly, divine, anything of excellence

Pathiyam- Regimen/ Prescribed diet for a patient

Boothana- the gross or physical body

Boothan- Purified soul

Prapathya- the protector of travellers

Pranatha -Strong, powerful

Megam- cloud

Vayastha- Young

Vanadurgi- goddess- a manifestation of Lord Durga

Rohini - heals the wounds and ulcers

Jivanika/ Jivanthi - life-promoting

Jivya- brilliant

Vijaya- victorious or conquers all the diseases

Sethaki - increasing vitality

Jiva priya - liked by all

Ayurvedic father - Lord Dhanvantari will always have "Kadukkai" with him, to cure all diseases. It is also said to be neutralize three humors

Usually "Karpa marunthugal" is simply made by the Siddhars to take us to the state of yoga in an easy way. Kadukkai plays an important role of in Yogam. Kadukkai - also known as Haritaki in Sanskrit. Haritaki--- means to cure all diseases.

Kadukkai alone can balance the trio with its 5 flavors. According to our Mooligai Gunapadam text, Kadukkai is said to cure all diseases due to 6 seasonal variations.[11]

Kadukkayundh thaayung karuthilonren raalum

Kadukkaith thaikathigang kaannee-kadukkainoi

Ooti yudartetrum uttravannai yosuvaigal

Ootiudar rettru muvandhu.

-Agathiyar gunavaagadam

The mother feeds food with six tastes that nourish the baby, but Kadukkai wards off physical ailments and soothes the body. Once the body's disease was eliminated, then only the eaten food will be used by the body to drive the disease out of

the body. Otherwise, the eaten food will not benefit the body. So Kadukkai is better than the mother because she feeds only food to her child.[10]

VIII. BOTANICAL DESCRIPTION

Height-50-80 feet

Branches - the round crown and spreading branches

Bark - dark brown with some longitudinal cracks.

Leaves - ovate and elliptical, with two large glands at the top of the petiole

Flower-Flowers appear May-June, the fruits July-December

Fruit - 1-2 inches in size. It has five lines or five ribs on the outer skin. Fruit is green when unripe and yellowish grey when ripe (Fruits were collected from January to April, fruit formation started from November to January)

Special identity

Taxonomic description of *T. chebula* Retz.

Kingdom: Plantae-Plants;

Subkingdom: Tracheobionta-Vascular plants;

Super division: Spermatophyta-seed plants;

Division: Magnoliophyta-flowering plants;

Class: Magnoliopsida-dicotyledons;

Subclass: Rosidae; Order: Myrtales;

Family: Combretaceae-Indian almond family;

Genus: *Terminalia* L-tropical almond;

Species: *T. chebula* (Gaertn) Retz. -myrobalan.[12]

IX. CHOOSING A KADUKKAI FOR MEDICINE PURPOSES.

Selection and Preparation

Kadukkai is immersed in the water. Drowning Kadukkai only should be used for medicinal purposes. All those "floating kadukkai are removed. [13]

Grading and Flotation

When detectives "floaters" are inspected by cutting in half, they usually show incomplete kernels (large airspaces, or whitish cork tissue with reduced brownish endosperm) [14] This above article mentioned this floating technique in recent days. But it was mentioned in ancient Siddha literature a few decades before.

X. IDENTIFICATION, HABITAT AND THERAPEUTIC ATTRIBUTES OF DIFFERENT VARIETIES OF KADUKKAI

Visayan Kadukkai

It is used for curing *Vatha* diseases and most ailments and is found in the Vindhya Mountain ranges.

Rohini Kadukkai

The fruits of this type of Kadukkai are round in shape and are mostly used for wound healing and cures *Muppini*, *Kaba* diseases. these are mostly found in the Kanniyakumari regions.

Pirithivi Kadukkai:

The fruits of this variety are small with thin skin and are mostly used *Pitha* diseases.and are usually found in the **Saurashtra** regions.

Amrita Kadukkai:

This Kadukkai variety has a thick fruit pulp which is found in the Kasi regions. It cures *Kaba* diseases, also it has purgative action.

Seevanthi Kadukkai:

The tree bears yellow-coloured flowers, and the dried fruits are used for curing all type of disorders and haemorrhoids. Mostly found in forest region.

Thiruviruthi Kadukkai:

The three-layered skin of the fruit is mostly used for external applications and these are mostly found in the Hills regions.

Abhayan Kadukkai:

The five-layered fruit skin of this variety is used for treating vision problems and are cultivated in the Pothigai hill.[10]

TABLE 3- GENERAL DESCRIPTION OF KADUKKAI [10]

CHARACTERISTICS	DESCRIPTION
Colour	Colour of the fruit rind varies from yellowish brown, uniform brown to light black owing to the variety and place of origin
Taste	Astringent, sweet, sour, pungent, bitter.
Potency	Hot
Division	Sweet
Indications in Siddha Medicine	<i>Athithoolam</i> (obesity), <i>pun</i> (ulcers), <i>Kamalai</i> (jaundice), <i>Silipatham</i> (filariasis), diseases of cheek, throat, tongue and male genitalia, <i>Pandu</i> (Anemia), <i>Moothrakireecharam</i> (Dysuria), <i>Moolam</i> (Haemorrhoids), <i>Thamaraganoi</i> (Cardiac diseases), <i>kannoikal</i> (Eye diseases), <i>Aanmainmai</i> (impotency), <i>Gunmam</i> (Gastro intestinal conditions) <i>Megharogam</i> (Sexually transmitted diseases), <i>Kuttam</i> (Skin diseases) etc

So, there is a need to be followed according to the particular seasonal requirement of *Kadukkai* with various adjuvant to maintain hormonal balance in our body & to be fit and healthy. Consumption of *Kadukkai* (pericarp of mature fruit of *Terminalia chebula*) in certain way with various adjuvant in respective season will boost our immunity and help to prevent diseases. It was explained in Figure;[13]

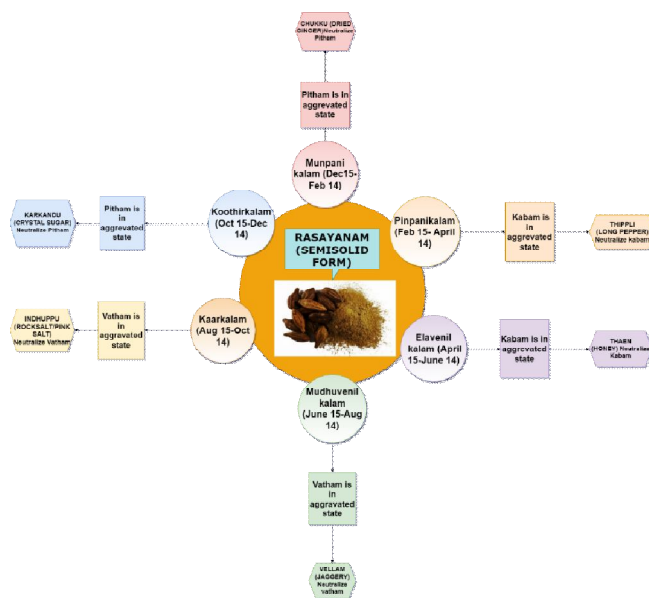


FIGURE 1- KADUKKAI CONSUMPTIONS WITH VARIOUS ADJUVANT IN RESPECTIVE SEASONS

TABLE 4- ADJUVANT OF KADUKKAI IN RESPECTIVE SEASONS [10]

SEASON/KAALAM	ADJUVANT
Illavenil kalam	Honey
Muthuvenil kalam	Jaggery
Kaar Kaalam kalam	Rock salt
Koothir Kaalam kalam	Sugar
Munpani kalam	Dried ginger
Pinpani kalam	Long pepper

It was advised that it should be taken in rasayanam form with respective adjuvants. Because Advantages of rasayanam form over other dosage forms it is highly palatable and easily digestible. Also, these adjuvants improve the absorption of *Kadukkai* into the gut. Another uniqueness of *Kadukkai* is it has 5 tastes among the six tastes except salt.

TABLE 5- VARIOUS TASTE PRESENT IN KADUKKAI [10]

PARTS OF KADUKKAI	TASTES ARE FOUND IN THE FRUIT OF KADUKKAI
Outer skin	Pungent
Ridge	Sour
Seed	Astringent
Stem	Bitter
Endosperm	Sweet

TABLE 6-PHYTOCONSTITUENTS OF T. CHEBULA RETZ. [15]

T. chebula is rich in tannins (about 32%-34%) {Tannins- Many physiological activities such as stimulation of phagocytic cells, host mediated tumor activity and a wide range of anti-infective action have been assigned to tannins}

Hydrolysable tannins (14 components)-gallic acid, chebulagic acid, punicalagin, chebulanin, corilagin, neochebulinic acid, ellagic acid, chebulinic acid, 1,2,3,4,6-penta-O-galloyl- β -D-glucose, 1,6-di-o-galloyl-D-glucose, casuarinin, 3,4,6-tri-o-galloyl-D-glucose, terchebulin
Phenolic components- chebulinic acid, ellagic acid and anthraquinones, Flavonol, glycosides, triterpenoids, coumarin conjugated with gallic acids called chebulin { Flavonoids are potent water-soluble super antioxidants and free radical scavengers which prevent oxidative cell damage have strong anti-cancer activity and protect against all stage of carcinogens. Flavonoids in the body are known to reduce the risk of heart diseases}
Polyphenols - corilagin, galloyl glucose, punicalagin, terflavin A, maslinic acid
Fatty acids - palmitic acid, linoleic acid and oleic acid
Triterpenoid glycosides - chebulosides I and II, arjunin, arjunglucoside, 2 α -hydroxyursolic acid and 2 α -hydroxymicromiric acid

XI. PHARMACOLOGICAL ACTIVITY

T. chebula is one of the most versatile plants having a wide spectrum of pharmacological and medicinal activities. *T. chebula* effective against different types of diseases

Antioxidant and free radical scavenging activity

Fruit of *T. chebula* possessed high antioxidant activity and phenolics were found to be responsible for this activity

Anticarcinogenic activity

Researchers have reported the inhibitory action on cancer cell growth by the phenolics of *T. chebula* Retz fruit and found that chebulinic acid, tannic acid and ellagic acid were the most growth inhibitory phenolics of *T. chebula*

Hepatoprotective activity

Ethanollic extract of *T. chebula* fruits showed strong hepatoprotective activity

Cardioprotective activity

Kadukkai has been reported to have cardioprotective activity.

Cytoprotective activity

Gallic acid (GA) was isolated from the extract of the herbal medicine the fruit of *T. chebula* as active principal that blocked the cytotoxic T- lymphocyte-mediated cytotoxicity.

Antiviral activity

- Four immunodeficiency virus type 1 (HIV-1) integrase inhibitors, GA (I) and three galloyl glucoses (II-IV).
- Galloyl moiety plays a major role for inhibition against the 3'-processing of HIV-1 integrase of the compounds
- Protects epithelial cells against influenza A virus
- It has an effect on human cytomegalovirus (CMV)[
- Kadukkai (*T. chebula*) against SARS-CoV-2 based on 3CLpro protease activity inhibition [14]

Hypolipidemic and hypocholesterolemic activity

Immunomodulatory activity

Aqueous extract of *T. chebula* produced an increase in humoral antibody titre and delayed type hypersensitivity in mice. Crude extract of *T. chebula* stimulated cell-mediated immune response in experimental amoebic liver abscess in golden hamsters.[12]

XII. ANTIOXIDANTS AS PROTECTIVE AGENTS

In recent years, antioxidants have gained much importance as prophylactic and therapeutic agents in curing human ailments. Antioxidants may function as immune modulators and used as a mainstream therapy in certain diseases.

Nature has endowed each and every cell in our body with adequate protective mechanisms against any harmful effects of free radicals such as glutathione peroxidase, glutathione reductase, thioredoxin, thiols and disulfide bonding are buffering systems in every cell. Other non-enzymatic antioxidants include carotenoids, flavonoids and related polyphenols, α -lipoic acid and glutathione, vitamins C and E. [16]

Imbued with these components, Kadukkai has the potential to boost immunity and provide effective treatment for various diseases.

XIII. CONCLUSION

As it is well said that "Prevention is better than cure", regulating our dietary habits right from the beginning can not only help us remain healthy but also prevent majority of ailments to affect our body, mind and soul. It was proved that if our digestive system is impaired our mental or psychological factor also get affected. It is inferred that, the Siddhars (usually referred as the olden day scientist) had the inner knowledge of the science of medicinal plants without the use modern technologies for medicinal activity of the plant. Therefore, it can be concluded that the increase in infectious diseases or pandemics will continue to transpire with the emergence of severe organisms or microbes; and an effective method of control and prevention will be of importance. Hence, the herbal drugs, concept of Siddha medicine and lifestyle proves that it is efficient and cost effective in the development of medications. This review reveals, Kadukkai possess immunomodulatory, anti-oxidant, anti-inflammatory and anti-viral properties which may have major role in the management of COVID-19 like infection and the uses of Siddha system of medicine to shed light along with the modern system of medicine to maintain stable and healthy lifestyle remarkably during pandemics.

II. NOTE:

THE STUDY HIGHLIGHTS THE EFFICACY OF "NATURAL HERBAL SOURCE" WHICH IS AN ANCIENT TRADITION, USED IN SOME PARTS OF INDIA. THIS ANCIENT CONCEPT SHOULD BE CAREFULLY EVALUATED IN THE LIGHT OF MODERN MEDICAL SCIENCE AND CAN BE UTILIZED PARTIALLY IF FOUND SUITABLE.

REFERENCES

- [1] Meyer C, Muto V, Jaspar M, et al. Seasonality in human cognitive brain responses. *Proc Natl Acad Sci U S A*. 2016;113(11):3066-3071. doi:10.1073/pnas.1518129113
- [2] Sambasivam Pillai TV. (1993). Introduction to Siddha medicine. 3rd Edition. Directorate of Indian medicine and Homeopathy, Chennai, 10.
- [3] Dopico, X. C. et al. Widespread seasonal gene expression reveals annual differences in human immunity and physiology. *Nat. Commun.* 6:7000 doi: 10.1038/ncomms8000 (2015).
- [4] Caroline D.Hoemann ET.AL., Immunological Responses in Orthopedics and Transplantation Encyclopedia of Biomedical Engineering 2019, Pages 359-373, <https://doi.org/10.1016/B978-0-12-801238-3.11009-8>
- [5] Shanmughavelu, H.P.I.M., Noinaadai Noimudhal Naadal Thirattu Part 1, First Edition, Published by D I M & H, Chennai, Pg no-17,72-75,79, 364.
- [6] Dr.Ko.Dhurairasan., Noi illa neri, 3rd edition-1993, Pg no-310-311
- [7] Shanmughavelu, H.P.I.M., Noinaadai Noimudhal Naadal Thirattu Part 1, First Edition, Published by D I M & H, Chennai, Pg no-17,72-75,79, 364.
- [8] Ochoa-Repáraz J, Kasper LH. The Second Brain: Is the Gut Microbiota a Link Between Obesity and Central Nervous System Disorders. *Curr Obes Rep.* 2016;5(1):51-64. doi:10.1007/s13679-016-0191-1
- [9] Dr.S.P.Thiagarajan. Sirappu Maruthuvam. 1st ed. Department of Indian Medicine and Homeopathy Publishers; 1998.
- [10] K.S.Murugesu mudhaliyar, Gunapadam mooligai vaguppu 7th edition 2003 pg no-324
- [11] G.Ramasamykom, Boghar karpam - 300, Sri ramachara vilasam press, 4th edition, 1969, Madurai
- [12] Bag A, Bhattacharyya SK, Chattopadhyay RR. The development of Terminalia chebula Retz. (Combretaceae) in clinical research. *Asian Pac J Trop Biomed.* 2013;3(3):244-252. doi:10.1016/S2221-1691(13)60059-3
- [13] Hakkim.Pa.Mohammad abdullah sayubu, "Kadukkai Vallarai thani maanbu", 2nd edition 1975, Indian Medicine and Homeopathy, Chennai-29
- [14] Upadhyay S, Tripathi PK, Singh M, Raghavendhar S, Bhardwaj M, Patel AK. Evaluation of medicinal herbs as a potential therapeutic option against SARS-CoV-2 targeting its main protease. *Phytother Res.* 2020;34(12):3411-3419. doi:10.1002/ptr.6802
- [15] P. Venkatalakshmi et.al., Role of phytochemicals as immunomodulatory agents: A review, *International Journal of Green Pharmacy* • Jan-Mar 2016 • 10 (1) | 1