Published online in http://ijam.co.in ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 11 (4), 594-615

Prevention of COVID 19 - Siddha perspective

Review Article

Anand Ganapathy A[1], Alaganandam Kumaran[2], Lekha G S[3]*

1. Chemical Sciences and Technology Division, CSIR-NIIST, Thiruvananthapuram.
2. Principal Scientist, Chemical Sciences and Technology Division, CSIR-NIIST, Thiruvananthapuram.
3. Research Officer, Siddha Regional Research Institute, Poojappura, Thiruvananthapuram.

Abstract

Introduction: Siddha is one of the ancient traditional medicine systems originated in South India which incorporates the extensive use of herbs, inorganic substances and animal products for maintaining a healthy life. Siddha system of medicine (SSM) has diverse and extensive use of natural resources for the prevention and management of comorbid conditions, widespread epidemic or pandemic diseases. Methodology: This article summarizes on Siddha methodologies and practices that are obtained from major scientific databases such as SciFinder, Pubmed, Scopus, Science Direct, Google Scholar and Springer using primary search terms as COVID-19, SARS-CoV-2, epidemic, immune-modulatory, antiviral, environmental sanitization and Siddha. The collected data's are extracted as SARS-COV-2 outline, Basic concepts, communicable diseases and preventive measures revealed in Siddha system of Medicine. Moreover the authors have tabulated the herbs used as health promoters and immune-modulators in Siddha, herbs used for fumigation and sanitization and the herbal ingredients used in important Siddha formulations for the management of infectious diseases. Conclusion: Many of the active principles present in the herbs are studied, proven to be effective immune-modulators, antivirals, anti-asthmatic and anti-inflammatory agents, which may also be effective towards the control of COVID-19. However, further scientific studies and data are required to support the use of Siddha medicines and herbs.

Key Words: *COVID-19, SARS-CoV-2, Siddha, Immune-modulatory, Antiviral, Sanitization.*

Introduction

The novel coronavirus pneumonia (coronavirus disease 2019, COVID-19) has now infected a total of 21,294,845 people and has claimed 761,779 deaths globally as on August 16, 2020 (1). Despite all the advancements in the 21st century in the field of medical sciences and advanced research, health problems and diseases have again led humankind to great distress. It has witnessed three major viral outbreaks in the current century- SARS-CoV, MERS and SARS-COV-2 (2) whereas the latter SARS-CoV-2, highlights the need for control in this highly pathogenic epidemic.

Due to the high infectivity of COVID-19, than its predecessors, more and more of the population are susceptible to higher respiratory infections and death (3). The high chance of human to human transmission is due to the presence of spike protein, which has a 10-20 times affinity for human angiotensin converting enzyme-2 (ACE2) for viral replication as compared to other SARS-CoVs (4).

Currently, there is no proven drug or vaccine for the treatment of COVID-19. The available methods include the use of supportive measures aimed at managing the symptoms such as fever, dehydration, respiratory disorders and other clinical symptoms. Due to the morbid and fatal nature of COVID-19, and the absence of any treatment measures, many of the clinically available antivirals, ACE2 inhibitors, immune-modulators, non-steroidal anti-inflammatory agents (NSAIDS) and corticosteroids, etc. are being repurposed.

Because of the numerous complications involved in the drug and vaccine development processes, the traditional systems of medicine are explored for their preventive and supportive care to the infected patients. In addition, some of the uncontrolled studies containing herbal products from traditional medicines claim a direct effect on the virus. Siddha system of medicine, practiced in South India has a close affinity towards Ayurveda and yet maintains a distinctive identity of its own by considering humans as a universal entity and implies that any change in the environment will have an influence on human existence and living. This system of medicine emphasizes the usage of botanical drugs for many severe respiratory diseases (5). Several of these drugs and formulations have been scientifically proven to be pharmacologically active against specific viruses such as Dengue and Chikungunya (6–8), and also possessing significant immune-modulatory effects (9). In this review, we present a brief outline on SARS-COV-2, and the Siddha concept of infectious and epidemic diseases along with their preventive measures in Siddha.

*** Corresponding Author:**

Lekha G S
Research Officer,
Sidda Regional Research Institute,
Poojappura, Thiruvananthapuram, India.
Email Id: lekha_doctor@yahoo.co.in

Methodology

The authors searched the Siddha medicinal literatures available in Siddha Regional Research Institute and CSIR library for information related to infectious and epidemic diseases and a total of nine important textbooks- *Siddha Vaidya Thirattu*, *Therayar Maha Karisal*, *Therayar Yamagam*, *Brahma Muni Karukkadai*, *Yogi Vatha Kaviyam*, *Agasthiyar Vallathi, Yugi vaidhya cinthamani, Noi illa neri* and *Agasthiyar Kanma Soothiram* were reviewed: Other research articles, literatures and books were also consulted for more details. The latest information regarding SARS-CoV-2 and COVID-19, were obtained through systematic search from major scientific databases such as SciFinder, Pubmed, Scopus, Science Direct and Springer. The keywords used were SARS-CoV-2, COVID-19, treatment, transmission. In addition to the same search engines, Google Scholar search was also performed to obtain evidence regarding Siddha drugs or formulations prescribed during epidemics. For this search, we used the terms Siddha, environmental sanitization, dengue, influenza, epidemic, antiviral, immunomodulatory and phytochemicals along with the names of drugs, according to their use. Time restriction was not made to extract the most useful information.

Brief outline on SARS-COV-2

Till date, seven human CoVs (hCoV) have been identified, capable of infecting humans: 229E and NL63 (alpha coronaviruses); OC4, HKU1, MERS-CoV and SARS-CoV (beta coronaviruses); and SARS-CoV-2 or COVID-19**.** Coronaviruses are enveloped, single stranded positive RNA viruses belonging to Coronaviridae family, consisting of a large club- or petal-shaped surface projections or spikes which resembles that of the solar corona (10). Member viruses of this family can cause respiratory failure, enteric and hepatic dysfunction as well as neurological disorders in different animal species including cattle, cats, camels and bats.

Preliminary genetic analysis studies of the earlier cases from China designated L and S strains of SARS-CoV-2, where the L-type was found to be more frequent (11). In addition, the virus was first discovered through the use of high-throughput sequencing and broncho-alveolar lavage fluid samples from infected patients (12). In addition, the extensive transmission of the virus over several continents summarize the fact for genetic diversity and the presence of three prominent sites in Orf1ab polyprotein in encoding Nsp6, Nsp11, Nsp13, and one in the Spike protein designate recurrent mutations, thereby suggesting convergent evolution and possible cause for adaptation in the human body (13).

The coronaviruses consist of four structural proteins, namely spike, membrane, envelop and nucleocapsid. Spike protein is composed of two functional subunits: S_1 and S_2 which are responsible for binding and fusion of the viral and cellular membranes (14). In 2003, it was identified that ACE2 was a functional receptor for SARS-CoV (4) and the structural and functional analysis revealed the high affinity of spike for SARS-CoV-2 to ACE2 (15,16). ACE2 expression was also found to be high in lung epithelial tissue as compared to other organs such as heart, ileum, kidney and bladder, indicating SARS-CoV-2 primarily affects the respiratory system, in spite other organs are also involved (17). The other notable feature is the cleavage of polybasic cleavage site (RRAR) at the junction of S_1 and S_2 subunits by furin and other proteases which is effective for the determination of viral infectivity as well as host range (18).

In addition, it is estimated that adults are more prone to COVID-19 than infants or young children (19). Some of the hypotheses include (i) the expression of ACE2 was more abundant in adults as the human lung epithelial cells continue to develop following birth (20) (ii) with ageing, the pro-inflammatory mediators also increase, that govern the neutrophil functions and the low capability of the T-cells at early stages of birth (21) (iii) the concurrent presence of other viruses also in the lung mucosa and airways are frequent in children and can lead to competition with SARS-CoV-2 and thereby limiting its growth (22).

Basic Concepts and infectious diseases in Siddha System

According to Siddha system, all substances in the universe are composed of five basic primal elements; earth, water, fire, air and space (23); where the human body is considered as an assortment of three humors and seven physical components. Any changes in the environmental factors- air, water, habitat and season are considered accountable for disease emergence (24). These environmental, epidemiological, seasonal and water-borne diseases can be compared and treated with the use of *Noi Nadal* (Siddha Pathology) concepts (23). In *Agasthyar Pallu*, 82 Siddha drugs are described which are extensively used to fight infectious and communicable diseases (24).

The Siddha system of medicine involves the concepts and relationships of humors within the body- *vali*/*vata* (wind), *azhal*/*pitta* (bile), and a*iya*/*kapha* (phlegm), where the respective pathological condition can be determined by the investigation of *nati* (pulse) to determine the nature of the humor responsible. According to *Siddha* concept, pulsation and its movement is exhibited as different types such as movement similar to that of a swan or peacock for cases of deranged *vata* humor and that of a hen or ant, if there is *pitta* imbalance; that of a fly or vulture in cases of vitiated *kapha* (24). An experienced Siddha physician is able to differentiate and identify status of humors through the pulse movements whether in right- or left-side body parts (25), thereby identifying the nature and cause of disease.

Epidemics/pandemics are mentioned as '*Uzhi Noi*' or '*Kothari Noi*' in Siddha system. In general, they are classified under "*Kollai Noikal*" which most commonly occur at the time of "*Ayana Santhi*" months (end a month of *Uthara Ayanam* & *Thatchana Ayanam*) fall on *Aadi* (mid of July to August) and *Margazhi* (mid of December to January) month in Tamil Calendar. It is believed that in those days, the immunity of human beings will be low; based on *Trithodam* or *Mukkutram*

theory (depended on three humors *vata, pitta* and *kapha*) the occurrence of diseases are raised based on the derangement of *Mukkutram*. Usually, *Thottru Noigal* (communicable diseases), associated with *Aiya kutram* (Respiratory-related illness), gets affected due to its *Sthiram gunam* (stability factor). *Guru Naadi* quoted that, *Thottru Noigal* is generally caused by *Kirumi* (Pathogens or Microbes). The symptoms are due to *Noiyinan vanmai* (immunity of an individual); if it is good, the individual will not be affected. Hence the Siddha formulations or habits are designed to neutralize the *Aiya kutram* (24,26) and to maintain the immuno-modulatory mechanism during this period.

In accordance to the Siddha system of medicine, COVID-19 can be effectively described as a *Thotru Noi* (communicable disease) which is caused due to the derangement of immune system of the body to fight the invading *Kirumi* (virus or pathogen) which directly causes *Aiya noigal* (respiratory related illness) due to changes in food, behaviour and surroundings. In addition, the symptoms of COVID-19 such as mild fever, sore throat, malaise, headache, shortness of breath, pneumonia and respiratory distress can be compared to that of *Kapha suram*. Also, people with low immune power or immunity are also susceptible to epidemics as described by *Tirumantiram* by Saint *Tirumular* (24).

In Siddha, all types of pyrexia including vector-borne diseases such as malaria, dengue etc. are classified as a total of 64 types and collectively called as *Suram*. Among them, Siddha equates dengue to *Pitta Suram,* because the symptoms such as haematuria, anorexia, vomiting, nausea, myalgia, dysentery, fever followed by chills are similar to those described in *Sura Vadagam,* which explains the treatment as well. Literatures such as *Siddha maruthuvam* also describe similar symptoms for dengue fever. Whereas *Agastiyar sura nool 300* describes that the 'Pitta suram' can cause bleeding correlating to haemorrhages (*kuruthi azhal*) in dengue fever and the symptoms described above corresponds with the definition of dengue fever by WHO (8,27).

In the same way Siddha equates COVID-19 to *Kapha suram*, because the symptoms of *Kapha suram/ Slethma suram* are fever, cough, throat pain, anosmia, dysgeusia, shortness of breath and fatigue which can be correlated with mild stage SARS-CoV-2. In severe stage, the symptoms are related with *Sanni* staging of *Kapha suram* or *Kabavatha suram* (28). The literatures in Siddha system explores various formulations for the treatment of *Kapha suram* or *Kabavatha suram* and *Sanni noi.*

Therefore, it is evident that without identifying the microbes and other detrimental substances, Siddha healers or scholars could recognize and apprehend the reason, source and mode of transmission of contamination, thereby managing infectious epidemics. Thus the theories and observations made above supports the effective use of Siddha medicine as a significant therapy against current health problems.

Prevention of epidemics as per SSM

From Siddha literatures, it is found apparent that the "*Pini anugaa vidhi*" (keeping diseases afar) are more important than the cure for the particular disorder. Therefore, the Siddhars have recommended some basic life guidelines that are to be followed for a healthy life and wellbeing. Some of the concepts such as *Thinai/ Nilam ozhukkam* (habitat disciplines), *Kaala ozhukkam* (seasonal discipline), *Naal ozhukkam* (daily regimen) and *Unavu* (diet) are still being followed along with *Kayakalpam* as a preventive measure against diseases.

Thinai ozhukkam stresses the importance of habitat in ancient Tamil literature depending on landscape and landforms- *Kurinchi* (mountains and surroundings), prone to fevers affecting hematopoietic systems; *mullai* (forest), prone to diseases affecting joints and nerves; *neithal* (sea shores and beaches), prone to liver and intestinal diseases, *palai* (dry and desert lands) are considered prone to all kinds of diseases; and *marutham* (agricultural land) is said to have all the humors in equilibrium and hence considered the best for living (23).

Kaala ozhukkam is based on the seasonal changes that affect the humors. The diet and drugs that help in normalizing these humors are also recommended by the *Siddhars*. During monsoon season, buttermilk mixed with dried ginger, root of *Piper longum* L. and *Plumbago zeylanica* L. are considered suitable along with food rich in fiber content; walking on wet surfaces with bare foot are to be strictly avoided. In the autumn season, diet containing pulses, rice, goat milk, amla, green and leafy vegetables are deemed essential and day time sleeping is to be avoided. In the winter season, urududal (split black gram) and a diet consisting of wheat should be included with breakfast regimens. The medicated oils that minimize *vata* should be applied on the head and body as recommended. In case of spring season, rice, ghee, *kezhvaragu* (ragi), fruits like drupe, plantains along with honey are to be included in the diet. Dried roots of *Vetiveria zizanioides* (L.) are highly recommended to be included while boiling water for drinking. During this season, sleeping at daytime are restricted and wakefulness at night are to be avoided. In case of summer season, easily digestible foods rich in high water and fiber content such as grapes, pomegranate, cardamom, ilupaipoo (flower of *Madhuca longifolia* (J. Konig) J.F. Macbr.), and palm jaggery are recommended. Moreover, alcohol consumption is to be strictly avoided during this season (24,26). The diet regimens and sleep patterns are to be strictly maintained in order for healthy wellbeing, according to Siddha concept.

Naal ozhukkam involves the daily discipline that has to be followed on a day; where an entire day is divided into six minor individual parts based on time, called *sirupozhuthu* (small periods) as each part is dominated by a particular humor. Daily lifestyle regimens such as waking up between 4 to 6 am, drinking pure water immediately after waking and use of twigs from *Asoku* (*Saraca asoca* (Roxb.) Willd), *Vembu* (*Azadirachta indica* A. Juss.), *Aathi* (beedi leaf

tree), *Aal* (Indian banyan), *Vael* (Gum Arabic tree) for brushing are considered to be very healthy and hygienic. Application of *Pancha karpam* which is a mixture of five herbal ingredients such as *Kasthuri manjal* (aromatic turmeric), *Milagu* (pepper), *Vembin vithu* (seed of neem), *Kadukkai thol* (*Terminalia chebula* Retz.. fruit) and *Nelli paruppu* (gooseberry seed) mixed with boiled milk, on head before bathing helps for keeping the body cool and balance the humors. Eating only when required and on a right quantity is essential to maintain the humor. The sleeping beds should be used according to the season and pathological conditions. For example, in cases of giddiness, vomiting and aggravated *pitta*, sleeping on *Thazhampai* (screw pine leaves) *padukkai* (mat) is advised (24).

Unavu involves the dietary regimens for a safe and healthy life. According to Siddha, *Unavae marunthu (Food is Medicine) as proclaimed* by the great Siddhar *Thiruvalluvar* in his famous work *Thirukkural.* The dietary regimen during the intake of Siddha medicine is termed as *pathyam* and *apathyam* (23,29,30).

Medicinal ingredients such as Velavarai (*Dolichos lablab* L.), Manathakkali (*Solanum nigrum* L.), Nerunchil (*Tribulus terrestris* L.), Mookiratai (*Boerhavia diffffusa* L. nom. cons.), Musumusukai (*Mukia maderaspatana* (L.) M. Roem.) etc. are recommended for the balancing of *Vata* humour. Whereas, Cucumber (Cucumis sativus), Vallarai (*Centella asiatica* (L.) Urban), Puliarai (*Oxalis corniculata* L.), Kovai (*Coccinia grandis* (L.) Voigt), Ponmusuttai (*Sida acuta* Burm.f.), Oritazhttamarai (*Ionidium suffrutiocosum* Ging.), Sundai (*Solanum torvum* Sw.) etc. are useful in the maintenance of *pitta* and; Brinjal, Peipudal (*Trichosanthes cucumerina* L.), Bittergourd, Pepper, Turmeric, Mustard, Sundai (*Solanum torvum* Sw.), Gooseberry etc. are essential for the control of *kapha* as per Siddha literature. Also, *Kayakalpa* drugs such as *Citrus limon* (L.) Burm. (elumicchai), *Terminalia chebula Retz.* (kadukkai), *Strychnos potatorum* Linn. (thettran), *Phyllanthus emblica* L. (nelli), *Aegle marmelos* (L.) Correa (vilvam) help in providing essential nutrients to the body and act as a preventive against most of the diseases (23). Meat and fish are strictly restricted in certain type of diseases and during Siddha treatment period. A number of immunomodulatory drugs that are encouraged during epidemics are given in **Table 1**.

Role of SSM in environmental sanitization

Fumigation, called "*Pugai"* in Siddha represents the artificial saturation of surroundings with fumes or smoke of any herb or aromatic substance. The purpose of this procedure is to control the microbial infections. *Pugai* is one among the 32 types of external therapies explained in Siddha literature *Theriyar Tharu* and was used as a preventive measure to protect themselves from communicable diseases (24). It is considered as one of the best methods employed for disinfection and sterilization of the environment and surroundings instead of chemical fumigants. During fumigation, the surroundings as well as the persons involved in the process are benefited by the usage of medicinal herbs (31).

Pugai involves fumigating the surroundings by burning dried medicated herbal juices or extracts over a cloth, where the cloth acts as *Thiri* (wick). Similarly, Thippili (*Piper longum* L.), Manjal (*Curcuma longa* L.*),* Omam (*Trachyspermum ammi* (L.) Sprague), and Milagu (*Piper nigrum L.*) are ground, then applied on a cloth and soaked with Neem oil. This mixture was allowed to smolder and the smoke was allowed to be inhaled by the patient and/or used as an environment sanitizer (31). Ellu (*Sesame indicum* L.), Payaru (*Vigna* radiate (L.) R. Wilczek), Kadugu (*Brassica juncea* (L.) Czern.), egg shell, fecal matter of dog, outer skin of the Poondu (*Allium sativum* L.), Kattamanaku (*Jatropha curcas* L.), Thulasi *(Ocimum sanctum L.),* Devadaru (*Cedrus deodara* (Roxb.) G.Don) are also used for the same purpose. *Karuvelam pisin* (Gum of Acacia Arabica), roots of Murungai (*Moringa oleifera* Lam.), Erukku (*Calotropis gigantea* (L.) Dryand.), azhinjil (*Alangium salviifolium* (L.f.) Wangerin) and Sivanar vembu (*Indigofera aspalathoides* Vahl. ex. DC.) are made into a fine powder, and a pinch is added to burning charcoal and was used to fumigate the surroundings as well as the patient (24).

Suruttu (medicated cigar) is made by rolling dry medicated leaves, for eg., *Adathodai suruttu*. The fumes of Sathakuppai (*Anethum graveolens* L.) dry leaves are extensively used around the patient's surroundings as a disinfectant. These fumes not only cleanse the affected areas but also relieves the mental stress of the subjects (31). In Siddha literature, Sage *Agasthiyar's Maanidakkirigai-64* explains the use of various drugs for *Pugai* in the treatment of Psychiatric ailments (24).

Nowadays, Padigara neer (alum) and turmeric water (*Curcuma longa L.*) are also used as an effective hand sanitizer. *Agasthiyar kuzhambu* was extensively used in the dose of 3 to 5 paddy weight to fumigate before the origination of chemical sprays or fumigants (31). Some of the other common herbs that are used for fumigation as well as sanitization in Siddha are: *Shorea robusta* Roth*., Argemone mexicana* L.*, Costus speciosus* (J. Konig) C. Specht*, Anethum graveolens* L.*, Boswellia serrata* Triana & Planch.*, Santalum album* L.*, Abutilon indicum* (Link) Sweet*, Cedrus deodara* (Roxb.) G. Don*, Nicotiana tabacum* L.*, Mangifera indica* L.*, Crinum asiaticum* L., *Aquilaria agallocha* Roxb.*, Lawsonia inermis* L., *Ruta chalepensis* L., *Justicia beddomei* (C.B. Cl) S.S.R. Bennet, *Madhuca longifolia* (J. Konig) J. F. Macbr., *Datura metel* L., *Solanum surattense* Burm. f., *Saccharum officinarum* L., *Rhus succedanea* L. (31). The information regarding these medicinal drugs along with other natural fumigants are available in **Table 2**.

Many of the medicinal herbs contain volatile and essential oils which can act as excellent antimicrobial, for example Manjal (*Curcuma longa* L.), Vembu (*Azadirachta indica* A. Juss.), Sadakuppi (*Anethum graveolens* L.), Milakukkirai (*Mentha piperita* L.), Karupuramaram (*Eucalyptus globulus*

Labill.), Thulasi (*Ocimum sanctum* L.), etc. provide pleasant aroma when burnt or incinerated.

It is evident that from **Table 2**, almost all of the medicinal herbs proposed for fumigation in Siddha literature are found to be antimicrobial or antiviral agents. In-spite of their pharmacological actions, there are no evidence based clinical studies suggesting the use of these herbs as fumigants. However, there are several sporadic studies that compared the herbal disinfectants which are recommended by Siddha to that of the chemical agents and found equally efficacious, safe and available at low cost (32,33). Yet clinical studies in a controlled manner and data reports are required to prove the efficacy and safety of these herbal fumigants (34,35).

Prevention of COVID-19: Siddha perspective

The data collected from the literatures and Manuscripts reveal the following preventive measures of COVID-19 in Siddha system of medicine.

According to the Siddha system of medicine, food is considered as medicine and proper intake of food can provide immunity to the body. A number of immunomodulatory herbs are reported in Siddha as a preventive during epidemics are given in **Table 1.** Immunomodulation is the ability to alter the immune response in humans and animals against infectious agents, stimulation of immune system is preferred for patients those who have compromised immunity and immune-suppressants are required for patients having inflammatory diseases.

In general, an infusion made up of half teaspoon of chukku (dried ginger) in two litres of water can be used for drinking; the use of inji (ginger) thenooral / inji tea / adhimaduram (liquorice) tea is recommended for immunomodulation. It is highly advised to avoid drinking milk before bedtime and if needed for children, adding a quarter teaspoon of manjal (turmeric) with milagu (pepper) is advised. Steam inhalation therapy by using *Tulasi* / *Nochi* / *Manjal* and gargling with a pinch of salt and turmeric is also highly recommended. The use of *karappan pandam* (allergic food) should be devoid from the daily diet. Also, the diet may include Nandu kanji (Crab soup), Pancha mutti kanji (5-grain gruel) and Irumurai vadittha kanji (double-cooked gruel) are highly recommended to include in the daily regimen as per the Siddha literatures (36,37) and the Ministry of AYUSH, Govt. of India (38).

In spite of the other resources, 108 medicinal herbs called as *karpa mooligaikal* are predominantly used in Siddha system for treating certain diseases and as an antioxidant & immunomodulator which were used extensively in case of dengue and HIV epidemics (8,39). These plants are also rejuvenators to boost health and thereby prevent chronic diseases and reduce ageing (40).

Kayakalpa (Kaya- Body, mind and psyche and Kalpa- Transmutation) is one of the significant and exclusive methods of Siddha system which combines both human and natural sources (herbs) for rejuvenation and transformation as prevention from diseases (23,24). The treatment regimen involves lifestyle measures and routines involving breathing regulation, sperm conservation, administration of carefully processed mineral drugs or potent herbs such as *Katrazhai* (*Aloe indica* Royle), *Bhringaraja* (*Eclipta alba* L. Hassk) and *Neem* (*Azadirachta indica* A. Juss.) etc. which are beneficial to the human internal system as a whole (41). Also, the intake of *Muppu*, which is a meticulously prepared mixture of three salts are considered to have prophylactic action besides the rejuvenation of body (13).

In addition, the effectiveness of a number of Siddha medicinal formulations or drugs are being scientifically validated and proven, thereby supporting and promoting the value of Siddha system of medicine. For example, *Brahmananda bairavam mathirai*, *Nilavembu Kudineer*, *Vishnu chakram* are effective against chikungunya infections (7,8,42). Evidence based Siddha medications such as *Nivalembu kudineer*, *Adathodai kudineer*, *Veppilai chooranam*, *Ammukkara chooranam*, *Amman Pachirisi karkam* for dengue infections (8,39); Urai mathirai for its immunomodulatory effect (9); *Kapa Sura*, *Sarva Sura* and *Visha Sura Kudineers* (decoctions) from the Siddha literature *Kaaviya Sura Nool* are also useful against Swine flu fever, as these formulations are found to contain major medicinal herbs and phyto-constituents that are proven to be antiviral and antipyretic agents (28,39,43,44). Other polyherbal Siddha preparations such as *Chitramutti Kudineer, Chukku kudineer, Adathodai manapagu* are some of the classical medications used by Government of Tamil Nadu, India, in the year 2012 when the state was plagued by dengue fever (45).

Urai mathirai is a Siddha formulation made up of 10 herbal ingredients of hot-potency and pungent taste, extensively used for the prevention of recurrent respiratory infections. The medication as a whole after the digestion in stomach gets transformed into a fire moiety which increases the *Azhal* (immunity) of the body. As according to Siddha system *"Vatamaai Padaithu, Pitta Vanniyai Kathu, Sethuma Seethamai Thudaithu"* meaning *Vata* is responsible for creation, *Pitta* for prevention and *Kapha* for destruction. Infection occurs if the immunity is challenged and it can be rectified with the increase of *Azhal.* The ingredients of Siddha polyherbal formulation *Urai mathirai* are chukku (*Zingiber officinale* Roscoe), adimathuram (*Glycyrrhiza glabra* L.), akkirakaram (*Anacyclus pyrethrum* (L.) Lag.), vashambu (*Acorus calamus* L.), catikkai (*Myristica fragrans* Houtt.), katukkai (*Terminalia chebula Retz.*.Retz.), masikkai (*Quercus infectoria* G.Olivier), acanam (*Allium sativum* L.), tippili (*Piper longum* L.) and perunkayam (*Ferula assa-foetida L.*) which are having immunomodulatory activity (7,8).

As COVID-19, is considered as a *Thotru noi* having similar symptoms as that of *Kabasuram* and *Sanni noigal* in Siddha literature, the effective management may be acquired by the use of anti-inflammatory, antiviral, antipyretic, immunomodulators in order to reduce or control the symptoms (24). Some

of the most extensively used Siddha formulations which are said to contain the above said pharmacological activities are (i) *Kaba Sura Kudineer* (ii) *Nila Vembu Kudineer* (iii) *Visha Sura Kudineer* (iv) *Sarva Sura Kudineer* (28,38,39,42,44). The contents of the said Siddha preparations are given in **Table 3**.

The four Siddha formulations contain a blend of medicinal herbs which are to be administered as a liquid at a dose of 60 ml twice a day before food. These formulations contain specific immunomodulators for respiratory care, antivirals, antipyretic and anti-inflammatory agents such as *Sitrarathai* (*Alpinia galanga* (L.) Willd.), *Amukkara* (*Withania somnifera* (L.) Dunal), *Kodiveli* (*Plumbago zeylanica* L.), *Charanai* ver (*Trianthema decandra* L.), *Peyputtal* (*Trichosanthes cucumerina* L.), *Koraik kilanku* (*Cyperus rotundus* L.), *Parpatakam* (*Mollugo cerviana* (L.) Ser.), *Nilavembu* (*Andrographis paniculata* (Burm.f.) Nees), *Keezhanelli* (*Phyllanthus niruri L.), Seenthil* (*Tinospora cordifolia* (Thunb.) Miers) which are individually proven for their respective pharmacological actions (8,28,39,43,44).

Siddha system of medicine also contains different formulations such as *Adathodai Managapu*, *NellikkaiIlagam*, *Vasantha Kusumakaram*, *Thalisathi Vadagam*, *Bramananda Bairavam*, *Thirithoda Mathirai*, *Seenthil Chooranam*, *Pachaikarpoora Mathirai*, *Swasakudori Mathirai*, *Thippili Rasayanam,* etc which are the effective herbal formulations in Siddha which can be employed for the control of *Kabasuram* – fever with Respiratory illness (38,46,47).

Conclusion

It can be summarized that prevention of epidemics are possible through the methods of Siddha system of medicine by maintaining a stable and healthy relationship with the human body and the environment. This review is aimed to update the readers about the classical Indian system of medicine, which is built on the vast experiences on observation and treatment regimens of the ancient saints of India. The Siddha concepts of sanitation, diet and immunomodulation are completely dependent on the mind and natural surroundings of human population. Therefore, Siddha system of medicine is a bundle of desirous information that has to be explored, explained and implemented to understand the ancient knowledge of maintaining a relationship with the environment for better wellbeing.

The medicinal herbs which are being long used in ancient cultures are now being proven to be effective through scientific studies although more controlled clinical data are of utmost importance. The concept of *pugai* as a mode of fumigation and sanitization of surroundings and environment, the use of herbal hand washes such as turmeric and the use of *kayakalpa* technique and various other polyherbal decoctions with respect to the daily and seasonal variations with a strict and proper diet lead to a long and healthy life to our ancestors.

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 and concept of Siddha medicine and lifestyle may prove effective and cheap products in the development of medications. This review suggests the use of traditional system of Indian medicine such as Siddha to shed light along with the modern system of medicine to maintain and stable and healthy lifestyle remarkably during pandemics.

Tables

Table 1: Herbs used as health promoters and Immunomodulators according to Siddha.

Botanical name and family	Siddha name	Part used	Location	Traditional uses	Constituent responsible	Mode of action or rationale	References
Cedrus deodara (Roxb.) G. Don, Pinaceae	Devadaru	Wood	Jammu and Kashmir, Himachal Pradesh, Nepal, China	Essential oil as insect repellant, aromatherapy, astringent, antifungal	Volatile oil constituents	Immunostimulant, anti-inflammatory, antioxidant	(48–50)
Cinnamomum tamala (Buch. Ham.) T. Nees & C.H. Eberm., Lauraceae	Lavanga pathiri	leaves	Bangladesh, Nepal, China, India	Antidiabetic, carminative, sedative, antidepressant, antidiarrhoeal, astringent, stimulant	A-type procyanidin oligomers	Immunomodulatory, antimicrobial	(37,51)
Alpinia galanga (L.) Willd., Zingiberaceae	Arathai	Rhizome	West Bengal, Assam, Cambodia, Thailand, Japan	Cold, sore throat, anti-emetic, analgesic	Neolignans and sesquineolignans	Immunomodulatory, antioxidant	(52–54)

Withania somnifera (L.) Dunal., Solanacea	Amukkara	Root	Tamil Nadu, Rajasthan, Andhra Pradesh, China, Yemen	Blood tonic, treat irregular menstruation, anaemia, erectile dysfunction	Withaferin A	Immunostimulant, anti-inflammatory	(55,56)
Tinospora cordifolia (Thunb.) Miers, Papilionaceae	Seenthil	Leaves	Haryana, Madhya Pradesh, Assam, China, Bangladesh, Vietnam, Malaysia, Sri Lanka	Memory booster, antispasmodic, antidiarrhoeal, stomachic, tonic, bronchitis, promotes longevity, anti-allergic	Alkaloids, flavonoids, saponins	Immunomodulatory, antiviral	(57,58)
Cynodon dactylon (L.) Pers., Poaceae	Arugampul	Juice	Madhya Pradesh, Himalayas, Pakistan, Indonesia, United States	Haemostatic, diuretic, antipyretic, treatment of bronchitis, leucoderma, diarrhea, hypertension	Protein fraction	Immunomodulatory, antioxidant	(50,59, 60)
Curcuma longa L., Zingeberaceae	Manjal	Rhizome	Most states in India, Pakistan, Malaysia, Indonesia, Ethiopia, Japan, China	Natural antiseptic, disinfectant, analgesic, remedy for skin diseases, indigestion, arthritis	Aqueous rhizome powder	Immunostimulant, anti-inflammatory	(51,61, 62)
Plumbago zeylanica L., Plumbaginaceae	Kodiveli	Root	Assam, Australia, Oman	Expectorant, astringent, laxative, abortifacient, memory booster,	Seselin	Immunomostimulant, anti-inflammatory	(63,64)
Justicia adhatoda L., Acanthaceae	Adathodai	Leaves	Eastern Ghats, Assam, Himalayas, China, Nepal	Cough, fever, asthma, dysentery	Vasicine	Immunostimulant, antioxidant, antimicrobial	(55,63, 65)
Enicostemma axillare Lam., Gentianaceae	Vellarugu	Whole	Tamil Nadu, West Bengal, Kerala	Stomachic, tonic, antipyretic, remedy for dyspepsia, malaria, leprosy	Swertiamarin	Immunomodulatory, antoxidant	(66,67, 68)
Indigofera aspalathoides Vahl. ex. DC.,Fabaceae	Sivanar vembu	Aerial part	Pakistan, Indonesia, Malaysia, Sri Lanka	Demulcent, sedative, analgesic, antispasmodic, remedy for leprosy, malaria, kidney stones	Kaempferol 5-O-β-D-glucopyranoside	Immunostimulant, anti-inflammatory	(61,69)
Senna alexandrina Mill., Fabaceae	Nilavarai	Seeds	Tamil Nadu, Egypt, South Africa, China	Remedy for dysuria, diabetes, night blindness, epilepsy	Rhein	Immunostimulant, antimicrobial	(70,71)

Morus alba Linn., Moraceae	Kambli chedi	Leaves	Haryana, China, Pakistan, Africa, South America	Tonic, laxative, reatment for cough, catarrh, fever, sore throat, dizziness, vertigo.	Methanol extract	Immunomodulatory, antioxidant	(36,59)
Terminalia arjuna (Roxb.) Wight & Arn., Combretaceae	Marudha maram	Bark	Madhya Pradesh, Rajasthan	Cough, cold, skin diseases, inflammation, asthma, excessive perspiration, remedy for viral and blood diseases	Tannins, arjunolic acid	Immunostimulant	(72,73)
Allium sativum L., Amaryllidaceae	Poondu	Garlic bulb	Asia, Iran, Egypt, Mexico	Stomachic, fever, cough, antibacterial, anti-inflammatory	Lectins	Immunomodulatory	(32,61, 58)
Boerhavia diffusa L. nom. cons., Nyctaginaceae	Mukkarattai	Root	Asia, South America and Africa	Remedy for reproductive disorders, jaundice, kidney problems, skin diseases, eye problems	Punarnavine	Immunomodulatory, Anti inflammatory, Antioxidant	(74,75)
Pteridium aquilinum (L.) Kuhn., Dennstaedtiaceae	Parnai	Bud	China, India, Indonesia	Treatment of tuberculosis, antiemetic, antiseptic, appetizer, tonic	Aqueous extract	Immunomodulatory, antioxidant	(55,76, 77)
Andrographis paniculata (Burm.f.) Nees., Acanthaceae	Nilavembu	Whole plant	Eastern Ghats, Sri Lanka, China, United States	Treatment of dyspepsia, influenza, dysentery, malaria, respiratory infections	Andro-grapholides	Immunomodulatory, antipyretic, antioxidant	(55,76, 78)

Table 2: Herbs used for fumigation and environmental sanitization as per Siddha system.

Botanical name and family	Siddha name	Part used	Location	Traditional use	Phytochemistry	Mode of action or rationale	References
Curcuma longa L., Zingeberaceae	Manjal	Rhizome	Most states in India, Pakistan, Malaysia, Indonesia, Ethiopia, Japan, China	Natural antiseptic, disinfectant, analgesic, remedy for skin diseases, indigestion, arthritis	Turmerone, zingiberene	Fumigation, antimicrobial, sanitizer	(51,79,80)
Azadirachta indica A. Juss., Meliaceae	Vembu	Leaves	India, China, Malaysia, Caribbean, South East Asia	Antibacterial, anti-inflammatory, natural antiseptic, antipyretic	Azadirachtin, Nimbin	Fumigation, insecticidal, antimicrobial	(51,61,81)
Anethum graveolens L., Apiaceae	Sadakuppai	Leaves	Central Asia, Mediterranian, USSR	Abdominal pain, eye diseases, uterine pains	Scopoletin, umbelliferone	Insecticidal, antibacterial	(66,82,83)

Piper longum L., Piperaceae	Thippili	Seeds	India, Pakistan, China, Europe	Relieve muscular pains, anti-inflammatory, stimulant, stomachic, antidiabetic	Piperine, piperlongumine	Antiparasitic, antimicrobial, antibacterial	(9,59,84)
Carum copticum (L.) Sprague ex Turrill., *Apiaceae*	Omam	Leaves, seeds	Kerala, West Bengal, Gujarat, Iran, Afghanistan, Pakistan	Carminative, antiseptic, expectorant, antimicrobial bronchodilatory, antitussive	Carvacrol, γ-terpinene	Insecticidal, antimicrobial	(66,85)
Piper nigrum L., Piperaceae	Milagu	Seeds	South India, Vietnam, Brazil	Cough, sinusitis, throat pain, infections, ear ache, gastrointestinal disorders	β-pinene, p-cymene	Antimicrobial, antibacterial	(86-88)
Sesamum indicum L., Pedaliaceae	Ellu	Seeds	Asia, Africa, Japan	Wound healing, antiviral, analgesic, hypolipidaemic	Sesamin, sesamol, sesaminol	Fungicide, antimicrobial	(36,66,89, 90)
Vigna radiata (L.) R. Wilczek,* Fabaceae	Cherupayaru	Seeds	India, China, Bangladesh	Antipyretic, anti-inflammatory	Catechin, gallic acid	Antimicrobial, antibacterial	(55,91,92)
Brassica juncea (L.) Czern., Brassicaceae	Kadugu	Seeds	Pakistan, India, Bangladesh, Japan, China, America	Stimulant, expectorant, diuretic, used as spice	Zeaxanthin, lutein	Fumigation	(61,93-95)
Allium sativum L., Amaryllidaceae	Poondu	Outer skin	Asia, Iran, Egypt, Mexico	Stomachic, fever, cough, antibacterial, anti-inflammatory	Allicin, alliin, diallyl sulfide	Fumigation	(32,96,97)
Jatropha curcas L.,* Euphorbiaceae	Kattamanaku	Leaves	Pakistan, India, South America, China	Lactogogue, stomachic, rubefacient, remedy for diabetes, arthritis, jaundice, malaria	Vitexin, isovitexin, gallic acid	Insecticidal	(51,61,98)
Ocimum sanctum L., Lamiaceae	Thulasi	Leaves	India and Southeast Asia	Bronchitis, malaria, diarrhea, dysentery, skin diseases, arthritis, eye diseases, insect bites, antibacterial, common cold	Methyl eugenol, carvacrol	Insecticidal	(70,97,99)
Cedrus deodara (Roxb.) G. Don, Pinaceae	Devadaru	Wood	Jammu and Kashmir, Himachal Pradesh, Nepal	Essential oil as insect repellant, aromatherapy, astringent, antifungal	Deodarin, cedeodarin, cedrusin	Antiparasitic, antimicrobial	(48,49,55, 64)

Moringa oleifera Lam., Moringaceae	Murungai	Roots	Asia and Africa	Immune booster, anti-inflammatory, abortifacient, cough, common cold	Isotrifolin, quercetin	Fumigation, antimicrobial	(66,86, 100)
Calotropis gigantea (L.) Dryand., Apocynaceae	Erukku	Root	Haryana, China, Thailand, Sri Lanka	Antipyretic, purgative, antimicrobial, wound healing activity	Calotropagenin, calotoxin	Fumigation, insecticidal	(51,101, 102)
Alangium salviifolium (L.f.) Wangerin,* Cornaceae	Azhinjil	Root	India, China, Phillipines	Emollient, anthelmintic, laxative, diuretic, antidote, purgative	Alangidiol, alangicine	Antifungal	(55,57, 103)
Indigofera aspalathoides Vahl. ex. DC.,* Fabaceae	Sivanar vembu	Root	India, Pakistan, Indonesia, Malaysia, Sri Lanka	Demulcent, sedative, analgesic, antispasmodic, remedy for leprosy, malaria, kidney stones	Afromosin, genistein	Insecticidal, antibacterial	(61,69,79, 104)
Shorea robusta Roth.,* Dipterocarpaceae	Kungiliyam	Resin	India, China, Russia	Astringent, detergent, wound healing effect, remedy for cold, piles, bronchitis and leucorrhoea	Fischinidol, Afzetechin tannins	Insecticidal	(51,105)
Argemone mexicana L.,* Papaveraceae	Kudiyotti poondu	Seeds	Madhya Pradesh, Eastern Ghats, Himalayas, South America, West Africa	Treatment of tumors, warts, skin diseases, inflammation, rheumatism, jaundice, leprosy, microbial infections, malaria	Oxyhydrastinine, Mexicanol, Mexicanic acid	Insecticidal, antibacterial	(55,57, 106, 107)
Costus speciosus (J. Konig) C. Specht., Costaceae	Kottam	Roots and rhizomes	Nagaland, Assam, Sri Lanka, Malaysia	Astringent, aphrodisiac, purgative, anthelmintic, depurative, febrifuge, expectorant, tonic, stimulant	Cycloartenol, diosgenin, lupeol	Fumigation	(108,109)
Boswellia serrata Triana & Planch., Burseraceae	Kuntharikkam	Resin	Assam, Bihar, China	Remedy for bronchitis, asthma, cough, diarrhea, dysentery, fever	β-Sitosterol, α-Thujene	Antifungal, fumigant	(32,57, 110)

Santalum album L., Santalaceae	Santhanum	Wood	Eastern Ghats, China,	Tonic for heart, stomach, liver, fever; treatment of diarrhea, piles, vomiting, eye infections and inflammation	Nuciferol, α-Curcumone	Fumigation	(35,55,57, 111)
Abutilon indicum (Link) Sweet,* Malvaceae	Thuthi	Seed	Tamil Nadu, Africa, Australia	Diuretic, laxative, demulcent, analgesic, antiulcer	Gossypetin, Vanillic acid, β-Sitosterol	Insecticidal	(70,75, 112)
Tinospora cordifolia (Thunb.) Miers.,* Papilionaceae	Seenthil	Leaves	Haryana, Madhya Pradesh, Assam, China, Bangladesh, Vietnam, Malaysia, Sri Lanka	Memory booster, antispasmodic, antidiarrheal, stomachic, tonic, bronchitis, promotes longevity, anti-allergic	Quercetin, monocrotaline	Insecticidal, antibacterial	(57,58,68)
Nicotiana tabacum L.,* Solanaceae	Pugayilai	Leaves	India, China, North America, Europe, Africa	Treatment of rheumatism, pulmonary ailments, conjunctivitis, bronchitis and pneumonia	Solavetivone, Nor-nicotine	Antibacterial	(55,113,114)
Mangifera indica L.,* Anacardiaceae	Maa	Leaves, flower	India, Africa, Middle East	Dentifrice, antiseptic, astringent, diaphoretic, stomachic, laxative, vermifuge	Mangiferin, fisetin	Insecticidal, antimicrobial	(59,68, 115)
Crinum asiaticum L.,* Amaryllidaceae	Vidamoongil	Leaves	Tropical Asia	Analgesic, antimicrobial, antiemetic, anthelmintic, laxative, skin infections, expectorant, wound healing property	Lycorine, isocraugsodine, criasbetaine	Insecticidal	(31,116, 117)
Aquilaria agallocha Roxb.,* Thymeleaceae	Akil	Wood	India, China, Indonesia	Mouth freshner, aphrodisiac, astringent, bitter, cardiotonic, stimulant, carminative, fragrant	Aromatic oil	Antimicrobial	(61,79, 118)
Lawsonia inermis L.,* Lythraceae	Alavanam	Seed	Eastern Ghats, Assam, China	Treatment of headache, hemicranias, lumbago, bronchitis, syphilis, scabies, dysuria, skin diseases	Lawsone, scopoletin, esculetin	Insecticide, antioxidant	(55,63, 119)

Ruta chalepensis L., Rutaceae	Aruvatha	Leaves	Kerala, China, North Africa	Anti-inflammatory, analgesic, antipyretic	Chalepin, graveoline, arborinine	Insecticide, fumigant	(66,120)
Justicia adhatoda L., Acanthaceae	Adathodaai	Leaves	Eastern Ghats, Assam, Himalayas, China, Nepal	Cough, fever, asthma, dysentery	Vasicine, Vasicinone, β-Sitosterol	Fumigation, antioxidant	(55,121)
Madhuca longifolia (J. Konig) J.F. Macbr., Sapotaceae	Illupai	Crushed cake of seed	Madhya Pradesh, Eastern Ghats	Emollient, skin diseases, rheumatism, headache, laxative, piles, hemorrhoids	A-Spinasterol, Betulinic acid	Fumigation	(51,68, 122)
Datura metel L.,* Solanaceae	Oomathai	Leaves	Haryana, Jammu and Kashmir, China, Brazil	Anti-fungal, anti-bacterial, antirheumatic, anti-inflammatory	Daturine, atropine	Antifungal, antimicrobial	(58,116, 123)
Solanum surattense Burm. f.,* Solanaceae	Kandangat hiri	Seed	Himalayas, Pakistan, Malaysia, Southeast Asia	Remedy for inflammatory problems, leprosy, dropsy, cough, hernia, dental caries and swelling	Solasonine Solamargine, esculin	Insecticidal	(61,113, 124)
Saccharum officinarum L.,* Poaceae	Karumbu	Sugar	Assam, Pakistan, New Guinea, Taiwan, China	Whooping cough, canes for broken bones, catarrh	Apigenin, Orientin, Ferulic acid	Insecticidal	(59,63, 125)
Rhus succedanea L.,* Anacardaceae	Karkadaka singi	Gall	Himalayas, Australia, New Zealand	Antidote, cholagogue, febrifuge, treatment of phthisis	Aromatic oil, Tannins	Insecticidal	(96,126)

*Studies regarding the fumigation effect of these herbs were not found on any of the search engines. However, scientific studies suggest the presence of bioactives that may provide santization and air-purifying effects on fumigation. Hence, these herbs provide a rationale for future research.

Table 3: Herbal ingredients used in important Siddha formulations for *Kabasuram*.

Botanical name and family	Siddha name	Part used	Location	Traditional uses	Major Pharmacological action	Siddha Formulation	References
Santalum album L., Santalaceae	Chandanam	Heart wood	Eastern Ghats, China	Tonic for heart, stomach, liver, fever; treatment of diarrhea, piles, vomiting, eye infections and inflammation	Anti-pyretic, treatment of common cold and bronchitis	Nilavembu, Visha Sura Kudineer	(55,57,111)
Terminalia chebula Retz., Combretaceae	*Kadukai*	Fruit	Arunachal Pradesh, Nagaland, China, Europe	Detoxifying agent, purgative, digestant, rejuvenator, wound healing property	Antiviral, antinociceptive	Visha Sura Kudineer	(87,127)
Anisochilus carnosus (L.f.) Wall., Lamiaceae	*Katpooravvalli*	Leaves	India, China, Indonesia	Gastric ulcer and skin diseases	Anti-pyretic, antimicrobial	Visha Sura Kudineer	(51,116,12 8)

Plectranthus vettiveroides (Jacob) N.P. Singh & B.D. Sharma, Lamiaceae	Vilamichai	Root	South India, Sri Lanka	Deodorant, treatment of headache, diarrhea, fever, hyperdipsia, leprosy, ulcer, nausea, giddiness	Analgesic, anti-inflammatory, antimicrobial	Nilavembu, Kaba Sura Kudineer	(66,129,130)
Tragia involucrata L., Euphorbiaceae	*Sirukaannchonri Ver*	Root	Assam, West Bengal, Kerala	Treatment of wounds, scabies, skin infections	Bronchodilator, anti-pyretic, anti-inflammatory	Visha Sura Kudineer	(66,131)
Cyperus rotundus L., Cyperaceae	Koraikilanku	Stem bark	Haryana, Africa, central Europe	Remedy for diarrhea, diabetes, inflammation, malaria, stomach, bowel disorder, fever	Antipyretic, anti-hypertensive	Nilavembu, Sarva Sura Kudineer	(43,132,133)
Piper nigrum L., Piperaceae	Milaku	Seed, Fruit	South India, Vietnam, Brazil	Cough, sinusitis, throat pain, infections, ear ache, gastrointestinal disorders	Antimicrobial, anti-pyretic, anti-inflammatory	Nilavembu, Sarva Sura Kudineer	(42,88)
Hygrophila auriculata Schumach., Acanthaceae	Neermulli ver	Root	South India, Sri Lanka	Treatment of cough, anal fistula, blood disorders, jaundice, anaemia, dropsy, aphrodisiac	Haematopoietic, anti-inflammatory	Visha Sura Kudineer	(39,67,134)
Sida acuta Burm.f.., Malvaceae	Vattathiruppi Ver	Root tuber	Tamil Nadu, Central America	Treatment of fever, skin diseases, diarrhea, dysentry	Antibacterial, antipyretic	Visha Sura Kudineer	(39,135)
Andrographis paniculata (Burm.f.) Nees., Acanthaceae	Nilavembu	Stem, leaves	Eastern Ghats, Sri Lanka, China, United States	Treatment of dyspepsia, influenza, dysentery, malaria, respiratory infections	Immunostimulant, anti-inflammatory	Nilavembu, Sarva Sura, Kaba Sura Kudineer	(8,28,44)
Hedyotis corymbosa (L.) Lam., Rubiaceae	Parpadaakam	Whole plant	India, Sri Lanka, East Asia	Antiviral, treatment of acne, hepatitis, eye diseases, skin ailments, bleeding, promotes diuresis	Antimicrobial, antioxidant, immunostimulant	Nilavembu Kudineer	(55,136,137)
Trichosanthes cucumerina L., Curcubitaceae	Peipudol	Gourd	Eastern Ghats, Sri Lanka, Malaysia	Treating headache, alopecia, fever, abdominal tumors, boils, diarrhea, haematurian skin allergy	Anti-inflammatory, antipyretic	Nilavembu, Sarva Sura Kudineer	(42,44,55, 61,138)
Zingiber officinalis Roscoe, Zingiberaceae	Sukku	Rhizome	Kerala, Andhra Pradesh, tropical Asia	Antiemetic, stomachic, expectorant, aphrodisiac	Antipyretic, anti-inflammatory	Nilavembu, Sarva Sura, Visha Sura, Kaba Sura Kudineer	(28,39,42, 44)

Vetiveria zizanioides (L.) Nash, Poaceae	Vettiver	Root	India, Senegal, Sri Lanka, Brazil	Cooling agent, tonic, blood purifier, treatment of skin disorders, indigestion, loss of appetite	Antioxidant, anti-inflammatory	Nilavembu, VIsha Sura Kudineer	(39,42,129)
Hemidesmus indicus (L.) R.Br., Apocyanaceae	Nannari ver	Root	Eastern Ghats, China	Demulcent, astringent, diaphoretic, diuretic, tonic, antipyretic, blood purifier, leprosy, bronchitis, syphilis, pruritis, urinary diseases	Anti-inflammatory, antipyretic	Visha Sura Kudineer	(39,55)
Justicia adhatoda L., Acanthaceae	Aadathodai	Leaves	Eastern Ghats, Assam, Himalayas, China, Nepal	Cough, fever, asthma, dysentery	Immunostimulant, antimicrobial, antitussive	Sarva Sura, Kaba Sura Kudineer	(55,63,139)
Glycyrrhiza glabra L., Fabaceae	Adimaduram	Root	Kerala, China, Central and South Western Asia	Sweetening and flavoring agent, expectorant, anti-tussive agent,	Anti-inflammatory, immunomodulatory	Sarva Sura, Visha Sura Kudineer	(57,66,140)
Aristolochia bracteolata Lam., Aristolochiaceae	Eechuramooli	Root	Nigeria, Ethiopia, India	Prevent seizures, immune booster, treatment of snake bites, intestinal pain, gall bladder pain, arthritis, gout, rheumatism	Antibacterial, anti-inflammatory	Visha Sura Kudineer Kudineer	(61,66,141)
Anacyclus pyrethrum (L.) Link, Asteraceae	Akkarakaram	Stem bark	Himalayas, Jammu and Kashmir, West Bengal, Spain, North Africa	Aphrodisiac, antidiabetic, antiasthmatic, throat problems, rejuvanant, carminative, diuretic, muscle relaxant	Antipyretic, anti-inflammatory, immunostimulant	Sarva Sura, Kaba Sura Kudineer	(53,93,116)
Vitis vinifera L. Vitaceae	Grapes/Plums	Fruit	Europe, Western Asia	Laxative, purgative, diuretic, aphrodisiac, appetizer, asthmatic, treatment of diarrhea, bleeding.	Antipyretic, anti-inflammatory	Sarva Sura Kudineer	(61,136,142)

Indigofera tinctoria L., Fabaceae	Neeli	Root	India, Pakistan, China	Treatment of epilepsy, nervous disorders, asthma, bronchitis, fever, stomach ache, rabies, skin diseases, wounds, sores, ulcers	Immunoprotective, anti-inflammatory	Visha Sura Kudineer	(39,61,143)
Syzygium aromaticum (L.) Merr. & L.M. Perry, Myrtaceae	*Karampu*	Fruit	Haryana, China, Indonesia	Anxiolytic, expectorant, antimicrobial, decongestant	Antipyretic, antiviral	Visha Sura Kudineer	(39,48)
Phyllanthus niruri L., Phyllanthaceae	Keezhkainelli	Whole plant	Central and south India, China, Nigeria, Guam	Treatment of jaundice, gonorrhea, antidiabetic, antiviral, skin ulcers, sores, antiallergic	Antiviral, antipyretic, analgesic	Sarva Sura Kudineer	(6,57)
Costus speciosus (J. Konig) C. Specht, Costaceae	Koddam	Root	Nagaland, Assam, Sri Lanka, Malaysia	Astringent, aphrodisiac, purgative, anthelmintic, depurative, febrifuge, expectorant, tonic, stimulant	Antipyretic, anti-inflammatory	Sarva Sura, Kaba Sura Kudineer	(63,93,109)
Elettaria cardamomum (L.) Maton, Zingiberaceae	Elam	Fruit	India, Nepal, Sri Lanka, Mexico, Tanzania	Culinary uses, remedy for asthma, gum infections, kidney disorders, cataracts, nausea, diarrhoea	Antibacterial, anti-inflammatory	Visha Sura Kudineer	(39,59,96)
Azadirachta indica A. Juss., Meliaceae	Vembu	Stem bark	India, China, Malaysia, Caribbean, South East Asia	Antibacterial, natural antiseptic, antipyretic	Antibacterial, anti-inflammatory, antiviral	Visha Sura Kudineer	(51,55,68)
Smilax chinensis L., Smilacaceae	Parankilanku	Stem bark	India, China, Taiwan, Japan	Used as energy tonic, remedy for impotency, seminal disorders, arthritis, syphilis, schizophrenia, epilepsy	Antipyretic	Sarva Sura Kudineer	(55,116,144)
Mollugo cerviana (L.) Ser., Molluginaceae	Parpadaakam	Aerial part	Rajasthan, south India	Fever, stomach ache, jaundice, gout, rheumatism	Antioxidant, antipyretic, spasmolytic, hypolipidemic	Sarva Sura Kudineer	(42,44,145)

Tinospora cordifolia (Thunb.) Miers, Papilionaceae	Seenthil kodi	Leaves	Haryana, Madhya Pradesh, Assam, China, Bangladesh, Vietnam, Malaysia, Sri Lanka	Memory booster, antispasmodic, antidiarrheal, stomachic, tonic, bronchitis, promotes longevity, anti-allergic	Antimicrobial, antioxidant, anti-inflammatory	Sarva Sura, Kaba Sura Kudineer	(57,68,132)
Alpinia galanga (L.) Willd., Zingiberaceae	Sitrarathai	Rhizome	West Bengal, Assam, Cambodia, Thailand, Japan	Cold, sore throat, anti-emetic, analgesic, antioxidant	Anti-inflammatory	Sarva Sura Kudineer	(53,54)
Abies webbiana Lindl., Pinaceae	Talisapathiri	Leaves	Himalayas, Northeast India	Carminative, expectorant, stomachic, tonic, as a remedy for respiratory problems, cold, tuberculosis, indigestion	Anti-tussive, anti-inflammatory	Sarva Sura Kudineer	(87,93,146)
Piper longum L., Piperaceae	Thipally	Root	India, Pakistan, China, Europe	Relieve muscular pains, anti-inflammatory, stimulant, stomachic, antidiabetic	Anti-inflammatory, analgesic	Sarva Sura, Kaba Sura Kudineer	(61,66,84)
Evolvulus alsinoides (Linn.) Linn., Convolvulaceae	Vishnukiraanthy	Whole plant	Eastern Ghats, Africa, Philippines	Cure fever, cold, venereal diseases, adenitis, depression, dementia	Antipyretic, anti-inflammatory, antidiarrheal	Sarva Sura Kudineer	(55,79,131,147)
Clerodendrum serratum (L.) Moon., Verbenaceae	*Siruthekku*	Root	Assam, Himalayas, Sri Lanka, South Africa, Australia	Remedy for cough, asthma, malaria, fever, urinary tract infections, itches, ulcerated wounds, dysmenorrheal, epilepsy	Anti-allergic, antipyretic, anti-inflammatory	Visha Sura Kudineer	(59,148,149)

References

1. World Health Organization (WHO), 2020. Coronavirus Disease (COVID-19) Situation Report 209. World Health Organization.
2. Čivljak R, Markotić A, Kuzman I. The third coronavirus epidemic in the third millennium: What's next? Croat Med J 2020;61:1–4. https://doi.org/10.3325/cmj.2020.61.1.
3. Vellingiri B, Jayaramayya K, Iyer M, Narayanasamy A, Govindasamy V, Giridharan B, et al. Science of the Total Environment COVID-19 : A promising cure for the global panic. Sci Total Environ 2020;725:138277. https://doi.org/10.1016/j.scitotenv.2020.138277.
4. Li W, Moore MJ, Vasllieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature 2003;426:450–4. https://doi.org/10.1038/nature02145.
5. Ram A, Arul Joseph D, Balachandar S, Pal Singh V. Medicinal plants from Siddha system of medicine useful for treating respiratory diseases. Int J Pharm Anal 2009.
6. Lee NYS, Khoo WKS, Adnan MA, Mahalingam TP, Fernandez AR, Jeevaratnam K. The pharmacological potential of Phyllanthus niruri. J Pharm Pharmacol 2016;68:953–69. https://doi.org/10.1111/jphp.12565.
7. Jain J, Pai S, Sunil S. Standardization of in vitro assays to evaluate the activity of polyherbal siddha

formulations against Chikungunya virus infection. VirusDisease 2018;29:32–9. https://doi.org/10.1007/s13337-018-0421-0.

8. Jain J, Kumar A, Narayanan V, Ramaswamy RS, Sathiyarajeswaran P, Shree Devi MS, et al. Antiviral activity of ethanolic extract of Nilavembu Kudineer against dengue and chikungunya virus through in vitro evaluation. J Ayurveda Integr Med 2019:1–7. https://doi.org/10.1016/j.jaim.2018.05.006.
9. Sathiyarajeswaran P, Shree Devi MS, Sunil Kumar Koppala Narayana, Muthu Tamizh Manoharn, Satheesh Durairaj, Brindha Sundaramoorty, Dhanaraj K PR. Quality Standards for Urai Mathirai-A Siddha Immunomodulator Formulation for Children Quality Standards for Urai Mathirai - A Siddha Immunomodulator Formulation for Children. J Phytopharm 2018;7 (1):40–4.
10. Li F. Structure, Function, and Evolution of Coronavirus Spike Proteins. Annu Rev Virol 2016. https://doi.org/10.1146/annurev-virology-110615-042301.
11. Tang X, Wu C, Li X, Song Y, Yao X, Wu X, et al. On the origin and continuing evolution of SARS-CoV-2. Natl Sci Rev 2020;7:1012–23. https://doi.org/10.1093/nsr/nwaa036.
12. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–33. https://doi.org/10.1056/NEJMoa2001017.
13. Van Dorp L, Acman M, Richard D, Shaw LP, Ford CE, Ormond L, et al. Emergence of genomic diversity and recurrent mutations in SARS-CoV-2. Infect Genet Evol 2020;83:104351. https://doi.org/10.1016/j.meegid.2020.104351.
14. Bosch BJ, van der Zee R, de Haan CAM, Rottier PJM. The Coronavirus Spike Protein Is a Class I Virus Fusion Protein: Structural and Functional Characterization of the Fusion Core Complex. J Virol 2003;77:8801–11. https://doi.org/10.1128/jvi.77.16.8801-8811.2003.
15. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Cell 2020. https://doi.org/10.1016/j.cell.2020.02.058.
16. Chen Y, Guo Y, Pan Y, Zhao ZJ. Structure analysis of the receptor binding of 2019-nCoV. Biochem Biophys Res Commun 2020;525:135–40. https://doi.org/10.1016/j.bbrc.2020.02.071.
17. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med 2020;14:185–92. https://doi.org/10.1007/s11684-020-0754-0.
18. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. Nat Med 2020;26:450–2. https://doi.org/10.1038/s41591-020-0820-9.
19. Lee PI, Hu YL, Chen PY, Huang YC, Hsueh PR. Are children less susceptible to COVID-19? J Microbiol Immunol Infect 2020. https://doi.org/10.1016/j.jmii.2020.02.011.
20. Jia HP, Look DC, Shi L, Hickey M, Pewe L, Netland J, et al. ACE2 Receptor Expression and Severe Acute Respiratory Syndrome Coronavirus Infection Depend on Differentiation of Human Airway Epithelia. J Virol 2005;79:14614–21. https://doi.org/10.1128/jvi.79.23.14614-14621.2005.
21. Wong H, Freishtat R, Monaco M, Odoms K, Shanley TP. Leukocyte subset-derived genomewide expression profiles in pediatric septic shock. Pediatr Crit Care Med 2010;11:349–55. https://doi.org/10.1097/PCC.0b013e3181c519b4.
22. Nickbakhsh S, Mair C, Matthews L, Reeve R, Johnson PCD, Thorburn F, et al. Virus-virus interactions impact the population dynamics of influenza and the common cold. Proc Natl Acad Sci U S A 2019;116:27142–50. https://doi.org/10.1073/pnas.1911083116.
23. Subbarayappa B V. Siddha medicine: An overview. Lancet 1997;350:1841–4. https://doi.org/10.1016/S0140-6736(97)04223-2.
24. Madhavan, V.R. and Subramanyam, S.V. Tirumandiram by Siddha medicine. Ist Editio. International institute of Tamil studies, Madras; 1983.
25. Lester RC, Daniel EV. Fluid Signs: Being a Person the Tamil Way. J Am Orient Soc 1987;107:353. https://doi.org/10.2307/602863.
26. Swamy K and P. History of Siddha medicine. Governament of Tamil Nadu Publications, Madras; 1979.
27. World Health Organisation. Dengue and severe dengue. WHO Fact Sheet 2014;117:1–4. https://doi.org/10.1111/1469-0691.12442.
28. Kiran G, Karthik L, Shree Devi MS, Sathiyarajeswaran P, Kanakavalli K, Kumar KM, et al. In Silico computational screening of Kabasura Kudineer - Official Siddha Formulation and JACOM against SARS-CoV-2 spike protein. J Ayurveda Integr Med 2020. https://doi.org/10.1016/j.jaim.2020.05.009.
29. Rao M, Rao KD, Kumar AS, Chatterjee M, Sundararaman T. Human resources for health in India. Lancet 2011. https://doi.org/10.1016/S0140-6736(10)61888-0.
30. Ajmal M, Raseeha R, Uma AP. Siddha Perspective on Healthy Living and Management of Lifestyle Diseases. Int J Curr Res Med Sci 2017;3:138–43. https://doi.org/10.22192/ijcrms.2017.03.07.020.
31. Lalitha S, Anavarathan V, Mahalakshmi V, Kumar NJM kumar. Pugai (fumigation) as a Pura maruthuvam (external therapy) in the Siddha system of medicine. Int J Ayurveda Pharma Res 2018;6:76–80.
32. Bhatwalkar SB, Shukla P, Srivastava RK, Mondal R, Anupam R. Validation of environmental disinfection efficiency of traditional Ayurvedic fumigation practices. J Ayurveda Integr Med

2019;10:203–6. https://doi.org/10.1016/j.jaim.2019.05.002.
33. Swathy Anand PJ, Athira S, Chandramohan S, Ranjith K, Raj VV, Manjula VD. Comparison of efficacy of herbal disinfectants with chlorhexidine mouthwash on decontamination of toothbrushes: An experimental trial. J Int Soc Prev Community Dent 2016;6:22–7. https://doi.org/10.4103/2231-0762.175406.
34. Kim S Il, Na YE, Yi JH, Kim BS, Ahn YJ. Contact and fumigant toxicity of oriental medicinal plant extracts against Dermanyssus gallinae (Acari: Dermanyssidae). Vet Parasitol 2007;145:377–82. https://doi.org/10.1016/j.vetpar.2006.12.021.
35. Kim J, Jang M, Shin E, Kim J, Lee SH, Park CG. Fumigant and contact toxicity of 22 wooden essential oils and their major components against Drosophila suzukii (Diptera: Drosophilidae). Pestic Biochem Physiol 2016;133:35–43. https://doi.org/10.1016/j.pestbp.2016.03.007.
36. Balasubramanian S, Roselin P, Singh KK, Zachariah J, Saxena SN. Postharvest processing and benefits of black pepper, coriander, cinnamon, fenugreek, and turmeric spices. Crit Rev Food Sci Nutr 2016;56:1585–607. https://doi.org/10.1080/10408398.2012.759901.
37. Widyaningsih TD, Mahar J, Wijayanti N, Rahmani, Najmuddin M. Immunomodulatory effect of instant tea powder from black cincau (Mesona palustris BL) in the treatment of Salmonella typhimurium-induced infection in BALB mice. Food Public Heal 2013;3:142–6. https://doi.org/10.5923/j.fph.20130303.05.
38. AYUSH. Guidelines for Siddha Practitioners for COVID 19 2020. https://doi.org/https://www.ayush.gov.in/docs/siddha-guidelines.pdf.
39. Shailaja R, Sugunthan S, Pitchaiah Kumar M. A review on polyherbal formulation- Vishasura Kudineer chooranam-A classical anti-viral drug used in Siddha system of medicine. Eur J Pharm Med Res 2017;4:184–92.
40. Vinitha G, Saibudeen K. Literature Review on Kaya Karpa Medicines From Various Siddha Literatures. Int J Trans Res Ind Med 2019;2019:13–21.
41. Trivedi A, Fatima N, Husain I, Misra A. An update on the therapeutic potential of Neem and its active constituents: A panacea for all diseases. Era's J Med Res 2019;6:1–6. https://doi.org/10.24041/ejmr2019.116.
42. Krishna S, Thileepan T. Pharmacological activity of Nilavembu decoction used in Suram (Fever). J Res Tradit Med 2019:1. https://doi.org/10.5455/jrtm.2018/301708.
43. Thillaivanan S, Parthiban P, Kanakavalli K, Sathiyarajeshwaran P. A Review on " Kapa Sura Kudineer " - A Siddha Formulary Prediction for Swine Flu. Int J Pharm Sci Drug Res 2015;7:376–83.
44. Nisha J, Jeeva Gladya R. A review on Siddha polyherbal formulation Sarvasura kudineer for the management of Pyrexia (fever). World J Pharm Res 2017;6:1100–16. https://doi.org/10.20959/wjpr201714-10043.
45. Pitha Suram (Dengue Fever) n.d. https://www.nhp.gov.in/pitha-suram-dengue-fever-_mtl (accessed July 16, 2020).
46. Lalitha N. Protecting traditional knowledge in Siddha system of medicine. J Intellect Prop Rights 2013;18:272–82.
47. Ram A, Arul Joseph D, Balachandar S, Pal Singh V. Medicinal plants from Siddha system of medicine useful for treating respiratory diseases. Int J Pharm Anal 2009;1:975–3079.
48. Makhaik M, Naik SN, Tewary DK. Evaluation of anti-mosquito properties of essential oils. J Sci Ind Res (India) 2005;64:129–33.
49. Chaudhary AK, Ahmad S, Mazumder A. Cedrus deodara (Roxb.) Loud.: A review on its ethnobotany, phytochemical and pharmacological profile. Pharmacogn J 2011. https://doi.org/10.5530/pj.2011.23.2.
50. Sheng-Ji P. Ethnobotanical approaches of traditional medicine studies: Some experiences from Asia. Pharm Biol 2001. https://doi.org/10.1076/phbi.39.7.74.5869.
51. Hong L, Guo Z, Huang K, Wei S, Liu B, Meng S, et al. Ethnobotanical study on medicinal plants used by Maonan people in China. J Ethnobiol Ethnomed 2015;11. https://doi.org/10.1186/s13002-015-0019-1.
52. Sheng-Ji P. Ethnobotanical approaches of traditional medicine studies: Some experiences from Asia. Pharm Biol 2001. https://doi.org/10.1076/phbi.39.7.74.5869.
53. Bendjeddou D, Lalaoui K, Satta D. Immunostimulating activity of the hot water-soluble polysaccharide extracts of Anacyclus pyrethrum, Alpinia galanga and Citrullus colocynthis. J Ethnopharmacol 2003;88:155–60. https://doi.org/10.1016/S0378-8741(03)00226-5.
54. Chaweepack T, Chaweepack S, Muenthaisong B, Ruangpan L, Nagata K, Kamei K. Effect of galangal (Alpinia galanga Linn.) extract on the expression of immune-related genes and Vibrio harveyi resistance in Pacific white shrimp (Litopenaeus vannamei). Aquac Int 2014;23:385–99. https://doi.org/10.1007/s10499-014-9822-2.
55. Reddy AM, Babu MVS, Rao RR. Ethnobotanical study of traditional herbal plants used by local people of Seshachalam Biosphere Reserve in Eastern Ghats, India. Herba Pol 2019;65:40–54. https://doi.org/10.2478/hepo-2019-0006.
56. Rasool M, Varalakshmi P. Immunomodulatory role of Withania somnifera root powder on experimental induced inflammation: An in vivo and in vitro study. Vascul Pharmacol 2006;44:406–10. https://doi.org/10.1016/j.vph.2006.01.015.
57. Jain M, Shrivastava PN, Samar R. Survey of Ethnobotanical Medicinal Plants Used by the People of District Guna, Madhya Pradesh, India. Int J Life-Sciences Sci Res 2018;4:1880–8. https://doi.org/10.21276/ijlssr.2018.4.4.5.

58. Singh N, Tailang M, Mehta SC. a Review on Herbal Plants As Immunomodulators | International Journal of Pharmaceutical Sciences and Research. Int J Pharm Sci Res 2016;7:3602–10. https://doi.org/10.13040/IJPSR.0975-8232.7(9).3602-10.
59. Bhattacharyya R, Medhi KK, Borthakur SK, Borkataki S. An ethnobotanical study of medicinal plants used against jaundice by tea tribes of Morigaon District, Assam (India). J Nat Remedies 2020;20:16–28. https://doi.org/10.18311/jnr/2020/23879.
60. Kaleeswaran B, Ilavenil S, Ravikumar S. Dietary supplementation with Cynodon dactylon (L.) enhances innate immunity and disease resistance of Indian major carp, Catla catla (Ham.). Fish Shellfish Immunol 2011;31:953–62. https://doi.org/10.1016/j.fsi.2011.08.013.
61. Id NJ, Kurniawan E, Eka C, Himayani S. An ethnobotanical study of medicinal plants used by the Tengger tribe in Ngadisari village, Indonesia 2020:1–16. https://doi.org/10.1371/journal.pone.0235886.
62. Yue GGL, Chan BCL, Hon PM, Kennelly EJ, Yeung SK, Cassileth BR, et al. Immunostimulatory activities of polysaccharide extract isolated from Curcuma longa. Int J Biol Macromol 2010;47:342–7. https://doi.org/10.1016/j.ijbiomac.2010.05.019.
63. Bhattacharyya R, Medhi KK, Borthakur SK, Borkataki S. An ethnobotanical study of medicinal plants used against jaundice by tea tribes of Morigaon District, Assam (India). J Nat Remedies 2020;20:16–28. https://doi.org/10.18311/jnr/2020/23879.
64. Checker R, Sharma D, Sandur SK, Khanam S, Poduval TB. Anti-inflammatory effects of plumbagin are mediated by inhibition of NF-kappaB activation in lymphocytes. Int Immunopharmacol 2009;9:949–58. https://doi.org/10.1016/j.intimp.2009.03.022.
65. Bishayi B, Adhikary R, Majhi A, Mahanti S. Immunomodulatory and anti-oxidant properties of methanolic extract of Adhatoda vasica Nees leaf after particulate antigen stimulation in mice. J Pharm Res 2014;8:1520–37.
66. Morvin Yabesh JE, Prabhu S, Vijayakumar S. An ethnobotanical study of medicinal plants used by traditional healers in silent valley of Kerala, India. J Ethnopharmacol 2014;154:774–89. https://doi.org/10.1016/j.jep.2014.05.004.
67. Vijayakumar S, Harikrishnan JP, Prabhu S, Morvin Yabesh JE, Manogar P. Quantitative Ethnobotanical Survey of Traditional Siddha Medical Practitioners from Thiruvarur District with Hepatoprotective Potentials through In Silico Methods. Achiev Life Sci 2016;10:11–26. https://doi.org/10.1016/j.als.2016.03.001.
68. Ilango K, Kammalla A kumar, Dubey GP, Agrawal A. Current status of Indian Medicinal Plants with Immunomodulatory potential - A Review. Vedic Res Int Phytomedicine 2013;1:73. https://doi.org/10.14259/pm.v1i2.39.
69. Bhagavan NB, Arunachalam S, Dhasarathan P, Kannan ND. Evaluation of anti inflammatory activity of Indigofera aspalathoides Vahl in Swiss albino mice. J Pharm Res 2013;6:350–4. https://doi.org/10.1016/j.jopr.2013.02.018.
70. Maria Francis Jeffrey Bose N, Aron S, Mehalingam P. An ethnobotanical study of medicinal plants used by the Paliyars aboriginal community in Virudhunagar district, Tamil Nadu, India. Indian J Tradit Knowl 2014;13:613–8.
71. Yamate Y, Hiramoto K, Yokoyama S, Ooi K. Immunological changes in the intestines and skin after senna administration. Pharm Biol 2015;53:913–20. https://doi.org/10.3109/13880209.2014.948636.
72. Halder S, Bharal N, Mediratta PK, Kaur I, Sharma KK. Anti-inflammatory, immunomodulatory and antinociceptive activity of terminalia arjuna roxb bark powder in mice and rats. Indian J Exp Biol 2009;47:577–83.
73. Verma SK, Jain V, Katewa SS. Blood pressure lowering, fibrinolysis enhancing and antioxidant activities of cardamom (Elettaria cardamomum). Indian J Biochem Biophys 2009;46:503–6.
74. Vasuki K, Murugananthan G, Banupriya C, Ramya R, Mohana Priya C, Shenjudar D. Investigation of immunomodulatory potential of whole plant of Boerhavia erecta Linn. Pharmacogn J 2018;10:241–4. https://doi.org/10.5530/pj.2018.2.42.
75. Esakkimuthu S, Sylvester Darvin S, Mutheeswaran S, Gabriel Paulraj M, Pandikumar P, Ignacimuthu S, et al. A study on food-medicine continuum among the non-institutionally trained siddha practitioners of Tiruvallur district, Tamil Nadu, India. J Ethnobiol Ethnomed 2018;14. https://doi.org/10.1186/s13002-018-0240-9.
76. Naik SR, Hule A. Evaluation of immunomodulatory activity of an extract of andrographolides from Andographis paniculata. Planta Med 2009;75:785–91. https://doi.org/10.1055/s-0029-1185398.
77. Latorre AO, Furlan MS, Sakai M, Fukumasu H, Hueza IMH, Haraguchi M, et al. Immunomodulatory effects of pteridium aquilinum on natural killer cell activity and select aspects of the cellular immune response of mice. J Immunotoxicol 2009;6:104–14. https://doi.org/10.1080/15476910902972465.
78. Aye MM, Aung HT, Sein MM, Armijos C. A review on the phytochemistry, medicinal properties and pharmacological activities of 15 selected myanmar medicinal plants. Molecules 2019;24. https://doi.org/10.3390/molecules24020293.
79. Ezuruike UF, Prieto JM. The use of plants in the traditional management of diabetes in Nigeria: Pharmacological and toxicological considerations. J Ethnopharmacol 2014. https://doi.org/10.1016/j.jep.2014.05.055.
80. Tripathi AK, Prajapati V, Verma N, Bahl JR, Bansal RP, Khanuja SPS, et al. Bioactivities of the Leaf Essential Oil of <I>Curcuma Longa</I> (Var.

Ch-66) On Three Species of Stored-Product Beetles (Coleoptera). J Econ Entomol 2009;95:183–9. https://doi.org/10.1603/0022-0493-95.1.183.

81. Michaelraj S, Sharma RK. Fumigant toxicity of neem formulations against Sitophilus oryzae and Rhyzopertha dominica. J Agric Technol 2006;2:1–16.
82. Seo SM, Kim J, Lee SG, Shin CH, Shin SC, Park IK. Fumigant antitermitic activity of plant essential oils and components from ajowan (Trachyspermum ammi), allspice (Pimenta dioica), caraway (Carům carvi), dill (Anethum graveoiens), geranium (Pelargonium graveoiens), and litsea (Litsea cubeba) oils against. J Agric Food Chem 2009;57:6596–602. https://doi.org/10.1021/jf9015416.
83. Attique Babri R, Khokhar I, Mahmood Z, Mahmud S. Chemical Composition and Insecticidal Activity of the Essential Oil of Anethum Graveolens L. SciInt(Lahore) 2012;24:453–5.
84. Yang YC, Lee SG, Lee HK, Kim MK, Lee SH, Lee HS. A piperidine amide extracted from Piper longum L. Fruit shows activity against Aedes aegypti mosquito larvae. J Agric Food Chem 2002;50:3765–7. https://doi.org/10.1021/jf011708f.
85. Mahmoodi L, Valizadegan O. Fumigant toxicity of Carum copticum L. (Apiaceae) essential oil on Trialeurodes vaporariorum (Westwood) (Hemiptera: Aleyrodidae) adults under greenhouse conditions. Arch Phytopathol Plant Prot 2014;47:1291–302. https://doi.org/10.1080/03235408.2013.840101.
86. Mutheeswaran S, Pandikumar P, Chellappandian M, Ignacimuthu S. Documentation and quantitative analysis of the local knowledge on medicinal plants among traditional Siddha healers in Virudhunagar district of Tamil Nadu, India. J Ethnopharmacol 2011;137:523–33. https://doi.org/10.1016/j.jep.2011.06.003.
87. Murtem G, Chaudhry P. An ethnobotanical study of medicinal plants used by the tribes in Upper Subansiri district of Arunachal Pradesh, India. Am J Ethnomedicine 2016;3:35–49.
88. Vinturelle R, Mattos C, Meloni J, Nogueira J, Nunes MJ, Vaz IS, et al. In vitro evaluation of essential oils derived from piper nigrum (Piperaceae) and Citrus limonum (Rutaceae) against the tick rhipicephalus (Boophilus) microplus (Acari: Ixodidae). Biochem Res Int 2017;2017. https://doi.org/10.1155/2017/5342947.
89. Mbaebie B, Omosun G, Uti A, Oyedemi S. Chemical Composition of Sesamum indicum L . (Sesame) Grown in Southeastern Nigeria and the Physicochemical Properties of the Seed Oil 2010:1–5.
90. Miraj S, Kiani S. Bioactivity of Sesamum indicum: A review study. Der Pharm Lett 2016;8:328–34.
91. Singh N, Kapur ML, Mahajan RK. Effect of fumigation on germination and vigour in chickpea and green gram during prolonged storage. Seed Sci Technol 2003;31:161–8. https://doi.org/10.15258/sst.2003.31.1.16.
92. Hou D, Yousaf L, Xue Y, Hu J, Wu J, Hu X, et al. Mung bean (Vigna radiata L.): Bioactive polyphenols, polysaccharides, peptides, and health benefits. Nutrients 2019;11:1–28. https://doi.org/10.3390/nu11061238.
93. Kichu M, Malewska T, Akter K, Imchen I, Harrington D, Kohen J, et al. An ethnobotanical study of medicinal plants of Chungtia village, Nagaland, India. J Ethnopharmacol 2015;166:5–17. https://doi.org/10.1016/j.jep.2015.02.053.
94. Furlan L, Bonetto C, Finotto A, Lazzeri L, Malaguti L, Patalano G, et al. The efficacy of biofumigant meals and plants to control wireworm populations. Ind Crops Prod 2010;31:245–54. https://doi.org/10.1016/j.indcrop.2009.10.012.
95. Kumar V, Thakur AK, Barothia ND, Chatterjee SS. Therapeutic potentials of Brassica juncea: an overview. Tang (Humanitas Med 2011;1:2.1-2.16. https://doi.org/10.5667/tang.2011.0005.
96. Radha, Puri S, Kumar S. An Ethnobotanical Study of Wild Medicinal Plants Used By Migratory Shepherds – a Tribal Community of Western Himalayas. Asian J Pharm Clin Res 2019;12:137–44. https://doi.org/10.22159/ajpcr.2019.v12i4.31130.
97. Singh A, Singh PK. An ethnobotanical study of medicinal plants in Chandauli District of Uttar Pradesh, India. J Ethnopharmacol 2009;121:324–9. https://doi.org/10.1016/j.jep.2008.10.018.
98. Oskoueian E, Abdullah N, Ahmad S, Saad WZ, Omar AR, Ho YW. Bioactive compounds and biological activities of Jatropha curcas L. kernel meal extract. Int J Mol Sci 2011;12:5955–70. https://doi.org/10.3390/ijms12095955.
99. Pattanayak P, Behera P, Das D, Panda S. Ocimum sanctum Linn. A reservoir plant for therapeutic applications: An overview. Pharmacogn Rev 2010;4:95–105. https://doi.org/10.4103/0973-7847.65323.
100. Prabsattroo T, Wattanathorn J, Iamsaard S, Somsapt P, Sritragool O, Thukhummee W, et al. Moringa oleifera extract enhances sexual performance in stressed rats. J Zhejiang Univ Sci B 2015;16:179–90. https://doi.org/10.1631/jzus.B1400197.
101. P R, T P, S M. Ethnomedicinal plants and novel formulations used by Hooralis tribe in Sathyamangalam forests, Western Ghats of Tamil Nadu, India. J Med Plants Res 2013;7:2083–97. https://doi.org/10.5897/jmpr2013.5074.
102. Karim MR, Alam MA, Habib MR, Nikkon F, Khalequzzaman M. Insecticidal Activity of Root Bark of Calotropis gigantea L. Against Tribolium castaneum (Herbst). World J Zool 2009;4:90–5.
103. Wuthi-udomlert M, Prathanturarug S, Wongkrajang Y. Antifungal activity and local toxicity study of Alangium salviifolium subsp hexapetalum. Southeast Asian J Trop Med Public Health 2002;33:125–54.

104. Tamilselvi N, Krishnamoorthy P, Dhamotharan R, Arumugam P, Sagadevan E. Analysis of total phenols,total tannins and screening of phytocomponents in Indigofera aspalathoides (Shivanar Vembu) Vahl EX DC. J Chem Pharm Res 2012;4:3259–62.
105. Wani TA, Chandrashekara HH, Kumar D, Prasad R, Gopal A, Sardar KK, et al. Wound healing activity of ethanolic extract of Shorea robusta Gaertn. f. resin. Indian J Exp Biol 2012;50:277–81.
106. Singh S, Pandey VB, Singh TD. Alkaloids and flavonoids of Argemone mexicana. Nat Prod Res 2012;26(1):16–21. https://doi.org/10.1080/14786419.2010.529809.
107. Simoes-Pires C, Hostettmann K, Haouala A, Cuendet M, Falquet J, Graz B, et al. Reverse pharmacology for developing an anti-malarial phytomedicine. The example of Argemone mexicana. Int J Parasitol Drugs Drug Resist 2014. https://doi.org/10.1016/j.ijpddr.2014.07.001.
108. Shen S, Qian J, Ren J. Ethnoveterinary plant remedies used by Nu people in NW Yunnan of China. J Ethnobiol Ethnomed 2010;6. https://doi.org/10.1186/1746-4269-6-24.
109. El-Far AH, Shaheen HM, Alsenosy AW, El-Sayed Y, Al Jaouni SK, Mousa SA. Costus speciosus: Traditional uses, phytochemistry, and therapeutic potentials. Pharmacogn Rev 2018. https://doi.org/10.4103/phrev.phrev_29_17.
110. Venkatesh HN, Sudharshana TN, Abhishek RU, Thippeswamy S, Manjunath K, Mohana DC. Antifungal and antimycotoxigenic properties of chemically characterised essential oil of Boswellia serrata Roxb. ex Colebr. Int J Food Prop 2017;20:1856–68. https://doi.org/10.1080/10942912.2017.1354882.
111. Barrett DR, Fox JED. Santalum album: Kernel composition, morphological and nutrient characteristics of pre-parasitic seedlings under various nutrient regimes. Ann Bot 1997;79:59–66. https://doi.org/10.1006/anbo.1996.0303.
112. Pandikumar P, Chellappandian M, Mutheeswaran S, Ignacimuthu S. Consensus of local knowledge on medicinal plants among traditional healers in Mayiladumparai block of Theni District, Tamil Nadu, India. J Ethnopharmacol 2011;134:354–62. https://doi.org/10.1016/j.jep.2010.12.027.
113. Khan M, Ahmad L, Rashid W. Ethnobotanical Documentation of Traditional Knowledge about Medicinal Plants used by Indigenous People in Talash Valley of Dir Lower, Northern Pakistan. J Intercult Ethnopharmacol 2018;7:1. https://doi.org/10.5455/jice.20171011075112.
114. Kumar SP, Darshit P, Ankita P, Palak D, Ram P, Pradip P, et al. Biogenic synthesis of silver nanoparticles using Nicotiana tobaccum leaf extract and study of their antibacterial effect. African J Biotechnol 2011;10:8122–30. https://doi.org/10.5897/ajb11.394.
115. Maldonado-Celis ME, Yahia EM, Bedoya R, Landázuri P, Loango N, Aguillón J, et al. Chemical Composition of Mango (Mangifera indica L.) Fruit: Nutritional and Phytochemical Compounds. Front Plant Sci 2019;10. https://doi.org/10.3389/fpls.2019.01073.
116. Kumar M, Paul Y, Anand VK. An Ethnobotanical Study of Medicinal Plants used by the Locals in Kishtwar, Jammu and Kashmir, India. J Ethnobiol Ethnomed 2009;13:1240–56.
117. Sun Q, Shen YH, Tian JM, Tang J, Su J, Liu RH, et al. Chemical constituents of Crinum asiaticum L. var. sinicum Baker and their cytotoxic activities. Chem Biodivers 2009;6:1751–7. https://doi.org/10.1002/cbdv.200800273.
118. Dash M, Patra JK, Panda PP. Phytochemical and antimicrobial screening of extracts of Aquilaria agallocha Roxb. African J Biotechnol 2008;7:3531–4. https://doi.org/10.5897/AJB08.623.
119. Hsouna A Ben, Trigui M, Culioli G, Blache Y, Jaoua S. Antioxidant constituents from Lawsonia inermis leaves: Isolation, structure elucidation and antioxidative capacity. Food Chem 2011;125:193–200. https://doi.org/10.1016/j.foodchem.2010.08.060.
120. Jeon JH, Kim MG, Lee HS. Insecticidal activities of Ruta chalepensis leavesisolated constituent and structure-relationships of its analogues against Sitophilus oryzae. J Korean Soc Appl Biol Chem 2013;56:591–6. https://doi.org/10.1007/s13765-013-3215-5.
121. Marathakam A, Kannappan N, Jasemine S, Santhiagu A, Sreejith M, Ajith MP. Studies on phytochemical and In-Vitro antioxidant potential of Justicia beddomei (Clarke) Bennett. Free Radicals Antioxidants 2012;2:26–31. https://doi.org/10.5530/ax.2012.4.5.
122. Yadav P. Review MADHUCA LONIGFOLIA (Sapotaceae): A review of its traditional uses, Phytochemistry and pharmacology. Int J Biomed Res 2012;3. https://doi.org/10.7439/ijbr.v3i7.292.
123. Asma R, Mejda DR, Afef L, Faten O, Imen R, Rabiaa H. Antifungal activity of Datura metel L. organic and aqueous extracts on some pathogenic and antagonistic fungi. African J Microbiol Res 2013;7:1605–12. https://doi.org/10.5897/ajmr12.2376.
124. Tekuri SK, Pasupuleti SK, Konidala KK, Amuru SR, Bassaiahgari P, Pabbaraju N. Phytochemical and pharmacological activities of Solanum surattense Burm. f.-A review. J Appl Pharm Sci 2019;9:126–36. https://doi.org/10.7324/JAPS.2019.90318.
125. Singh A, Lal UR, Mukhtar HM, Singh PS, Shah G, Dhawan RK. Phytochemical profile of sugarcane and its potential health aspects. Pharmacogn Rev 2015;9:45–54. https://doi.org/10.4103/0973-7847.156340.
126. Wu PL, Lin S Bin, Huang CP, Chiou RYY. Antioxidative and cytotoxic compounds extracted from the sap of Rhus succedanea. J Nat Prod 2002;65:1719–21. https://doi.org/10.1021/np0201467.

127. Rathinamoorthy R, Thilagavathi G. Terminalia chebula - Review on pharmacological and biochemical studies. Int J PharmTech Res 2014.
128. Muthuraman MS, Santharam L, Ariraman S, Pemaiah B. Studies on anticancer and antimicrobial efficacy of Anisochilus carnosus wallich - extract. Int J Pharm Pharm Sci 2012;4:132–5.
129. Chou ST, Lai CP, Lin CC, Shih Y. Study of the chemical composition, antioxidant activity and anti-inflammatory activity of essential oil from Vetiveria zizanioides. Food Chem 2012;134:262–8. https://doi.org/10.1016/j.foodchem.2012.02.131.
130. Hisham A, Padmaja V, Sivakumar N, Al-Saidi S, Al-Kindy S, Rameshkumar KB. Composition and antimicrobial activity of essential oil of Plectranthus vettiveroides (Jacob) Singh & Sharma. Curr Top Phytochem 2012;11:59–65.
131. Gobalakrishnan R, Kulandaivelu M, Bhuvaneswari R, Kandavel D, Kannan L. Screening of wild plant species for antibacterial activity and phytochemical analysis of Tragia involucrata L. J Pharm Anal 2013;3:460–5. https://doi.org/10.1016/j.jpha.2013.07.001.
132. Gitika, Kumar M. Ethnobotanical Study of Some Medicinal Plants of Haryana, India. World J Pharm Pharm Sci 2016;5:1717–36. https://doi.org/10.20959/wjpps20168-7420.
133. Jebasingh D, Jackson DD, Venkataraman S, Emerald BS. Physiochemical and toxicological studies of the medicinal: Plant Cyperus rotundus L (Cyperaceae). Int J Appl Res Nat Prod 2012;5:1–8.
134. Singh A, Handa SS. Hepatoprotective activity of Apium graveolens and Hygrophila auriculata against paracetamol and thioacetamide intoxication in rats. J Ethnopharmacol 1995;49:119–26. https://doi.org/10.1016/0378-8741(95)01291-5.
135. Karou D, Savadogo A, Canini A, Yameogo S, Montesano C, Simpore J, et al. Antibacterial activity of alkaloids from Sida acuta. African J Biotechnol 2006;5:195–200.
136. Sharma H, Kumar A. Ethnobotanical studies on medicinal plants of Rajasthan (India): A review. J Med Plants Res 2011;5:1107–12.
137. Ramanathan M, Subramanian L, Poongodi T, Manish S, Muneeswari E, Pavithra P, et al. Formulation and Evaluation of Nilavembu Kudineercapsules. Asian J Pharm Res Dev 2019;7:41–5. https://doi.org/10.22270/ajprd.v7i1.468.
138. Arawwawala M, Thabrew I, Arambewela L, Handunnetti S. Anti-inflammatory activity of Trichosanthes cucumerina Linn. in rats. J Ethnopharmacol 2010;131:538–43. https://doi.org/10.1016/j.jep.2010.07.028.
139. Vinothapooshan G, Sundar K. Immunomodulatory activity of various extracts of Adhatoda vasica Linn. in experimental rats. African J Pharm Pharmacol 2011;5:306–10. https://doi.org/10.5897/AJPP10.126.
140. Chellappandian M, Pandikumar P, Mutheeswaran S, Gabriel Paulraj M, Prabakaran S, Duraipandiyan V, et al. Documentation and quantitative analysis of local ethnozoological knowledge among traditional healers of Theni district, Tamil Nadu, India. J Ethnopharmacol 2014. https://doi.org/10.1016/j.jep.2014.03.028.
141. Negi PS, Anandharamakrishnan C, Jayaprakasha GK. Antibacterial Activity of Aristolochia bracteata Root Extracts. J Med Food 2003;6:401–3. https://doi.org/10.1089/109662003772519994.
142. Valli Kanagarla et al. A Review on Benefits and Uses of Vitis Vinifera (Grape). Trade Sci Inc 2013;7:175–80.
143. Saraswathi Motamarri N, Karthikeyan M, Rajasekar S, Gopal V. Indigofera tinctoria Linn - A Phytopharmacological Review. Int J Pharm Biomed Sci 2012.
144. Raghunadha Reddy S, Rajani P, Divi K, Naidu YK, Sarath Chandiran I, Kalyan Reddy MP. Anti-inflammatory and analgesic activity of smilax chinensis. Res J Pharm Biol Chem Sci 2010;1:1–8.
145. Sadique J, Chandra T, Thenmozhi V, Elango V. The anti-inflammatory activity of Enicostemma littorale and Mollugo cerviana. Biochem Med Metab Biol 1987;37:167–76. https://doi.org/10.1016/0885-4505(87)90023-5.
146. Yasin M, Hussain Janbaz K, Imran I, Gilani AUH, Bashir S. Pharmacological studies on the antispasmodic, bronchodilator and anti-platelet activities of Abies webbiana. Phyther Res 2014;28:1182–7. https://doi.org/10.1002/ptr.5112.
147. Kumar M, Ahmad A, Rawat P, Khan MF, Rasheed N, Gupta P, et al. Antioxidant flavonoid glycosides from Evolvulus alsinoides. Fitoterapia 2010;81:234–42. https://doi.org/10.1016/j.fitote.2009.09.003.
148. Patel JJ, Acharya SR, Acharya NS. Clerodendrum serratum (L.) Moon. - A review on traditional uses, phytochemistry and pharmacological activities. J Ethnopharmacol 2014;154:268–85. https://doi.org/10.1016/j.jep.2014.03.071.
149. Khan SA, Shahid S, Ahmad W, Ullah S. Pharmacological Importance of Clerodendrum Genus : A Current Review. Int J Pharm Sci Res 2017; 2:22–30.

*****