Review Article

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POTENCY OF KARA SOODA SATHU PARPAM, A HERBO MINERAL SIDDHA DRUG IN THE MANAGEMENT OF KALLADAIPPU NOI (UROLITHIASIS): A DRUG REVIEW

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ABSTRACT
Siddha is one of the Indian systems of medicine which is widely practised in Tamil Nadu, India. Siddha insists to lead a healthy life both physically and mentally by keeping pace with the laws of nature. Siddhas have classified 4448 diseases, based on the three humoral pathologies. Among them Kalladaippu noi (Urolithiasis) is classified under neerinai arukkal noigal. They consider that the dietary factor play a vital role in the formation of calculi. Also pitha humor is said to be the major causative factor of this disease. Many formulations are indicated for Urolithiasis in Siddha literature. Kara sooda sathu parpam is a herbo mineral drug indicated for urolithiasis. The ingredients are strongly indicated for the disease. Here the article is focused to explore the efficacy of the drug for urolithiasis in various literatures and scientific studies.
Keywords: Urolithiasis, Siddha, Nature, Kalladaippu

INTRODUCTION

Siddha, a traditional healing science of India is an age old holistic medicine which emphasizes the maintenance of relaxed mind and body harmony and insists to keep pace with the laws of nature. In Siddha system besides herbs, metals and mineral drugs are used as medicines[1]. All the medicines have their own way of preparation and prescribed with specific dosage and with specific anupaanams and thunai marundhu in this system. Siddhars classify kalladaippu noi under neerinai arukkal noigal. They define that the dietary factors play an important role in the formation of calculi. Derangement in the pitha humour results in highly concentrated urine and accumulation of salts in the urinary tract[2]. The features mentioned in kalladaippu noi can be compared with urolithiasis mentioned in modern medicine. Since the beginning of recorded history, human beings have grappled with the consequences of unwanted precipitation of insoluble salts from body fluids, especially within the urinary tract[3]. Urinary calculi consist of aggregates of crystals containing small amounts of proteins and glycoproteins. Different types occur with different frequencies in different parts of the world, probably as a consequence of dietary and environmental factors, but genetic factors may also make a significant contribution[4]. Urolithiasis is a recurrent renal disease affecting 4-8 % in U.K, 15 % in U.S, 20 % in Gulf countries and 11 % population in India. Stone formation tends to recur at very high rate; without preventative measures after a first stone. After 3 years this is about 40 %, by 10 years up to 75 % and by 25 years virtually every patient has formed at least one more stone[5]. There are several types, most commonly consisting of calcium oxalate and calcium phosphate; others are composed of magnesium ammonium phosphate (struvite), uric acid or cysteine[6]. Epidemiological data suggests that 60-80 % of stone is composed mainly of Calcium oxalate (CaOx). Stone formation occurs when urinary concentrations of stone forming salts, exceed limit of metastability for that salt in solution. This most often reflects excessive excretion of one or more stone constituents, deficient inhibitory activity in urine, or simply a low urine volume resulting in excessively concentrated urine[7]. The pathogenesis of calcium oxalate stone formation is a multi-step process, which includes nucleation, crystal growth, crystal aggregation and crystal retention[8]. Various substances in the body have an effect on one or more of the above stone forming process, thereby influencing a person's ability to promote or prevent stone formation. Promoters of stone formation facilitate stone formation whilst inhibitors prevent it. Low urine volume, low urine pH, calcium, sodium, oxalate and urate are known to promote stone formation[9]. In spite of technological and conceptual developments in the present practice of medicine, the formation and growth of renal calculi continues to afflict mankind. The recognition of different types of urinary calculi resulted in more options of medical treatment[10]. Endoscopic stone removal and Extrcorporeal Shock Wave Lithotripsy (ESWL) have revolutionized the treatment of urolithiasis but do not prevent the likelihood of new stone formation[11]. Even improved and high cost treatment of ESWL in therapeutic doses may cause acute renal injury, decrease in renal function and an increase in stone recurrence. In addition, persistent residual stone fragments and possibility of infections after ESWL represent a serious problem in the treatment of stones[12]. Regardless of these advances, recurrence rates continue to be high and one of every 2 patients will develop other renal calculi within 5 years of the initial incidence, conforming a need to develop new drugs and treatments in order to prevent the recurrence of kidney stones[13]. There are no satisfactory drugs in modern medicine, which can prevent the formation of stone[14]. Medicines in Siddha, indicated for calculi may exert their beneficial effects in urolithiasis by multiple mechanisms like[15].

- Helps in spontaneous passage of calculi by increasing urine volume, pH and anti-calcifying activity (Diuretic)
- Balance the inhibitor and promoter of crystallization in urine and affects the crystal nucleation, aggregation and growth (Crystal inhibition activity)
- Relieves the binding mucin of calculi (Lithotriptic activity)
- Regulates the crystalloid colloid imbalance and improve renal function, thus prevents recurrence of calculi
- Improve renal tissue anti-oxidant status and cell membrane integrity and prevent recurrence (Anti-oxidant activity)
- Exerts significant anti-infective action against the major causative organisms (Anti-microbial activity)
- Reveals marked improvement in symptoms of urinary calculi like pain, burning micturition (Analgesic and anti-inflammatory activity)

The study drug, Kara sooda sathu parpam is a herbo mineral drug and the ingredients are strongly indicated for urolithiasis. Here the article is focused to explore the efficacy of the drug for urolithiasis in various literatures and scientific studies.

Drug Details
Study drug: Kara sooda sathu parpam
Reference: Chikitsarathnadeepam Part 2 vaithya sindhamani
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Preparation of the drug
Ingredients
- Fried Vengaaram (Borax / Sodium bi borate) 1/2 palam (17.5 g)
- Karpoora silasathu (Gypsum) 1/2 palam (17.5 g)
- Vediuppu (Potassium nitrate / salt petre) 1/2 palam (17.5 g)
- Chitrandathol (Egg shell) 1/2 palam (17.5 g)
- Palagarai (*Cyprea moneta*. Linn) 1/2 palam (17.5 g)
- Padigaaram (Alum / Alumen) 1/2 palam (17.5 g)
- Lemon juice (*Citrus limon*) required quantity

Method of Preparation
The purified ingredients ground with lemon juice and made into pellets and subjected to pudam with 7-8 cow dung cakes. The calcinized pellets are ground to fine powder and stored in an air tight glass container.
Route of administration: Oral
Dosage of medicine: 1 -1 ½ panavedai (488-732 mg)
Duration of treatment: 45 days.
Anupaanam: Tender coconut water, Lemon juice.
Indications: Kalladaippu, Neeradaippu, Neerchurukku, Sadhaiadaippu.

Profile of Individual Drugs
Vengaram (Borax/sodium Bi Borate)
Borax, also known as sodium bi borate, sodium tetra borate, or disodium tetra borate, is an important boron compound, a mineral, and a salt of boric acid. Powdered borax is white, consisting of soft colorless crystals that dissolve easily in water[16].

Natural sources
Borax occurs naturally in evaporate deposits produced by the repeated evaporation of seasonal lakes. The most commercially important deposits are found in Turkey; Boron, California; and Searles Lake, California. Also, borax has been found at many other locations in the Southwestern United States, the Atacama desert in Chile, newly discovered deposits in Bolivia, and in Tibet and Romania. [17]

Siddha literature
Vengaram has sweet and astringent taste. When taken internally it has coolant, diuretic, lithontriptic, emmenogogue activities. On external use it has emollient, antiseptic and astringent activities.

"Vengaram sethumathai verupannume kadugu
Thangusila neermuriya thaanvaangum"

It relieves kaba and urinary diseases[18].

Scientific validations
Toxicity study
Borax, sodium tetra borate decahydrate, according to one study, is not acutely toxic[19]. It's LD_{50} (median lethal dose) score is tested at 2.66 g/kg in rats[20]. Sufficient exposure to borax dust can cause respiratory and skin irritation. Ingestion may cause gastrointestinal distress including nausea, persistent vomiting, abdominal pain, and diarrhea. Effects on the vascular system and brain include headaches and lethargy, but are less frequent[21].

Anti-inflammatory
Tankana bhasma (Borax) has got potent anti-inflammatory and healing properties. Hence, it has been used as a treatment in chronic tonsillitis in the form of a gargle. To ensure scientific validity of the efficacy, a comparative study was conducted between Aspirin tablet and Tankana bhasma which was statistically analysed. In the study Tankana bhasma showed significant relief of symptoms that were statistically significant[22].

Anti-histaminic and bronchodilator activity
Antihistaminic activity of Linga mathirai (LM), where borax is an ingredient, was studied in guinea pigs using histamine-induced bronchospasm where pre convulsive dyspnoea was used as an end point following exposure to histamine aerosol. It was evaluated for antihistamine and bronchodilator activities and it administrated at the doses of 100, 200 and 400 mg/kg body weight. A dose response curve for histamine + LM is lower, when compared with histamine induced contraction ($p < 0.05$) at moderate dose level. The LM at moderate dose level significantly

prolonged the latent period of convulsions as compared to control following the exposure of histamine aerosol[23].

Ovulation inducing and folliculogenetic activity

This study has been undertaken to investigate the effect of Uppu parpam on folliculogenesis, relative ovary and uterus weight and number of ovarian surface follicles in female Wistar albino rats. Significant increase in FSH, LH and estradiol levels, ovarian and uterine weight was noticed along with increased folliculogenesis in the experimental groups treated with Uppu parpam. Thus the results suggested the significant ovulatory response in female rats, and can be used clinically in reproductive hormonal disorders and in infertility condition of female[24].

Karpoora Silasathu (Gypsum)

Gypsum is a soft sulfate mineral composed of calcium sulfate dihydrate, with the chemical formula $CaSO_4.2H_2O$[25]. Gypsum is moderately water-soluble (~2.0–2.5 g/l at 25°C) and, in contrast to most other salts, it exhibits a retrograde solubility, becoming less soluble at higher temperatures[26].

Occurrence

Gypsum is a common mineral with thick and extensive evaporate beds in association with sedimentary rocks. Deposits are known to occur in strata from as far back as the Archaeaneon. It is often associated with the minerals halite and sulfur[27]. In India, significant occurrences of gypsum are at Nellore, Prakasam and Guntur in Andhra Pradesh and Bikaner, Barmer, Jaisalmer, Nagaur, Ganganagar and Pali in Rajasthan, India. There are some other occurrences also reported in the states of Gujarat, Jammu and Kashmir, Himachal Pradesh, Uttar Pradesh and Tamil Nadu, India[28].

Siddha literature

According to siddha literatures Karpoora silasathu has diuretic, lithontriptic, astringent and styptic activity.

"Kalladaippu megam gana thoolam vithirathy
Solladaikku neerarugal sonithakkaan"

Karpoora silasathu is indicated for urolithiasis, obesity and urinary tract infections[18].

Scientific validations

Toxicity study

In this study, the acute and sub-acute toxicity of Vedikara silasathu parpam (VSP) and Nerunjil kudineer (NK), the two siddha formulations given in combination for urinary tract infection was evaluated in Wistar albino rats. In acute toxicity study, both VSP and NK were administered orally at the maximum dose of 2000 mg/kg/p.o. VSP and NK were tested once daily at the dose of 500 mg/kg/p.o for 28 days in sub-acute toxicity study. When compared with the control group, the results of the test group did not show any significant changes in food, water intake, body weight, liver and kidney function test and haematological parameters. Histopathological changes and gross pathological changes were not noted in the vital organs. VSP and NK are safe for the treatment in urinary tract infection at the dose of 500 mg/kg/p.o[29].

Anti-inflammatory and anti-nociceptive activity

In the carrageenan induced paw oedema technique, rats at the dosage of 500 mg/kg/p.o of VSP and NK, significant ($p < 0.001$) inhibition of inflammatory progression was observed than the control group. In the tail flick method, Vedikara silasathu parpam (VSP) and Nerunjil kudineer (NK) at dosage of 500/kg, increased the tail withdrawal time significantly ($p < 0.001$) when compared to the control group; this study has established the significant anti- inflammatory and anti-nociceptive activity of VSP and NK[30].

Anti-microbial activity

The drug Silasathu paavanai contains essential elements like Mg, Zn which are considered to be stone inhibitors and the aqueous extract has good anti-microbial activity against *E. coli* which is the commonest urinary tract infection among patients with urolithiasis[31].

Diuretic activity

In this present study, Karpura shilajit bhasma, an Ayurvedic herbo-mineral formulation, currently used in the Ayurvedic clinical practice as a diuretic drug, was investigated chemically and pharmacologically. Calcium was found to be the major element (24.6044 % w/w). The LD_{50} was found to be 4.625 g/kg p.o. Karpura shilajit bhasma produced mild reduction in motor coordination and mild sedation during the first 2 h after administration at the doses of 500-5000 mg/kg p.o. in mice. The diuretic activity was found to be significant ($P < 0.01$) at minimum dose of 200 mg/kg p.o. in rats and dose dependant up to 1000 mg/kg p.o. Furthermore, natriuretic effect was found to be significant ($P < 0.01$), while no significant change was observed on urinary potassium excretion[32].

Anti-ulcer activity

Silasathu parpam showed significant anti-ulcer activity tested by phenyl butazone induced and stress induced gastric ulceration in Wistar rats[33].

Vediuppu (Potassium nitrate)

Potassium nitrate is a chemical compound with the formula KNO_3. It is an ionic salt of potassium ions K^+ and nitrate ions NO_3^-. It occurs as a mineral niter and is a natural solid source of nitrogen. Potassium nitrate is one of several nitrogen-containing compounds collectively referred to as saltpeter[34].

Natural occurrence

Niter occurs in natural deposits in desert regions. Fairly large amounts are found in the north western provinces of China, and it was well known to early Chinese alchemists. They called it xiao shi (solve stone), and it was first recognized in the 4th century CE[35].

Siddha literature

Vediuppu is a coolant, diaphoretic and diuretic according to siddha medicine.

"Mallaarum attakunmam madhar udhara katti
Kallaam adhaippu neerkattu – ellaame"

By the above verse it is understood that vediuppu is indicated in acid peptic disease, urinary infections and urinary retention[18].

Scientific validations

Toxicity study

Vediuppu Chendhuram (VC) is a traditional Siddha mineral formulation used to treat Urinary tract dysfunction such as burning micturition and retention of urine. Animals were found to be safe up to 300 mg/kg body weight in acute oral toxicity study. Repeated toxicity study of VC has revealed that up to 200 mg/kg body weight; all the treated animals have survived throughout the dosing period of 28 days. But at the dose of 400 mg/kg, exhibits mortality on 21st day of treatment. No significant changes in the body weight, food and water intake have been observed. Complete urine, haematology, biochemical analyses, gross necropsy and histopathological examination at the end of treatment did not reveal any abnormalities[36].

Anti-androgenic potential

Vedi Annabedi Chenduram is a traditional formulation used for the treatment of various ailments in siddha system of medicine. In the present study, anti-androgenic potential and protective effect of Vedi Annabedi Chenduram (6.3 mg/kg) over Benign Prostatic Hyperplasia was assessed in male Wistar rats. The anti-androgenic potential of the formulation has been utilized to test the preventive effect on Benign Prostatic Hyperplasia (BPH). The results show a preventive effect of the formulation on BPH by decreasing the elevated serum acid phosphatase level, elevated organ weights and restoring the normal cellular pattern of prostate gland[37].

Anti-platelet aggregation and thrombolytic activity

Cheenalinga chendhuram [CLC] is a mineral drug made with Lingam, Vediuppu and Padikaaram as in literature is mentioned for its use in cardiac ailments predominantly angina and MI in which thrombus is the pathological background. In this study, CLC was evaluated for its *in vitro* anti platelet aggregation and thrombolytic activity which showed effective at the dose of 300 µg/ml and 75 µg/ml respectively. It has been concluded that CLC is an effective drug in the treatment of cardiovascular diseases and cerebrovascular accidents[38].

Anti urolithiatic activity

Vediyuppu cheyaneer has been widely used in Siddha system of medicine for various diseases. The liquid form of Vediyuppu cheyaneer showed a significant inhibitory effect when screened at 500 mg/kg, for the *in vivo* anti urolithiatic activity on ethylene glycol induced hyperoxaluria rats. The standard frusemide (20 mg/kg) and Cystone (750 mg/kg) were used as comparison for diuretic and anti urolithiatic activity respectively[39].

Ovulation induction and folliculogenetic activity

This study has been undertaken to investigate the effect of Uppu parpam (Vediuppu is the main ingredient) on folliculogenesis, relative ovary and uterus weight and number of ovarian surface follicles in female Wistar albino rats. Significant increase in FSH, LH and estradiol levels, ovarian and uterine weight was noticed along with increased folliculogenesis in the experimental groups. Thus the results suggested the significant ovulatory response in female rats[40].

Chitradathol (Egg shell)

An eggshell is the outer covering of a hard-shelled egg and of some forms of eggs with soft outer coats. Bird eggshells contain calcium carbonate and dissolve in various acids, including the vinegar used in cooking. While dissolving, the calcium carbonate in an egg shell reacts with the acid to form carbon dioxide[41]. According to Thapon and Bourgeois, 1994 shell is approximately 11 % of the total weight of the egg and it presents contents of calcium carbonate (94 %), calcium phosphate (1 %), magnesium carbonate (1 %) and organic substances (4 %). So, egg shell is a rich source of mineral salts, mainly calcium carbonate[42]. Eggshells contain calcium and trace amounts of other micro elements, i.e. magnesium, boron, copper, iron, manganese, molybdenum, sulphur, silicon and zinc. Eggshell calcium is probably the best natural source of calcium and it is about 90 % absorbable. It is a much better source of calcium than limestone or coral sources[43].

Siddha literature

It is mentioned as a demulcent, laxative and useful in vatha and kaba diseases and heals ulcers[18]. It is one of the raw materials from zoological origin for chunnam preparation[44].

Scientific validations

- Increases bone mineral density[45].
- The egg shell powder with vitamin D3 was able to improve bone mineral density without significantly increasing the blood calcium levels[46].
- Anda Odu Parpam produced a protective effect against reproductive toxicity induced by the Tetrachlorodibenzo-P-Dioxin (TCDD) in male rats and confirmed that this Siddha drug may be beneficial for male infertility[47].

Palagarai (*Cyprea moneta*)

Monetaria moneta, commonly known as the money cowry, is a species of small sea snail, a marine *Gastropod mollusk* in the family Cypraeidae, the cowries. The species is called money cowry because the shells were historically widely used in many Pacific and Indian Ocean countries as a form of exchange before coinage was in common usage. It is still used in divination rituals by some African animist tribes[48].

Natural occurrence

This is a very common species which is found widely in Indo-Pacific tropical waters. It is present in numerous regions, including East and South Africa, Madagascar, the

Red Sea and the Persian Gulf, eastern Polynesia, Galapagos, Clipperton and Cocos islands off Central America, southern Japan, Midway and Hawaii, and northern New South Wales and Lord Howe Island[48].

Siddha literature
It possesses bitter taste and is an expectorant and febrifuge. It is indicated in fever, eye diseases, thirst, vatha, indigestion, jaundice, hepato spleenomegaly and bronchial asthma[18].

"Mandham dhaagam grahani maavida suram kannoi
Thondham parinaamasoolai kayam"

Scientific validations
Toxicity study
Animals (mice) treated with Kaparadika bhasma did not show any sign of toxicity in the acute toxicity study. Acute and sub chronic toxicity study showed nontoxic nature and high safety profile in rodents[49]

Anti-pyretic, wound healing and anti-microbial activity
Processed shells of *Cyprea moneta* efficiently reduced the body temperature of rats that was made hyper thermic by yeast injection. The wound healing process ended with the production of scar indicating complete tissue regeneration in *C. moneta* administered rats. The anti-microbial activity was maximum in *Proteus vulgaris* followed by *Micrococcus sps* and *Solmonella abory*[50].

Other studies
Shell powder is proved to be good anti-inflammatory and effective in conjunctivitis. It is also used as a good calcium supplement in humans and animals and an inhibitor of cancer in mice[51]. High content of calcium confirms its medicinal role in bone formation. Sodium present in it is an extracellular cation involved in the regulation of plasma volume, acid base balance, and nerve and muscle contraction. Iron plays crucial roles in haemopoiesis, control of infection and cell mediated immunity[52].

Chemical constituents
The ash of *Cyprea moneta* contains phosphate, fluoride and carbonate of calcium, magnesium, phosphate and manganese[53]. Kaparadika bhasma is highly crystalline calcium carbonate in the calcite form with presence of trace elements like Mg, Al, K, Fe and Zn[54].

Padikaram (Alum)
Alum is both a specific chemical compound and a class of chemical compounds. The specific compound is the hydrated potassium aluminium sulfate (potassium alum) with the formula $KAl(SO_4)_2.12H_2O$. The wider class of compounds known as alums have the related empirical formula, $AB(SO_4)_2.12H_2O$. Alums are useful for a range of industrial processes. They are soluble in water; have an astringent, acid, and sweetish taste; react acid to litmus; and crystallize in regular octahedra. When heated they liquefy; and if the heating is continued, the water of crystallization is driven off, the salt froths and swells, and at last an amorphous powder remains[55].

Siddha literature
It is referred as an astringent, styptic, anti-septic and anti-spasmodic in Siddha.

"Seenamenum kaaramadhu seerivarum pallaranai
Aanaikkaal kannoi anilamodu maanilathil"

It is indicated in filariasis, eye diseases, bleeding disorders, diarrhea, dysentry, gum diseases, menorrhagia and leucorrhoea[18].

Scientific validation
Chronic toxicity and tumourogenicity study
The tumorigenic potential of Aluminium potassium sulphate [A1K $(SO_4)_2$ $12H_2O$, APS], a compound which exists widely in the environment, was investigated in B6C3F1 mice. APS was administered in the diet for 20 months at dose levels of 1.0, 2.5, 5.0 and 10.0 % (w/w). One group receiving the basal diet served as the control. Body weight gain in both sexes was decreased in the 10.0 % APS treated group, and increased in the 1.0 and 2.5 % APS treated groups. The survival rates at the end of the dosing period were 73.3 % (male) and 78.3 % (female) in the control group, and 86.7-95.0 % (male) and 86.7-91.7 % (female) in the APS treated groups. The survival rate showed a tendency to increase in both sexes in all the APS treated groups. In the tumour pathology, the incidence of hepatocellular carcinoma was significantly decreased in the males in the 10 % APS treated group. The incidence of hepatocellular carcinoma was significantly decreased in females in all groups including the control group. The results of the present study indicate that long-term administration of APS does not exert tumorigenic or any other toxic actions in B6C3F1 mice[56].

Anti-platelet activity
Traditionally known as a haemostatic agent, alum shows a paradoxical effect of increased prothrombin and partial thromboplastin times. This study investigated the *in vivo* effect of alum on platelet aggregation and bleeding time in rabbits. The collagen-induced platelet aggregation of platelet-rich plasma samples from 14 healthy rabbits was measured turbidometrically using a platelet aggregometer, before and 1 hour after intravenous injection of alum. Collagen-induced platelet aggregation was significantly reduced after alum injection. Bleeding time from an ear puncture in 8 rabbits was also significantly prolonged after intravenous alum injection. These results suggest that the use of alum as an oral anti platelet drug could be explored further, taking into account possible side-effects especially in renal compromised patients[57].

Anti-bacterial activity
The antibacterial activity of different concentrations of Alum (Hydrated Aluminium Potassium Sulphate) was examined against *Proteus mirabilis* that causes upper urinary tract infections. It was found that this bacteria loss the motility on semi-solid media in 0.6 mg/ ml of alum (Hydrated Aluminium Potassium Sulphate) after 24 hours

incubation but the Minimum Inhibition Concentration (MIC) of Alum was 0.8 mg/ml. The study revealed that Alum has the potential effect against *P. mirabilis*[58]. Kodasuri veeravaiuppu is one of the siddha formulations prepared by many inorganic compounds available in nature like Mercuric Chloride, Mercury, Sodium Chloride, Rock Salt, Potassium alum, Ammonium Chloride, Oxides of Calcium and Potassium, Copper Sulphate and Potassium Nitrate. It is a proven medicine for rheumatoid arthritis and as an antibacterial. The present study tested the anti-bacterial property of this drug on human pathogenic bacteria *Bacillus cereus, Bacillus subtilis, Proteous mirabilis, Citro bacter spp., Staphyllococcus aureus. Escheritia coli, Vibrio chlorae, Salmonella typhi, Pseudomonas aeuriginosa* and *Klebsialla pneumoniae*. The results were encouraging when compared to standard drug Ciprofloxacin[59].

Elumichai (*Citrus limon*)

The lemon (*Citrus limon*) is a small evergreen tree native to Asia, and the tree's ellipsoidal yellow fruit. The fruit is used for culinary and non-culinary purposes throughout the world, primarily for its juice, though the pulp and rind (zest) are also used in cooking and baking. The juice of the lemon is about 5 % to 6 % citric acid, which gives lemons a sour taste. The distinctive sour taste of lemon juice makes it a key ingredient in drinks and foods such as lemonade[60].

Anti-oxidant activity

Peel, including the flavedo and albedo of *C. limon* fruits contained higher amounts of the marker substances. The albedo also had higher contents of the phenols and flavonoids and was superior in its ability for DPPH scavenging and reduction[61].

Anti-microbial activity

The fresh crude lemon juice showed highest anti-microbial activity against *Solmonella para* B and *Shigella sonnei*. The efficacy was compared with Ampicillin[62].

Anti-nociceptive effect

The anti-nociceptive activity of *Citrus limon* essential oil (EO) was assessed in mice. EO (50, 100, and 150 mg/kg) significantly reduced the number of writhes, and, at highest doses, it reduced the number of paw licks. Whereas naloxone antagonized the anti-nociceptive action of EO (highest doses), this suggested, at least, the participation of the opioid system. Further studies currently in progress will enable us to understand the action mechanisms of EO[63].

Anti urolithiatic activity

In synthetic urine, the inhibition rate of calcium oxalate crystallization increases gradually with the lemon juice concentration. In natural urine, researchers noted that the kinetics of crystallization of calcium oxalate, before and after ingestion of lemon juice, is comparable. *In vivo,* after ingestion, a small increase in mean urinary pH (from 6.7 ± 0.1 to 6.9 ± 0.1) was noted. Indeed, oxalate, calcium means and citrate excretion increased during this period with 33.41 %, 6.85 % and 3.53 % respectively. This increase in the oxalate excretion is probably explained by the conversion of the exogenous ascorbic acid contained in the lemon juice. These results show that the lemon juice presents an important inhibitory effect *in vitro*. The ingestion of the lemon juice seems to dissipate an effect of great quantity of citrates which in turn increases the excretion of oxalates. The presence of these two elements simultaneously: citrate and oxalate compensate for their opposite effect[64].

Potency of the ingredients of Kara sooda sathu parpam in the management of Urolithiasis

S. No.	Name of the ingredients	Strengths as in siddha literature	Strengths as per scientific validations
1	Vengaram (Borax)	Diuretic, Lithontriptic	Anti inflammatory[22]
2	Karpoora silasathu (Gypsum)	Diuretic, Lithontriptic	Anti inflammatory[30], Anti nociceptive[30], Anti microbial[31], Diuretic[32]
3	Vediuppu (Potassium nitrate)	Coolent, Diuretic	Anti urolithiatic[39]
4	Chitrandathol (Egg shell)	Demulcent	
5	Palagarai (*Cyprea moneta*)	Febrifuge	Anti pyretic[50], Anti microbial[50], Anti inflammatory[51]
6	Padikaram (Alum)	Anti-septic, Anti spasmodic, Styptic	Anti microbial[58]
7	Elumichai (*Citrus limon*)	Helpful in pitha diseases	Anti microbial[62], Anti nociceptive[63], Anti urolithiatic[64]

CONCLUSION

By various literature searches it is well understood that each ingredient of Kara sooda sathu parpam has good activity related to the management of Urolithiasis. Vengaram, Karpoora silasathu and lemon juice have direct indication for Urolithiasis. Vengaram, Vediuppu and Karpoora silasathu are good diuretics. The other ingredients will be helpful in reducing the associated symptoms like fever, Urinary tract infections, hematuria, renal colic etc. it can be concluded that the formulation will be much helpful in the management of Urolithiasis.

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