



A REVIEW ON TRADITIONAL MEDICINAL PLANTS FOR THE MANAGEMENT OF URTICARIA (KANAAKADI)

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ABSTRACT

Nature has bestowed us with a wide variety of medicinal plants out of which 8000 herbs have been used in the traditional medicine of India. The Siddha system of Medicine that has emerged through the supreme intuition of the Siddhars has its origin in southern parts of India and it is well known for its holistic treatment approach. Urticaria is a commonest health problem worldwide which is coined by the term “*Kanaakadi*” in *Siddha* classical literature. This health issue is caused due to allergens including dust mites, pollen, cosmetics, food, and mold spores. Present day pharmacological management of allergic diseases includes anti-allergic medication and immunotherapy for specific allergens, most commonly antihistamines, anticholinergics and corticosteroids that are not free from its side effects. Currently, natural medicine provides imperative resources to meet the global health care at affordable prices and hence it is important to analyze the safety and efficacy comparable to conventional therapeutic drugs. This article deals with selective traditional herbs with anti-allergic properties that can be used for the management of urticaria.

KEYWORDS: Siddha, Ttraditional systems, Urticaria, *Kanaakadi*, Allergic disorders.

INTRODUCTION

The medical term “Urticaria” is derived from the Latin word “Urtica” which means “to burn”. Urticaria is characterized by a notable skin rash with dark red colored, raised, itchy Wheals affecting almost nearly 15-20% of the population atleast once in their life time.^[1-3] 30% among the affected individuals suffer from chronic Urticaria with recurrent episodes of skin rashes and itching at least twice a week for about 6 weeks.^[4] The itchy wheals may be single or in clusters and may vary in size from a few millimeters to hand sized lesions due to vasodilatation and increased vascular permeability. Urticaria may also exist with Angioedema (Tissue swelling) often notable in the face, oropharynx and genitalia as a result of local increase in vascular permeability.^[5] Though the most common cause of Acute Urticaria, may be due to a state of hypersensitivity to food or drugs, and it may also result from microorganisms such as viral, bacterial or parasitic infection.^[6-10]

While the pathogenesis of Urticaria in most of the cases is still unknown, this disease causes frustration to both patients and treating physicians due to its low response to

conventional antihistamines and steroids which may lead to side effects on long term use. The disease is also associated with lower quality of life to patients^{11, 12}. The *Siddha* system of medicine, has described several drugs from indigenous plant sources in the treatment of all the variety of allergic disorders¹³. The following are few of the selective herbs that have been analyzed towards then effective management of Urticaria. According to Siddha, pathogenesis of diseases pertaining to skin like Urticaria (*Kanaakadi*) owes to predominant imbalance of *Vatham* since the *Siddha* literature emphasis, “*Vathamalathu meni kedaathu*” which means disease pertaining to skin is associated with deranged *Vatham*. This imbalance in *Vatham* is inturn is followed by derangement of *Pitham* and *Kabam* resulting in itching, redness, burning sensation and raised lesions.^[14]

Scientific validation of traditional medicinal plants for urticaria

1. *Cynodon dactylon* (Tamil -Arugampul) Family: Poaceae



Cynodon dactylon commonly known as Bermuda grass belongs to the Poaceae family. It is the sacred plant of India next to *Ocimum* since age old times. It is common weed grass with enormous therapeutic potential.^[15] The phytochemical analysis showed that *Cynodon dactylon* contained alkaloids, flavanoids, glycosides, terpenoides, steroids, saponins, tannins, resins, phytosterols, reducing sugars, carbohydrates, proteins, volatile and fixed oils. The aqueous extract of *Cynodon dactylon* (50-400 mg/ml) was reported to have the antimicrobial activity against *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus mirabilis*.^[16]

Savali et al (2010), studied the anti-anaphylactic and mast cell stabilization effect of *Cynodon dactylon* compound (CDC) isolated by bio-assay guided fractionation by using rat peritoneal mast cells.^[17] The results revealed that *Cynodon dactylon* produced significant inhibitory effect on compound 48/80 induced anaphylactic reaction and mast cell. Besides a study on the immunomodulatory activity of *Cynodon dactylon* performed by Mangathayaru et al., (2009) in mice using the humoral antibody response showed that oral administration of the juice at 250 and 500 mg/kg in mice increased humoral antibody response upon antigen challenge evidenced by a dose-dependent, significant increase in antibody titer in the haemagglutination antibody assay and plaque forming cell assay.^[18]

Aqueous extracts of *Cynodon dactylon* (200, 400, and 600 mg/kg of bw orally) was reported to have anti-inflammatory activity in carrageenan, serotonin dextran and histamine induced rat paw edema within 7 days of treatment.^[19,20] *Cynodon dactylon* also showed significant analgesic and anti-pyretic activities and in one of the study the *Cynodon dactylon* extract possessed significant decrease in rectal temperature of mice similar to that shown by paracetamol.^[21,22] The diuretic activity of aqueous extract of *Cynodon dactylon* was evaluated in rats. Aqueous extract of *Cynodon dactylon* at a dose of 100, 250, 500mg, 750 mg/kg bw orally, showed diuretic activity.^[23] The extract of *Cynodon dactylon* also showed its ability to scavenge free radicals in a concentration dependant manner and increased the levels

of enzymatic antioxidants like super oxide dismutase, glutathione peroxidase and catalase and non-enzymatic antioxidants like reduced glutathione, vitamin A and vitamin E on the administration of ethyl acetate extract (80 µg in 100 µl of DMSO, ip).^[24,25]

Toxicity study: The acute toxicity test was carried out in swiss albino mice by up and down procedure of OECD guidelines to LD 50 thereby establishing the therapeutic index. The overnight fasted animals were administered with different doses of *Cynodon dactylon* hydro alcoholic extract in a single dose viz., 1.75mg, 55 mg, 175 mg, 550 mg and 2000 mg/kg body wt and observed up to 72 hours. The observation showed that the LD50>2000MG/KG which confirmed its safety for human consumption.^[26]

2. *Ocimum Sanctum* (Tulsi) Family: Lamiaceae



Ocimum sanctum commonly known as holy basil is an important symbol in Hindu tradition. It is found in tropical regions of the world and widespread as cultivated herb and weed.^[27] It has various uses medicinally due to the presence of the essential oil. In Siddha system, is well known for its curative potential in allergic skin and respiratory diseases. Sridevi et al., studied the mast cell stabilizing potential of *Ocimum sanctum* extract when challenged with horse serum that possessed Mast cell stabilizing potential, *O.sanctum* extract at 400 mg/kg, p.o., for 2 weeks of pretreatment in sensitized animals resulted in a significant reduction in the number of disrupted mast cells (P <0.001). Also the antihistaminic action of *Ocimum sanctum* was investigated in histamine induced bronchospasm of guinea pigs and anti-anaphylactic activity was investigated and confirmed in rats using active anaphylactic model.^[28]

In another study by Mediratta et al., the immunomodulatory effect of *O. sanctum* L. seed oil was evaluated in both non-stressed and stressed animals. *Ocimum sanctum* L. seed oil (3 ml/kg, Ip) produced a significant increase in anti-sheep red blood cells (SRBC) antibody titer and a decrease in percentage histamine release from peritoneal mast cell of sensitized rats showing humoral immune responses and decrease in food pad thickness and percentage leucocyte migration inhibition showing cell-mediated immune responses respectively.^[29] These pharmacological properties of *Ocimum sanctum* may be due to the presence of volatile

oil in the leaf consisting of eugenol, euginal and urosolic acid.^[30] A study also reports that the Antiallergic action of *O.sanctum* has been found to be associated with significant production of IgE antibodies.^[31]

Toxicity Study. The acute and subacute toxicity study performed in *Ocimum sanctum* showed that the extract did not cause death or any toxic signs in treated male and female mice at limit dose of 2000mg/kg. Also, the Subacute studies in rats did not show any change in hematological, liver functions and spleen with 800mg/kg *Ocimum sanctum* extract when administered for 28 days.^[32]

3. *Leucas aspera* (Thumbai) Family: Lamiaceae



Leucas aspera is commonly distributed throughout India from Himalayas to Ceylon.^[33] Flowers are valued as stimulant, expectorant, aperient, diaphoretic, insecticide and emmenagogue. Leaves are considered useful in chronic rheumatism, psoriasis and other chronic skin eruptions. Bruised leaves are applied locally in snake bites.^[34] *Leucas aspera* is reported to have significant anti-histaminic, bronchodilatory, anti-inflammatory, mast cell stabilizing, anti-allergic and anti-spasmodic activity. Phytochemical analysis performed on the whole plant of *Leucas aspera* L confirmed the presence of alkaloids, flavanoids, steroid, triterpenoids and saponins. The disease control group mice treated with boiled or cooled milk (4mg/kg, s.c.) similarly showed increase in leucocytes and eosinophil count.

Also the anti-inflammatory effect of methanolic extract of *Leucas aspera* was investigated in egg albumin induced paw edema that caused inflammation in hind paw of rat. It was observed in the study that rats treated with *L. aspera*, showed a decrease hind paw volume after egg albumin injection which proves the anti-inflammatory activity. Also the methanolic extract of *L. aspera* showed significant inhibition of Acetylcholine and histamine induced contractions in guinea pig ileum and tracheal chain preparation confirming its antihistaminic effect.^[35]

Toxicity study: Acute and subacute toxicity study was performed in ethanolic extract of *Leucas aspera* on albino and Wistar rats respectively. The results of acute toxicity study revealed the safety at 2000mg/body

weight. In subacute toxicity study the morphological, biochemical and hematological parameters were within the normal limits and the histopathological study also revealed no evidence of toxicity.^[36]

4. *Azadirachta indica* (Vembu) Family: Meliaceae



Neem is a native of East India, Burma and South East Asia and it belongs to the family *Meliaceae*. This tree has been considered as the mother of all therapeutic herbs since centuries. Various phytochemicals such as Azadirachtin, Nimbidin, Nimbin, Nimbinin, Nimbidinin, Nimbolide, Nimbidic acid and Nimbidin poses antipyretic, antiviral, analgesic, antibacterial, hepatoprotective effect and several other pharmacological effects.^[37] Nimbidin which is primarily obtained from the oil of Neem seed kernels has been shown to poses an Anti-inflammatory activity in formalin induced arthritis in rats and also has antihistaminic effect by blocking H2 receptor.

Azadirachta Indica has been studied extensively for its capability to bring under control the generation of chemiluminescence by activated human polymorphonuclear neutrophils (PMN), in which this compound indicate the inhibition of oxidative burst of PMN during inflammation. Moreover, a polysaccharide obtained from Neem bark is said to prevent the inflammation of the induced Carrageenin into the mouse.^[38-40] *Azadirachta indica* also acts as immune stimulant by boosting lymphocytes and other cell mediated systems such as Killer cells which involve in the inflammatory mechanism.^[41]

Toxicity study: Acute oral toxicity study was performed in the extract of *Azadirachta indica* leaf at a dose of 20 mg/kg, 200mg/kg or 2000mg/kg and the incidence of mortality was checked in the first 24 hours and the study was extended up to 14 days. The result revealed no significant changes and no mortality were observed in the behavioural or autonomic responses in mice after treatment with different doses of *Azadirachta indica* leaf extract. in another study which evaluated the the no-observed-adverse-effect level (NOAEL) of exposure and target organs of Neem oil in mice, The results showed that the serum biochemistry and organ coefficient in

experimental groups had no statistical difference compared with those of the control group.^[42,43]

5. *Acalypha indica* (*Kuppai meni*) Family: Euphorbiaceae



Acalypha indica belonging to the family Euphorbiaceae is a common herb of India and it is widely utilized by the tribal communities for the treatment of the various kinds of the disorders since centuries. The Phytochemical screening of the percentage crude yields of extracts studied has shown that the leaves of *Acalypha indica* Linn were rich in lignans, flavonoids, glycosides, sterols, sugars, amino acids and triterpenoids.^[44] Aqueous extract of *Acalypha indica* was studied on the histamine and acetylcholine aerosol induced bronchospasm in guinea pigs at doses of 200 and 400 mg/kg. Treatment with aqueous extract of *Acalypha indica* showed significant protection against histamine and acetylcholine aerosol induced bronchospasm in guinea pigs with significant decrease in the total leukocyte and differential leukocyte count in the the egg albumin sensitized guinea pigs.

The study results concluded that *Acalypha indica* extract decreased the infiltration of inflammatory cells in the airway and inhibition of release of histamine like mediators.^[44] Another study by Gupta and Srma on the effect of *A.indica* on in vitro mast cell degranulation by compound 48/80 (Sigma-Aldrich Chemical Co., USA) was found to significantly ($p < 0.001$) inhibit in vitro rat peritoneal mast cell degranulation induced by compound 48/80 as compared to base line value.^[45]

Toxicity study: In the acute toxicity study, the rats were treated with different concentration of *Acalypha indica* from the range of 5mg/kgb. wt to 2000mg/kg b.wt which did not produce signs of toxicity, behavioral changes, and mortality in the test groups as compared to the controls when observed during 14 days of the acute toxicity experimental period.^[46]

6. *Alium cepa* (*Vengayam*) Family: Liliaceae



Alium cepa (Family Liliaceae) is a well-known Indian medicinal herb that is indicated in Siddha literature as an effective remedy for several skin and allergic ailments. It has been consumed for its reputed nutritional and health benefits for centuries. It is well known to have potential antihistamine, anti-inflammatory, and antioxidant activities.^[47] A study on Anti-allergic activity of *Allium cepa* was conducted against various events responsible for Type I allergic reactions. The results showed that the herbal fraction (ALC-02) from *A. cepa* (bulb) inhibited histamine release and attenuated intracellular calcium levels in Compound 48/80- induced rat peritoneal mast cells.

Further, it also prevented compound 48/80-mediated systemic anaphylaxis while lowering histamine levels in plasma. Another study on anti-inflammatory effect of fresh onion juice was assessed by applying carrageenan sub plantar injection to Sprague-Dawley rats. The obtained results illustrated a significant analgesic property for fresh onion juice in both pain phases compared with positive control group ($Pv \leq 0.05$); the effects were similar to that of morphine (5 mg/kg) as the standard treatment. The results proved that fresh onion juice was capable to decrease the hind paw thickness significantly in comparison with control group ($Pv \leq 0.001$). Hence the study proved the potential of *Alium cepa* in inhibiting acute and chronic inflammation.^[48]

Toxicity study: A study on acute toxicity of *Alium cepa* showed that the LD 50 was found to be more than 3000 mg/ kg BW p.o. in acute toxicity testing. The therapeutic dose 300mg/ kg BW p.o. was calculated as 1/10 th of the lethal dose for the purpose of wound healing investigation.^[49]

7. *Solanum xanthocarpum* (Kandankathiri) Family: Solanaceae



Solanum xanthocarpum is known as Indian night shade or yellow Berried Night Shade plant belonging to the family Solanaceae. *Solanum xanthocarpum* is a prickly diffuse, bright green perennial herb found throughout India, mostly in dry places as a weed along roadsides and waste lands. Phytochemicals such as solasonine, β -sitosterol, solanacarpine, solamargine, aesculetin, aesculin, carpesterol, diosgenin, campesterol, daucosterol and triterpenes like cycloartanol and cycloartenol were reported from the whole plant and fruit. The plant is extensively studied for the various pharmacological activities like antiasthmatic, hepatoprotective, cardiovascular, hypoglycemic and mosquito repellent properties.^[50]

Another study result suggested that the plant possess antihistaminic, mast cell stabilizing and decreased capillary permeability effect and hence possesses potential role in the treatment of asthma and allergic disorders. The plant saponins extracted from *Solanum xanthocarpum* extract has been shown to protect sensitised mast cells from degranulation on antigen shock as it inhibited antigen induced histamine release from sensitised mast cells.^[51,52] The anti-anaphylactic and mast cell stabilizing effect of *Solanum Xanthocarpum* might be attributed to the presence of Phytoconstituents, which are known for their mast cell stabilizing potential against antigen-antibody reaction or due to the suppression of IgE antibody production, which is responsible for degranulation mast cells.^[53]

Toxicity study: Acute toxicity studies on *Solanum xanthocarpum* was performed orally as a single dose to mice at different dose levels of 250, 500, 1000, 1500 and 2000 mg/kg b.w. Animals were observed periodically for the symptoms of toxicity and death within 24 h and then daily for 14 days. The results revealed that *Solanum xanthocarpum* did not produce any mortality at 2000 mg/kg.^[54]

8. *Taxus baccata* (Thalisapatri) Family: Taxaceae.



Taxus is an evergreen tree with linear leaves that are dark green in color on upper surface and yellow green on lower surface. It belongs to the family Taxaceae.^[55] Four taxoids (taxusin, baccatin VI, baccatin III and 1beta-hydroxybaccatin I), five lignans and taxol an important phytochemical were isolated from the heartwood of *Taxus baccata* L. (Taxaceae).^[56]

In siddha system of medicine, *Taxus baccata* has been indicated for treating fever, asthma, vomiting, diarrhoea, indigestion. A study was designed to evaluate the bronchodilator activity of aqueous extract of *Taxus baccata* (AET) on the histamine and acetylcholine aerosol induced bronchospasm in guinea pigs. Treatment with AET at the doses of 200 and 400 mg/kg, p.o., for 7 days showed significant protection against histamine and acetylcholine aerosol induced bronchospasm in guinea pigs. Significant decrease in the total leukocyte and differential leukocyte count in the egg albumin sensitized guinea pigs AET dose dependently protected the mast cell disruption induced by compound 48/80. Hence the study proved that it improves bronchial hyper-reactivity by decreasing the infiltration of inflammatory cells in the airway and inhibiting the release of histamine like mediators through its mast cell stabilizing activity.^[57]

Toxicity study: The LD50 of taxol a chief phytochemical was over 200 mg/kg. The mice received SC injections on 6 days per week for 4 weeks. And all the animals were observed for 3 months. Though a slight body weight loss was initially observed, no mortality, no histological damage and no toxic effects were observed in the mice treated with taxol.^[58]

9. *Cyperus rotundus* (Korai kizhangu) Family: Cyperaceae.



Cyperus rotundus belonging to *Cyperaceae* family is a major weed and a grass-like herb that is found throughout India. It has tuberous roots or rhizomes that are fragrant. The chemical investigation on this plant revealed a number of chemical constituents belonging to different classes such as fat, gum resins, carbohydrates, essential oils alkaloids, saponins, flavonoids, albuminous matters, fibers and ash, the major constituents of the oil are glycerides of oleic, palmitic and linoleic acids with small quantities of essential oil.^[59-61] Another study revealed the extract of the rhizomes of *Cyperus rotundus* (CRE) containing the sesquiterpene derivatives (valencene, nootkatone, and caryophyllene α -oxide), monoterpenes (β -pinene, and limonene) and 4-cymene that were responsible for their anti-allergic activity in vitro and in vivo.

Also a research study showed that CRE inhibited leukotrienes production and β -hexosaminidase release at 300 μ g/mL. The chemical constituents valencene and nootkatone significantly inhibited the delayed-type hypersensitivity reaction in mice when administered orally at 50-300 mg/kg. So it was finalized that *C. rotundus* and its constituents, valencene, nootkatone, and caryophyllene α -oxide, exerted anti-allergic activity in vitro and in vivo.^[62] In another study, Ethanol/water (1:1) extract of dried rhizome, at a concentration of 0.001 g/ml, was active on guinea pig ileum and showed antihistaminic activity.^[63] The alcoholic extract (70% alcohol) possessed anti-inflammatory activity against carrageenan induced oedema and also found effective against formaldehyde induced arthritis in albino rat.^[64]

Toxicity study: Acute toxicity test performed on administration of 95% ethanol extract from the rhizomes of *C. rotundus* at the dose of 5,000 mg/kg, all rats did not exhibit signs of toxicity and mortality. Results of the subacute toxicity showed that administration of the ethanol extract from the rhizomes of *C. rotundus* at a dose of 1,000 mg/kg daily over 14 days did not cause mortality or behavioral changes.^[65]

10. *Curcuma longa* (Manjal) Family: Zingiberaceae



Turmeric (*Curcuma longa*) has traditionally been used to treat pain, fever, allergic and inflammatory diseases such as bronchitis, arthritis, and dermatitis. A study was conducted by Shin et al., to evaluate the anti-allergic action of turmeric in mice that were orally challenged with 50 mg ovalbumin and treated with turmeric extract

(100 mg/kg), Curcumin (3 mg/kg or 30 mg/kg) for 16 days. The results revealed that turmeric significantly attenuated food allergy symptoms induced by ovalbumin. Further turmeric also inhibited IgE, IgG1, and mMCP-1 and type 2 helper cell (Th2)- related cytokines and enhanced a Th1-related cytokine.

Furthermore, the anti-allergic effect was reported to be obtained through promoting Th1 responses on Th2-dominant immune responses in immunized mice.^[66] The main active ingredient of *Curcuma longa* is curcumin alkaloid. Curcumin suppressed compound 48/80-induced rat peritoneal mast cell (RPMC) degranulation and histamine release from RPMCs. Curcumin inhibited compound 48/80-induced systemic anaphylaxis in vitro and anti-DNP immunoglobulin E (IgE) mediated passive cutaneous anaphylactoid response in vivo. Curcumin has an ability to inhibit nonspecific and specific mast cell-dependent allergic reactions.^[67]

Toxicity study: Acute toxicity study of *Curcuma longa* conducted in rats, guinea pigs and monkeys showed that there was no adverse effect on health or gross or histological change in the liver, kidneys and heart of adult rats, guinea pigs and monkeys (*Macacus sp.*) which were given turmeric (*Curcuma longa*), 2.5 g/kg bodyweight, or its alcoholic extract, 300 mg/kg, for 3 weeks.^[68]

11. *Aegle marmelos* (Vilvam) Family: Rutaceae



Aegle marmelos, commonly known as Bael belonging to the family *Rutaceae*, has been widely used in indigenous systems of Indian medicine due to its various medicinal properties.^[69] It has been reported to contain several phytoconstituents such as marmenol, marmin, marmelosin, marmelide, psoralen, alloimperatorin, rutaretin, scopoletin, aegelin, marmelin, fagarine, anhydromarmelin, limonene, α -phellandrene, betulinic acid, marmesin, imperatorin, marmelosin, luvangentin and auroptene.^[70] Marmin is a coumarine derivative isolated from stem bark and root of *Aegle marmelos*.^[71] Nugroho et al. studied the effect of marmin isolated from *Aegle marmelos* on (Guinea pig tracheal chain) GPT contraction induced immunologically by endogenous histamine and to determine the relaxation effect of marmin. The study results revealed that Marmin inhibited the guinea pig tracheal contraction through the

inhibition of histamine released from mast cells.^[72] Krishnakanth et al., studied analgesic action and anti-inflammatory action of the leaf extract and fruit extract at doses 200mg/kg and the results showed that it had significant analgesic and anti-inflammatory action.^[73]

Toxicity study

Acute and subacute toxicity studies of *Aegle marmelos* when administered intraperitoneally at doses of 50, 70, 90 and 100 mg/kg body weight for 14-consecutive day to male and female Wistar rats was considered to be safe with no remarkable changes in histopathological studies.^[74]

12. *Nigella sativa* (Karuncheeragam) Family: Ranunculaceae



Nigella sativa belonging to Ranunculaceae family is commonly known as black cumin and has a wide spectrum of pharmacological action such as antihypertensive, hepatoprotective, diuretics, digestive, anti-diarrheal, analgesics, anti-bacterial, antioxidant properties, etc. The seed oil is rich in several phytochemicals such as thymoquinone, carvone, D-limonene, melanthin, tannins, *p*-cymene, α -pinene, thymol, dithymoquinone, thymohydroquinone and alkaloids. Most of the therapeutic properties of this plant are due to the presence of thymoquinone which is major bioactive component of the essential oil. Several studies showed that Thymoquinone and Nigellone showed antihistamine activities and antioxidant activities in ethanol treated rats which showed increased myeloperoxidase and histamine levels suggesting that it could partly shield gastric mucosal lining from acute alcohol-induced damage.

The inhibitory outcome of nigellone on histamine release from rat peritoneal mast cells was shown to be mediated by diminishing intracellular calcium as low concentration of nigellone effectively inhibited the histamine release from the mast cells, indicating an anti-asthmatic role. Further administration of *N. sativa* oil to patients with allergic problems, like allergic rhinitis, atopic eczema, and bronchial asthma decreased the immunoglobulin E, and eosinophil count. The aqueous extract of *N. sativa* was found to possess anti-inflammatory and analgesic effect.^[75]

Toxicological study

Acute toxicity study on *N. sativa* fixed oil showed no toxic effects when given to mice via the stomach. In a chronic toxicity study no changes were observed in key hepatic enzyme levels. Moreover, no abnormality was found in the histopathological results and LD₅₀ value suggested a wide margin of safety for therapeutic doses.^[76]

13. *Indigofera tinctoria* (Avuri) Family: Fabaceae



Indigofera tinctoria is an annual herb of Fabaceae family. It grows upto a height of 4-6 feet. The plant tastes bitter and it has thermogenic, laxative, expectorant, hepatoprotective, anticancer, antihelminthic actions and used in treating gastropathy, splenomegaly, cephalalgia and cardiopathy. *Indigofera tinctoria* contains naturally occurring antioxidants that scavenges the free radicals and also used in treating, chronic bronchitis, asthma and skin diseases.^[77]

Qualitative analysis of phyto constituents of plant shows less toxicity and more medicinal values because of its antioxidants.^[78] It contains phyto chemicals such as flavonoid, saponins, tannins, steroidal terpenes, phenols and anthroquinones with potent medicinal values.^[79] In a study by Katti H. R et al., the antiarthritic activity of indigofera was determined and the standard drug Diclofenac and extracts of *Indigofera tinctoria* L were tested to significantly inhibit ($p < 0.05$ to $p < 0.001$) of histamine from both blood and liver tissue thereby reducing the edema and inflammation mediated by histamine. The study results showed that significant decreased paw edema volume in Diclofenac and *Indigofera tinctoria* extract animals might be due to the inhibition of histamine or prostaglandins release by blocking through cyclo-oxygenase pathway.^[80] In another study, the ethanolic extracts of leaves of *Indigofera tinctoria* Linn. (500 & 1000 mg/kg bwt) showed potent anti-inflammatory activity when compared to control as well as positive control Ibuprofen (standard drug) group.

Toxicity study

Acute oral doses of *Indigofera tinctoria* at doses of 250, 500 and 1000 mg/kg did not provoke any gross behavioral changes or manifestations of toxic symptoms in experimental animals.^[81,82]

14. *Ziziphus oenoplia* (Soorai) Family: Rhamnaceae



The shrub *Ziziphus oenoplia* of family Rhamnaceae commonly known as jackal jujube. Some pharmacological properties of this plant are febrifuge, antiulcer (Root), antioxidant, anthelmintic, anti-plasmodial, angiogenic, antibacterial activity, wound healing activity and blood purifying property.^[83] Ethanolic extract of *Ziziphus oenoplia* root has significant anthelmintic activity of against *Pheretima posthuma* shows significant action at 50 mg/ml with the standard reference Albendazole (20mg/ml) and distilled water as control.^[84]

In a study performed by Butle A et al., in isolated ZOSL (*Ziziphus oenoplia* seed lectin) for its in vivo anti-allergic and anti-inflammatory activity through Arthus reaction and anaphylactic shock on Wistar albino rats, Lectins from some of the plant species were reported to possess immunomodulatory activity. lectin isolated from the seed cotyledons of *Ziziphus oenoplia* is found to be effective in preventing both Arthus reaction and anaphylactic to a great extent. Therefore confirming its action as an anti-allergic and anti-inflammatory drug.^[85-87] *Z. oenoplia* showed antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, *Salmonella enterica*, *Enterobacter aerogenes*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *in-vitro* by agar disc diffusion technique.^[88]

Toxicity study

All the fractions of alcoholic extract were found to be nontoxic when administered orally to mice in the dose 3000mg/kg b.w. and its LD50 was found to be safe in the same dose.^[89] In another study, *Ziziphus oenoplia* (L.) Mill root extracts at a dosage of 1000-4000mg/kg and were subjected for acute toxicity study according to the recommended method, the results showed that the dose caused no mortality and was well tolerated.^[90]

DISCUSSION

The traditional Siddha system offers both external and internal therapy for the management of urticaria which may be single herbal therapy or polyherbal formulations. The present literature search on traditional herbs for the management of urticaria validates the scientific rationale of the above selected herbs that are mentioned in ancient Siddha literature. According to Siddha philosophy, disease originates from the extrinsic and intrinsic influences which act on humans. The natural ability

(Innate immunity) can be correlated with “*Thega vanmai*” which is present at birth due to genetic trait, season, age, sex etc. The acquired ability varies according to diet, physical activity and thought. Any imbalance in these factors is said to affect the three humours *Vatham*, *Pitham* and *Kabam* that exists as subtle life forces to regulate the harmonial function of the human body.

Therefore each herb is a dynamic composition of its unique taste (suvai) which primarily owes to its phytoconstituents and contributes to its pharmacological activity such as anti-inflammatory, analgesic, antihistaminic, antioxidant and immunomodulatory action for the management of urticaria. These subtle concept of Siddha pharmacology stands as the backbone for the selection of specific herbs towards disease management, thereby balancing the deranged humours *Vatham Pitham* and *Kabam* responsible for symptoms of urticaria such as itching, redness, burning sensation and raised lesions. Further this preliminary effort also provides the safety profile of each herbs through previous research studies thereby confirming the traditional claims on humans.

Cynodon dactylon, *Solanum xanthocarpum*, *Taxus baccata* has been found to have significant anti anaphylactic and mast cell stabilization effect. The volatile oil of *Ocimum sanctum* has been found to be associated with significant production of IgE antibodies that can effectively reduce the symptom of itching in urticaria. *Leucas aspera*, *Neem* and *Acalypha indica*, *Alium cepa* has been reported to have significant anti-inflammatory properties to alleviate the wheal formation and erythema in urticaria. Studies on *Curcuma longa* and *Aegle marmelos* have showed that they possess both immunomodulatory and antihistaminic activity. Nigellone from *N. sativa* and *Indigofera tinctoria* was found to possess anti-inflammatory and analgesic effect by blocking through cyclo-oxygenase pathway. Lectins from *Ziziphus oenoplia* was found to have immunomodulatory, anti-allergic and anti-inflammatory action.

CONCLUSION

Through this preliminary effort on analyzing the traditional medicinal plants for the management of Urticaria, the safety and potential of few of the selected the medicinal plants have been discussed and they have shown significant anti histaminic activity and mast cell stabilizing activity. These herbs with cost effectiveness, high therapeutic value, easy availability and least side effects may provide an outbreak to further explore its anti-allergic effects through preclinical and clinical studies in future.

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