

Anti-asthmatic activity of Siddha polyherbal formulation *Thoothuvalai Nei*

Research Article

Suvedha P^{1*}, Thirunarayanan G², Amala Hazel AM³, Meenakshi Sundaram M⁴

1. PG Scholar, 3. Guide & Associate Professor, 4. Professor, Department of Kuzhandhai Maruthuvam,
2. Medical Officer,
National Institute of Siddha, Chennai, Tamil Nadu, India.

Abstract

Background: Siddha medicine is a traditional Indian system of medicine which provides a comprehensive treatment for different kinds of diseases among which are respiratory problems. The Siddha system of medicine uses different types of herbals, minerals and therapeutic methods to handle respiratory ailments like wheezing, coughing and shortness of breath. *Thoothuvalai Nei* is a siddha polyherbal formulation with a traditional use in respiratory health. **Objectives:** This paper discusses the anti-asthmatic activity of *Thoothuvalai Nei* by means of pre-clinical experimentation. **Materials and Methods:** The study was carried out by giving *Thoothuvalai Nei* to Guinea pigs to find out if it had bronchodilator effect against histamine induced bronchospasm. **Results:** The research proved that after the treatment the Pre-convulsive Time (PCT) was much longer and thus the formulation appeared to be of great help in bronchospasm relief. The dose dependent reaction proved the therapeutic efficacy of the medicine, with the higher doses showing a greater protection. **Conclusion:** The above mentioned facts confirm the pharmacological value of *Thoothuvalai Nei* and it is better to include it as evidence based respiratory care in the healthcare practice. Thus, it is a way to connect traditional knowledge of siddha medicine with the latest and the best scientific knowledge of medical science.

Keywords: Anti-Asthmatic activity, Bronchodilator activity, Respiratory illness, *Solanum trilobatum*, *Thoothuvalai Nei*.

Introduction

Siddha system of medicine is an ancient Indian medical system that offers complete treatment plans for many conditions including respiratory problems. Herbs, minerals, and therapeutic techniques are used in the Siddha system of medicine to treat respiratory diseases such as wheezing, coughing, and shortness of breath(1). *Thoothuvalai Nei*, a Siddha poly herbal formulation known for its wide benefits to respiratory health(2, 3). In terms of years, asthma ranks 16th in living with disability and burden of illness, asthma ranks 16th and 28th globally, respectively, based on disability-adjusted life years. Globally, there are over 300 million asthma sufferers and by 2025, another 100 million people might probably be affected. Asthma severity, mortality, and prevalence vary greatly by geography. The majority of asthma-related death happens in low-middle income nations despite the fact that asthma prevalence is greater in high income countries(4).

The botanical name of *Thoothuvalai* is *Solanum trilobatum* Linn. (5) which is a natural beginning and

the credibility of home remedies for respiratory illnesses. *Thoothuvalai Nei* is a medicated ghee preparation which not only renders it convenient in its way of administration but also aids in quick absorption and right nutrition support, thus improving the therapeutic efficacy.

The various active compounds in *Solanum trilobatum* Linn. play a role in the detailed pharmacological profile which is in aggregate expectorant, protective effect, anti-inflammatory and anti-oxidant activity(6). Therefore this wide range of biological activities verifies its multi-purpose therapeutic nature for the variety of diseases like asthma. In particular, historical use of *Thoothuvalai Nei* as a remedy for a wide range of respiratory ailments, including *Kabha Thodam*, *Sayam* (Tuberculosis), *Elai* (Cold), *Irumal* (Cough), *Kasam*, *Seththumanoi*, *Megam*, *Uttinanoi* and *Vaayvu*, reflects its well-established reputation as an effective respiratory tonic(2,7). However, *Thoothuvalai Nei* is an established therapeutic siddha medicine, through an intensive investigation of thirty Guinea pigs after long fasts, will give hopes to fill the information gap between mainstream knowledge and current scientific evidence. This study hopes to provide clarification on the protective features of *Thoothuvalai Nei* against histamine aerosol evoked bronchospasm using comparison between asthma control, reference control and varying doses of *Thoothuvalai Nei*.

* Corresponding Author:

Suvedha P

PG Scholar, Department of Kuzhandhai Maruthuvam,
National Institute of Siddha,
Chennai, Tamil Nadu, India.
Email Id: suvevas95@gmail.com

Materials and Methods

Ingredients of Thoothuvalai Nei(2,7)

Thoothuvalai (*Solanum trilobatum* Linn.), Mulli(*Solanum anguivi* Lam), Kandangkattari (*Solanum surattense*, Burm.f), Kanchori (*Tragia involucrata*.Linn), Adathodai (*Justicia adhatoda* Clarke.), Milagu (*Piper nigrum*.Linn), Thippili (*Piper longum*), Kadukkai (*Terminalia chebula*. Retz), Chirukanchori (*Tragia cannabina*.Linn), Cow's Ghee, Cow's Milk, Chukku (*Zingiber officinale*, Rose), Thantrikkai (*Terminalia bellerica* (Gaertn.) Roxb.), Nellikkai (*Phyllanthus emblica* Linn.), Thaliam (*Taxus baccata* Linn.), Kottam (*Costus speciosus* (Koenig ex Retz) J.E.Smith), Akkarakaram (*Anacyclus pyrethrum* DC), Vaivilangam(*Embelia ribes*.Burm.f), Chirakam (*Cuminum cyminum*.Linn), Omam (*Carum copticum* Benth&Hook.f), Valmilagu (*Piper cubeba*.Linn f), Chittaratai (*Alpinia officinarum* Linn.), Perarattai (*Alpinia galanga* Linn.), Elam (*Elletaria cardamomum*, Maton.), Kirambu (*Syzygium aromaticum* (Linn) Merrill & Perry), Sathikkai (*Myristica fragrans* Houtt), Sathipathiri (*Myristica fragrans* Houtt).

Collection of raw drugs

The roots of *Thoothuvalai*, *Mulli*, *Kandangkattari*, *Kanchori*, *Chirukanchori*, *Adathodai* were collected from Villages in Salem district, Tamilnadu, India. Other raw drugs were bought from well-known reputed country drug shops in the Chennai district.

Source of sample

After getting authentication from Medicinal Botanist at National Institute of Siddha, Chennai, the trial drug *Thoothuvalai Nei* was prepared in the *Gunapadam* laboratory of National Institute of Siddha after proper purification under the supervision of the guide.

Preparation of Thoothuvalai Nei

Part I

Thoothuvalai - 25 palam (875 gm), *Mulli* - 4 palam (140 gm), *Kandangkattari* - 4 palam (140 gm), *Kanchori* - 4 palam (140 gm), *Adathodai* - 4 palam (140 gm), *Milagu* - 4 palam (140 gm), *Thippili* - 4 palam (140 gm), *Kadukkai* - 4 palam (140 gm), *Chirukanchori* - 4 palam (140 gm), *Water* - 2 thooni (43 litres)(2,7).

Part II

Cow's Ghee - 2 padi (2.68 litres), *Cow's Milk* - 2 padi (2.68 litres)(2,7).

Part III

Thirikadugu-3¼ varagan (15.6 gm), *Thiriphala* - 3¼ varagan (15.6 gm), *Thaliam* - 3¼ varagan (15.6 gm), *Kottam* - 3¼ varagan (15.6 gm), *Akkarakaram* - 3¼ varagan (15.6 gm), *Vaivilangam* - 3¼ varagan (15.6 gm), *Chirakam* - 3¼ varagan (15.6 gm), *Omam* - 3¼ varagan (15.6 gm), *Valmilagu*- 3¼ varagan (15.6 gm), *Chittaratta*-3¼ varagan (15.6 gm), *Peraratta*-3¼

varagan (15.6 gm), *Elam*- 3¼ varagan (15.6 gm), *Kirambu*-3¼ varagan (15.6 gm), *Sathikkai*-3¼ varagan (15.6 gm), *Sathipathiri* - 3¼ varagan (15.6 gm).

The decoction was made from the ingredients from part I. The ingredients of part II were added to the decoction. Part III ingredients were made as a paste by using cow's milk. After adding the grounded paste to the above decoction, the mixture was brought allowed to boil till it reach its consistency. Then it was kept in an airtight container(2,7).

Experimental Animals

Guinea pigs weighed 300–400gms and were of either sex provided by Biogen laboratory animal facility, Bangalore. Animals were acclimated for 10 days before dosing. Animals were randomized to treatment groups and housed in polypropylene cage. Temperature was 24±2°C and relative humidity 30–70%. The circadian rhythm was 12:12 hours with a light: day cycle. All animals were provided free access to water and fed with standard commercial pelleted (M/s. Hindustan Lever Ltd, Mumbai). All experimental procedures and protocols employed in this study were approved by the Institutional Animal Ethics Committee (688/PO/Re/S/02/CPCSEA) and were in accordance with Institutional Ethics Guidelines(8).

Bronchodilator Activity

Thirty Guinea pigs that had fasted for overnight were split up into five groups of five. Group I was designated as the asthmatic control group, Group II as the reference control group, and Group III, IV, and V as the oral administration of *Thoothuvalai Nei* 1.25ml/kg, 2.5ml/kg, and 5ml/kg, respectively. Guinea pigs were used to induce bronchospasm by subjecting them to a histamine aerosol (0.2%) created by an ultrasonic nebulizer within a Perspex glass aerosol chamber measuring 24 x 14 x 24 cm. Every animal was put in the histamine chamber and exposed to 0.2% histamine aerosol prior to receiving medication therapy. When exposed to histamine aerosol, guinea pigs gradually developed respiratory problems that eventually resulted in convulsions, asphyxia and death(9). Each animal's time required for the histamine-induced pre-convulsive dyspnea to manifest was noted. Pre-convulsion time (PCT) was defined as the interval between aerosol exposure and the start of dyspnea that precedes convulsion presentation. Upon detecting pre-convulsion dyspnea (PCD), the animals were taken out of the chamber and allowed to recover in an environment with clean air. The baseline value was noted as pre-convulsive dyspnea. After that, the guinea pigs were given a 24-hour period for recovery from dyspnea. The animals were again exposed to histamine aerosol after a 24-hour period, with intervals of one hour, four hours, and twenty four hours after the oral administration of *Thoothuvalai Nei* to the group III, IV, V and Chlorpheniramine Maleate (reference control) to group II in order to determine PCT. The treatment's protection was estimated following the administration of *Thoothuvalai Nei* at one hour, four hours, and twenty-four hours (Image 1,2,3) (8,10).

$$\text{Protection percentage} = (1 - T1/T2) \times 100$$

Where,

T1 = T1 is the mean PCT before test drug administration,
T2 = T2 is the mean PCT after 1 hour, 4 hours and 24 hours after test drug administration.

GraphPad was used to perform Dunnett's "t" test. P less than 0.05 was considered significant (8).

Results

In this study, *Thoothuvalai Nei* significantly raised the incidence of Pre-convulsion dyspnea after histamine aerosol exposure, the time between the beginning of convulsion symptoms, like breathing difficulties leading to convulsions, hypoxia and death is called preconvulsion time(9) and showed maximum protection of 51.76%, 54.89%, and 57.86% at 1 hour, 4 hours, and 24 hours, respectively, at the dose of 5ml/kg, while the control group's maximum protection, at 2 mg/kg of chlorpheniramine maleate, exhibited protection of 56.03%, 54.98%, and 58.63% at 1 hour, 4 hours, and 24 hours, respectively. Statistical analysis revealed ***P<0.001 vs Induced Control which is considered as significant. Effect and Percentage protection of *Thoothuvalai Nei* on histamine induced broncho spasm in guinea pigs are tabulated in Table 1 and 2.



Statistical Analysis

Mean± SEM was used to represent the data. Oneway ANOVA was used to analyse the data, and then

Table 1: Effect of *Thoothuvalai Nei* on histamine induced bronchospasm in guinea pigs

Groups & Drug Treatment	Pre-convulsive Time (Secs) Basal Value	Pre-convulsion Dyspnoea (Secs)		
		1 hour	4 hours	24 hours
Group I - Asthmatic control	124.80±3.72	127.40±2.75	126.6±1.47	136.60±0.93
Group II - Chlorpheniramine Maleate (2mg/kg)	127.60±3.03	290.20±4.13***	283.40±4.68***	308.40±4.78***
Group III - <i>Thoothuvalai Nei</i> (1.25ml/kg)	125.80±3.49	175.80±3.17*	184.60±1.81*	182.00±4.01*
Group IV - <i>Thoothuvalai Nei</i> (2.5ml/kg)	126.60±2.12	210.60±3.02**	223.40±2.38**	236.20±3.12***
Group V - <i>Thoothuvalai Nei</i> (5ml/kg)	123.40±2.04	255.80±2.75***	273.60±5.18***	292.80±3.76***

Values are in mean ± SEM (n=5), *P<0.05, **P<0.01, ***P<0.001 Vs Induced Control

Table 2. Percentage protection of *Thoothuvalai Nei* on histamine induced broncho spasm in guinea pigs

Groups & Drug Treatment	% Protection		
	After 1hour	After 4hours	After 24 hours
Group I - Asthmatic Control	2.04	1.42	8.64
Group II - Chlorpheniramine Maleate (2mg/kg)	56.03	54.98	58.63
Group III - <i>Thoothuvalai Nei</i> (1.25ml/kg)	28.44	31.85	30.88
Group IV - <i>Thoothuvalai Nei</i> (2.5ml/kg)	39.89	43.33	46.40
Group V - <i>Thoothuvalai Nei</i> (5ml/kg)	51.76	54.89	57.86

Discussion

The aim of the study was to find out the anti-asthmatic properties of a Siddha polyherbal preparation *Thoothuvalai Nei* which is well known for its traditional use in the treatment of various respiratory ailments due to its herbal components(2, 7). Asthma is a major non-communicable disease (NCD) that affects both children and adults and is the most common chronic disease in children(11). The Global Burden of Disease estimates the total asthma burden in India at 34.3 million, which is 13.09% of the global burden. It was also found that 13.2 people die from asthma per thousand(12). In this study, the Siddha polyherbal preparation *Thoothuvalai Nei* significantly inhibited histamine-induced contraction in guinea pigs, indicating its H1-receptor antagonist activity and supporting the anti-asthmatic properties of the Siddhadrug(13). Histamine induced broncho constriction is a traditional immunological model of antigen induced airway obstruction. When

inhaled, histamine causes hypoxia and convulsions in guinea pigs and causes very strong smooth muscle contraction, profound hypotension and capillary dilation in the cardiovascular system(14). A significant effect caused by histamine causes severe broncho constriction in guinea pigs, leading to suffocation and death. Bronchodilators may delay the onset of these symptoms(15). The results of the study confirmed the bronchodilator properties of the siddha medicine *Thoothuvalai Nei*. On the other hand, the dose-dependent response demonstrates that the formulation possesses greater therapeutic efficacy, as higher doses provide increased protection against bronchospasm. The percentage of protection observed in this study is relatively higher compared to similar studies conducted on other formulations such as *Linga Mathirai*(16), thereby supporting its traditional use in the treatment of bronchial asthma and other respiratory disorders.(2, 7). The molecular docking study of phytochemicals

retrieved from *Thoothuvalai Nei*, including solasodine, ascorbic acid, apigenin, quercetin, vasicoline, piperic acid, piperine, gingerenone-A, chebuloside, betulonic acid, phellandrene, diosgenin, palmitic acid, embelin, beta-sitosterol, germacrene, nerolidol, kaempferol, and elemicin, revealed significant interactions with the core active amino acid residues of the histamine H1 receptor(17). These interactions suggest that the observed anti-asthmatic effects of *Thoothuvalai Nei* in this study may be attributed to the above mentioned phytochemical constituents.

Conclusion

This study emphasizes the anti-asthmatic effect of *Thoothuvalai Nei* against Histamine induced broncho spasm, this finding open the way for further bronchodilator studies against other inflammatory mediators can be devoted to the mechanism of action and its efficacy in clinical practice in order to utilize the therapeutic possibilities of *Thoothuvalai Nei* in the management of respiratory health.

Conflict of interest:

The authors announce that there are no competing interests.

Acknowledgements:

We greatly acknowledge Prof. Dr. R. Meenakumari, Director, National Institute of Siddha, Chennai, and Faculty members of Department of Kuzhanthai Maruthuvam, National Institute of Siddha, Chennai for their constant support and help throughout this work.

References

1. Muthukumar N.J, Visweswara. S. Siddha System of Medicine- The Science of Holistic Health. New Delhi; Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH), Government of India; 2019.1,53,63p.
2. Kuppusamy Mudhaliyar, Uthamarayan. Siddha Vaidhiya Thiratu. 1sted, Chennai; Department of Indian Medicine & Homoeopathy; 2014. 250p.
3. Siddha Treatment Guidelines for Selected Diseases. Chennai; National Institute of Siddha (An Autonomous Body under Department of AYUSH), Ministry of Health & Family Welfare, Government of India; 2014. 75p.
4. Dharmage S.C, Perret J.L, Custovic A. Epidemiology of Asthma in Children and Adults. *Front Pediatr.* Jun ,2019; 18;7:246.
5. Somasundharam. Taxonomy of Angiosperms. 1st ed. Tirunelveli; *Ilangovan Pathippakam*; 2006. 149p.
6. Ranjith M.S, Ranjitsingh A.J, Shankar S.G, Vijayalaksmi G.S, Deepa K, Babu K, Sidhu H.S. *Solanum trilobatum* in the management of atopy: Through inhibition of mast cell degranulation and moderation of release of interleukins. *Pharmacognosy Res.* Jan,2010;2(1):10-4.
7. The Siddha Formulary of India Part-I. 1st ed. Delhi; Ministry of Health and Family Welfare Department of Health, Government of India; 1992. 133-134p.
8. Kumar D, Bhujbal S.S, Deoda R.S and Mudgade S.C. In-vitro and In-vivo Antiasthmatic studies of *Ailanthus excelsa* Roxb. on Guinea Pigs. *Journal of scientific research.* 2010; 2 (1), 196-202.
9. Vir D.K, Evaluation of AntiAsthmatic and Anti-Cholinergic Activity of Ethanolic Extract Of *Artocarpus Heterophyllus* Linn Leaves. *J. Adv. Pharm. Edu. & Res.* 2016; 6(4): 22-26.
10. Singh, Surender, Agrawal, Shyam S. Bronchorelaxant Activity of *Belamcanda Chinensis* (Adans). *Indian Journal of Pharmacology.* Apr-Jun,1990; 22(2): 107-109.
11. <https://www.who.int/news-room/fact-sheets/detail/asthma> dated 06- 05- 2024
12. Singh S, Salvi S, Mangal D.K, Singh M, Awasthi S, Mahesh P.A, Kabra S.K, et al. Prevalence, time trends and treatment practices of asthma in India: the Global Asthma Network study. *ERJ Open Res.* May,2022; 30;8(2):00528-2021.
13. Nayampalli Sunanda S, Desai N.K, Ainapure S.S, Antiallergic Properties of *Tinospora Cordifolia* in Animal Models. *Indian Journal of Pharmacology.* Oct-Dec,1986; 18(4); 250-252.
14. Taur D.J, Patil R.N, Patil R.Y. Antiasthmatic related properties of *Abrus precatorius* leaves on various models. *J Tradit Complement Med.* Jan,2017; 12;7(4):428-432.
15. Srivastava A.K, Nagar H, Srivastava R, Ahirwar V, Chandel H.S. Evaluation of antitussive and anti-asthmatic activity of *Tabernaemontana divaricata* (L.) R. Br. *Ex Roem. And Schult. Ayu.* Jul-Dec,2016;37(3-4):256-263.
16. Parthiban P, Kanagavalli K, Sathiyaraj Rajeswaran P, Anbu J, Parthiban N.T, Evaluation of Anti-Histaminic and Bronchodilator Activity of *Linga Mathirai*. *International Journal of Pharma Research & Review,* May 2013; 2(5):8-12
17. Suvedha P, Thirunarayanan G, Eswari S, Amala Hazel A.M, Meenakshi Sundaram M, Molecular Docking Study to Evaluate Anti-Allergic and AntiInflammatory Activity of Siddha Poly Herbal Formulation *Thoothuvalai Nei*. *Indian Journal of Natural Sciences.* October,2024; 15(86); 81014-81027.
