Research Article

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EVALUATION OF ANTI-INFLAMMATORY ACTIVITY OF SIDDHA HERBO-MINERAL FORMULATION: SURANGUSA PARPAM

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ABSTRACT

Introduction: Medicinal plants, minerals and some marine products can potentially treat medical conditions in the long term based on error and trial methods. Surangusa parpam, one of the Siddha herbo-mineral formulations, is mentioned in the classical Siddha text and indicated for respiratory illnesses like cough, cold, fever, bronchial asthma and intestinal tuberculosis. Objectives: This study was designed to evaluate the anti-inflammatory activity of the trial drug Surangusa parpam. Materials and Methods: The trial drug Surangusa parpam is prepared as per literature and inflammation is induced in the experimental animal's carrageenan-induced paw oedema model. The trial drug Surangusa parpam and standard indomethacin are given orally for the anti-inflammatory effects. The anti-inflammatory effects were measured at regular intervals, and the percentage of the inhibition of paw oedema was to compare the effect of the trial medicine with the control and standard. Results: The trial drug showed significant improvement in the percentage inhibition of paw oedema in graded doses compared to control in the carrageenan-induced paw oedema model. 15 and 35 mg/kg of the trial drug showed significant inhibition of paw oedema at 55.9 % and 58.9 % compared with the control. Conclusion: Anti-inflammatory activity is seen with the graded dose of the trial drug. It can be concluded that the herbo-mineral formulation showed significant anti-inflammatory activity.

Keywords: Anti-inflammatory, Carrageenan-induced paw oedema, Herbo-mineral preparation, Siddha formulation, Surangusa parpam.

INTRODUCTION

Inflammation is the body's response against invading pathogens, typically characterized by redness, swelling, pain, and heat. Several reports have provided evidence that inflammation is involved in the pathogenesis of many diseases [1]. Acute inflammation is a process that consists of the overproduction of free radicals, activation of a complex enzyme, and release of several inflammatory and pro-inflammatory mediators. The carrageenan-induced paw oedema is a well-known acute inflammation model widely used for screening novel anti-inflammatory compounds. Carrageenan injection into the sub-plantar surface of rat paw-induced biphasic oedema. The early phase observed around 1 h is related to the release of histamine, serotonin, bradykinin, and to a fewer extent, prostaglandins produced by cyclooxygenase enzymes (COX), whereas the delayed phase (after 1 h) is attributed to neutrophil infiltration, and the continuing of the prostaglandin generation [2]. Release of the neutrophil-derived free radicals, nitric oxide (NO) and pro-inflammatory cytokines such as tumour necrosis factor (TNF-α) and interleukin-1 β (IL-1 β) also involved in the delayed phase of carrageenan-induced acute inflammation[3]. Different observations suggest that drugs targeting COX enzyme, free radical formation and pro-inflammatory protein expression (e.g., inducible nitric oxide synthase; iNOS) might provide better control over inflammatory states than the available therapeutic agents [4]. Carrageenan-induced paw oedema is one of the most popular tests to screen African spices and vegetables for anti-inflammatory activity [5].

It is a susceptible and reproducible test for nonsteroidal anti-inflammatory drugs and has long been established as a valid model for studying new anti-inflammatory drugs [5,6]. Carrageenan-induced inflammation is useful in detecting orally active anti-inflammatory agents; therefore, it has significant predictive value for anti-inflammatory agents acting through mediators of acute inflammation [7]. Developing oedema induced by carrageenan injection causes an acute and local inflammatory response. In the early phase (0–1 h), histamine, serotonin, and bradykinin are the first mediators involved, whereas prostaglandins and various cytokines such as IL-1β, IL-6, IL-10, and TNF-α are implicated in the second phase [8]. According to the WHO report, about 70–80% of the world's population rely on nonconventional medicine, mainly from herbal sources, in their primary health care [9]. Its demand is increasing daily in developing countries where the cost of consulting a physician and the price of medicine are beyond the limit of most people.

Many formulations for respiratory illness are mentioned in the Siddha system of medicine. Surangusa Parpam (SP) is one of the Siddha drugs mentioned in the Siddha text [11], and it is useful to treat kapha (Phlem) diseases like cough, Bronchial asthma, fever, intestinal TB etc. The ingredients of Surangusa Parpam (SP) are Manosilai (arsenic di sulphide), Sangu (conch – Shell – *Turbinella pyrum L*), and Milagu (Pepper - *Piper longum*). When traditional literature was reviewed, it revealed that Manosilai (arsenic di sulphide) has antimicrobial [12], anti-asthmatic properties [13], and Sangu (conch – Shell – *Turbinella pyrum L*) has anti-inflammatory and antipyretic properties [14]. The research articles revealed that the individual of some ingredients of SP

possesses anti-inflammatory activity. Still, as a finished product, no pharmacological activities had been carried out for this formulation. Based on the abovementioned, this study aimed to assess the anti-inflammatory effect of Surangusa parpam in carrageenan-induced paw oedema in rats.

MATERIALS AND METHODS

Ingredients of SP

1. Purified Manosilai (Arsenic di sulphide) - 4 Varagan (14 g)
2. Purified Sangu (Conch – Shell – *Turbinella pyrum L*) - 4 Varagan (14 g)
3. Purified Milagu (Pepper - *Piper longum*) - 4 Varagan (14 g)

Uses

1. Suram (Fever)
2. Kaasam (Cough)
3. Ulaimaanthai (Tuberculosis of the lung or incurable internal abscess)

The raw drugs were procured from a well-reputed country shop in Parrys Corner, Chennai. All the ingredients were purified and the medicine was prepared in the Gunapadam (Siddha Pharmacology) laboratory of the National Institute of Siddha, Chennai – 47. The plant material Milagu (Pepper - *Piper longum*) was identified and authenticated by the Assistant Professor, Department of Medicinal Botany, National Institute of Siddha. The raw drug Manosilai (Arsenic di sulphide) and Sangu (Conch – Shell – *Turbinella pyrum L*) was authenticated by the faculty member, Department of Gunapadam (Siddha Pharmacology), National Institute of Siddha, Chennai – 47.

Purification of the raw drugs: All the drugs mentioned here were purified as per the Siddha literature.

Purification of Manosilai (Arsenic di sulphide): Red orpiment (35 grams) is made into small pieces and kept soaked in 175 g of fermented buttermilk in a clay vessel. It was isolated and kindling was done frequently. In the evening, it is washed in water. The same procedure was repeated three times to get purified form [15].

Purification of Sangu (Conch – Shell – *Turbinella pyrum L*): Take equal quantities of limestone and fuller earth and add water eight times the weight of the conch. Put the conch into it and boil it well to purify it [15].

Purification of Milagu (Pepper - *Piper longum*): *Piper nigrum* is soaked in buttermilk for 1 ½ hours and then dried and roasted to purify it [15].

Method of Preparation

The above ingredients are soaked in goat urine 2 ½ palam (Siddha Measurement) (87.5 g) and kept for 3 days. On the fourth day, the contents are rubbed for 3 days with the same urine in which they are soaked. Then they are made into pellets and dried. The dried pellets are placed in a mud plate and then covered by a similar mud plate. The margins are covered by a mud-pasted cloth, dried and then subjected to pudam (Incineration) with cow dung cakes 20 times the weight of sealed mud plates. Again the process is repeated once. Being cooled, the lid is opened, and the processed medicine thus obtained is collected and kept in an airtight container. The dosage of the SP is 1 – 2 Kundri (Siddha Measurement) (130 – 260 mg), Twice a Day, after food, and the adjuvant and duration are honey and 48 days, respectively [11].

Ethical Clearance

Before the commencement of the study, the Anti-inflammatory activity experimental protocol was approved by the Institutional Animal Ethics Committee of the National Institute of Siddha, Chennai – 47, with approval number NIS/IAEC-V/09082017/07.

Animals

The present study was conducted in experimental animals, i.e., Albino Wistar rats. The animals were kept in polypropylene cages with husk bedding in the animal house. Wistar rats of either sex weighing between 140 and 160 g (6 – 8 weeks old) were chosen for the carrageenan-induced paw oedema model. They were maintained under standard laboratory conditions (12 h light and dark cycle), temperature (24°C ± 3°C), humidity (30 - 60% ± 10%) with access to food and water ad libitum as per the Organization for Economic Cooperation and Development guidelines, revised draft guidelines 425 and by the Committee for the Purpose of Control and Supervision of Experiments on Animals [16]. The acclimatization period is about 2 weeks before subjecting them to experimentation.

Assessment of anti-inflammatory activity – Carrageenan-induced paw oedema method

The anti-inflammatory activity was evaluated in male albino rats of the Wistar strain (140 - 160 g) by carrageenan-induced rat paw oedema. The animals were divided into 4 groups of 6 animals each. The first group received 10 ml/kg b.wt of honey orally and served as a control. The second animal group was administered indomethacin (10 mg/kg b.wt, p.o.). The animals of groups 3 and 4 were treated with SP (15 mg/kg b.wt and 35 mg/kg b.wt, orally). Acute inflammation was produced by sub-plantar injection of 0.1 ml of 1% suspension of carrageenan in normal saline in the right hind paw of the rats, 1 h after oral drug treatment. The paw volume was measured by a plethysmography method at 0, 1, 2 and 3 h after the carrageenan injection. Each paw volume was measured by dipping in a mercury plethysmometer up to the mark described by Chattopadhyay *et al.* [17]. Readings were re-up taken at 1, 2, and 3 h [18]. The difference between the two readings was taken as the volume of oedema, and the inhibitory percentage of inflammatory reaction was determined for each animal by comparing it to the control and calculated by the formula described by Sudjarwo Agus [19, 20].

$$\text{Percentage of inhibition} = (1 - Et/Ec) \times 100$$

Where Ec = Edema of the control (Group I)
Et = Edema of the treated (Group II–V)

Table 1: Anti-inflammatory activity of SP by carrageenan-induced paw oedema method in rats.

Treatment	Paw volume (ml) (Percentage of Inhibition)			
	0 h	1 h	2 h	3 h
Group I - Control (Honey)	1.66±1.09 (0.0)	1.74±0.73 (0.0)	1.80±0.71 (0.0)	1.68±0.05 (0.0)
Group II –Indomethacin 10mg/kg	1.60±0.82 (3.6)	1.27±0.87 (27)	0.89±0.81(50.5)	0.50±0.72* (70.2)
Group III – SP 15mg/kg	1.64±0.41 (1.2)	1.35±0.13 (22.4)	0.98±0.69 (45.5)	0.74±0.24* (55.9)
Group IV – SP 35mg/kg	1.65±0.10 (0.6)	1.29±0.95 (25.8)	0.95±0.63 (47.2)	0.69±0.56* (58.9)

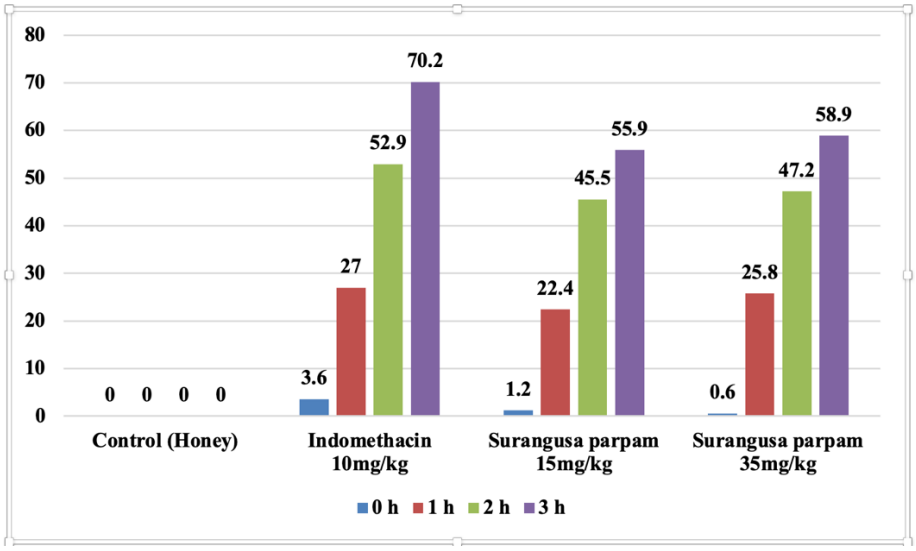

Figure 1: Anti-inflammatory activity of SP on rats by carrageenan-induced paw oedema model showing percentage inhibition

RESULTS AND DISCUSSION

In the carrageenan-induced rat paw oedema test, the SP at 15 and 35 mg/kg showed gradual inhibition of paw oedema at the end of 1st h after giving the carrageenan in the rat paw in comparison to the control. At the 1st h, the doses of 15 and 35 mg/kg showed a 22.4 % and 25.8% percentage inhibition compared to the control. On the other hand, at 35 mg/kg, the SP showed significant inhibition ($P < 0.05$) of paw oedema at the end of 3rd h after giving the carrageenan in the rat paw compared to the control. At the 2nd h, the doses of 15 and 35 mg/kg showed percentage inhibition of 45.5 % and 47.2 % in comparison to the control, and at the end of the 3rd h, the graded doses of SP showed a percentage inhibition of 55.9 % and 58.9 % in comparison with control. Whereas the standard drug Indomethacin showed very significant inhibition of paw oedema of rats ($P < 0.05$) 3rd h with percentage inhibition of 70.2 %, in comparison to the control [Table 1 and Figure 1].

The Carrageenan model is commonly used for anti-inflammatory evaluation as it is highly reproducible with apparent and no systemic side effects. Carrageenan develops oedema in the rat's paw in a biphasic event [21]. The initial phase of inflammation produced by carrageenan causes the release of histamine and serotonin in the 1st hour. While the second phase is related to the release of prostaglandin-like substances, protease and lysosome in 2 – 3 hours and these mediators produce oedema in the rat paw [8, 22]. These mediators contribute to the dilation of vessels with extravasations of fluid and plasma proteins with the formation of oedema [23]. These mediators, as the metabolites of arachidonic acid and its cyclooxygenase pathway, can produce the characteristic signs of inflammation: vasodilatation, hyperemia, pain, oedema, and cellular filtration. Oral administration of SP at the doses 15 mg/kg and 35 mg/kg showed significant ($P < 0.05$) per cent inhibition of oedema at the end of 2 and 3 h as compared to the control [Table 1 and Figure 1].

CONCLUSION

Herbo-mineral medicines have been used for various illnesses for many centuries. Due to better availability, affordable cost, and fewer side effects, they have immense potential. Ingredients of SP Manosilai (Arsenic di sulphide), Milagu (*Piper nigrum*) and Sangu *(Turbinella pyrum)* have various medicinal values. Therefore, the present study was planned to evaluate the medicinal properties of herbo-mineral preparation of SP. The ingredients of SP were found to have various pharmacological actions due to their various constituents. Anti-inflammatory activity was noted in a dose-dependent manner in acute (carrageenan-induced hind paw oedema model). The anti-inflammatory activity of SP is due to its major ingredients of Manosilai (Arsenic di sulphide), Milagu (*Piper nigrum*) and Sangu *(Turbinella pyrum)*. They decrease the chemical mediators of inflammation. It can be concluded that the herbo-mineral preparation SP in graded doses (15 mg/kg and 35 mg/kg) demonstrated significant anti-inflammatory activity on experimental animals in this study.

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REFERENCES

1. Ghorbanzadeh B, Mansouri MT, Hemmati AA, Naghizadeh B, Mard SA, Rezaie A. A study of the mechanisms underlying the anti-inflammatory effect of ellagic acid in carrageenan-induced paw oedema in rats. Indian Journal of Pharmacology. 2015;47(3):292.
2. Gilligan JP, Lovato SJ, Erion MD, Jeng AY. Modulation of carrageenan-induced hind paw oedema by substance P. Inflammation. 1994;18(3):285–92.
3. Halici Z, Dengiz GO, Odabasoglu F, Suleyman H, Cadirci E, Halici M. Amiodarone has anti-inflammatory and anti-oxidative properties: An experimental study in rats with carrageenan-induced paw oedema. European Journal of Pharmacology. 2007;566(1-3):215–21.
4. Ronchetti D, Borghi V, Gaitan G, Herrero JF, Impagnatiello F. NCX 2057, a novel no-releasing derivative of ferulic acid, suppresses inflammatory and nociceptive responses in *in vitro* and *in vivo* models. British Journal of Pharmacology. 2009;158(2):569–79.
5. Winter CA, Risley EA, Nuss GW. Carrageenin-induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. Experimental Biology and Medicine. 1962;111(3):544–7.

6. Willoughby DA, DiRosa M. Studies on the mode of action of non-steroid anti-inflammatory drugs. Annals of the Rheumatic Diseases. 1972;31(6):540–.
7. Morio F, Susumu T. The effect of locally injected anti-inflammatory drugs on the carrageenin granuloma in rats. Biochemical Pharmacology. 1969;18(2):475–84.
8. Crunkhorn Pearl, Meacock SC. Mediators of the inflammation induced in the rat paw by Carrageenin. British Journal of Pharmacology. 1971;42(3):392–402.
9. Ramsay S. Who launches first global strategy on traditional medicines. The Lancet. 2002;359(9319):1760.
10. Barua CC, *et al*. Antinociceptive activity of methanolic extract of leaves of *Achyranthes aspera* Linn. (Amaranthaceae) in Animal Models of Nociception. Indian J Exp Biol. 2010;48(8):817-21. PubMed PMID: 21341540.
11. PM Abdullah Saibu, Anuboga Vaithiya Navaneetham Part III; Ramachandran SP, editor. 2nd ed. Chennai: Thamarai Noolagam: 2001. p. 90.
12. Lokesh Kumar G, Mahendra S, Richa S, Rajesh D. Pharmaceutico analytical study and comparative antimicrobial effect of Hartala bhasma and Hartalagodanti bhasma. Int J Ayu Pharm Res [Internet]. 2015 Dec.13:1(3).
13. Mashru M, Shukla VJ, Ravishankar B, Prajapati PK, Galib R. Effect of Sameera pannaga rasa (arsenomercurial formulation) in the management of Tamaka Shwasa (bronchial asthma) - randomized double blind clinical study. AYU (An International Quarterly Journal of Research in Ayurveda). 2013;34(4):346.
14. Walter TM. Pharmacological evaluation of the anti-inflammatory activity of Sangu Parpam (conch) – a Siddha medicine [Internet]. Academia.edu. 2014 [cited 2023Mar3]. Available from: https://www.academia.edu/541492/Pharmacological_evaluation_of_the_Anti_inflammatory_activity_of_Sangu_Parpam_Conch_A_Siddha_Medicine.
15. Aanaivaari Anandhan, editor. Sarakku Suthi Sei Muraigal, 1st ed. Chennai: Siddha Maruthuva Nool Veliyettu Pirivu, Department of Indian Medicine and Homeopathy 2008, p. 72, 110, 13.
16. Test no. 425: Acute oral toxicity: Up-and-down procedure: En [Internet]. OECD. [cited 2023Mar3]. Available from: https://www.oecd.org/env/test-no-425-acute-oral-toxicity-up-and-down-procedure-9789264071049-en.htm
17. Chattopadhyay RN, Chattopadhyay R, Roy S, Moitra SK. A simple method for plethysmometric measurement of paw volume of small laboratory animals in evaluation of anti-inflammatory effects. Bull Calcutta School Trop Med. 1986;34:5–8.
18. Sattayasai J, Bantadkit J, Aromdee C, Lattmann E, Airarat W. Antipyretic, analgesic and anti-oxidative activities of *Aquilaria crassna* leaves extract in rodents. Journal of Ayurveda and Integrative Medicine. 2012;3(4):175.
19. Sudjarwo SA. The potency of piperine as an anti-inflammatory and analgesic in rats and mice. Folia Med Indones 2005;41:190-4.
20. Kolawole O. Evaluation of anti-inflammatory and antinociceptive potentials of *Khaya senegalensis* A. Juss (Meliaceae) stem bark aqueous extract. British Journal of Medicine and Medical Research. 2013;3(2):216–29.
21. Vinegar R, Schreiber W, Hugo R. Biphasic development of carrageenin edema in rats. J Pharmacol Exp Ther. 1969;166(1):96-103.
22. Oates JA, Wood AJJ, Brooks PM, Day RO. Nonsteroidal anti-inflammatory drugs — differences and similarities. New England Journal of Medicine. 1991;324(24):1716–25.
23. Peana A, Moretti M, Manconi V, Desole G, Pippia P. Anti-inflammatory activity of aqueous extracts and steroidal sapogenins of *Agave americana*. Planta Medica. 1997;63(03):199–202.

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