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An *Ex Vivo* Analysis of Siddha Herbo-Marine Formulation *Muthuchippi Parpam* for Evaluation of Antihistamine Potential

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Abstract: Allergic reactions are mediated by histamines, which cause various symptoms like itching, sneezing, and inflammation. Antihistamines are commonly used to counter these effects. *Muthuchippi Parpam*, a traditional Siddha medicine, has been used for its purported antihistamine properties. This study aims to evaluate the antihistamine activity of *Muthuchippi Parpam.* The antihistamine activity of *Muthuchippi Parpam* was assessed using *ex vivo* method. *Ex vivo* studies involved histamine-induced contraction of isolated chick ileum at various concentrations of *Muthuchippi Parpam* to determine the dose-dependent effect. The *ex vivo* results demonstrated that *Muthuchippi Parpam* significantly inhibited histamine-induced contractions of the chick ileum and maximum inhibition of 36.8% was exhibited at a concentration of 20 µg. *Muthuchippi Parpam* exhibits significant antihistamine activity, supporting its traditional use in managing allergic reactions. These findings suggest that *Muthuchippi Parpam* could be a potential natural alternative to conventional antihistamines, warranting further clinical studies to confirm its efficacy and safety in humans.

Keywords: *Muthuchippi Parpam*, Antihistamines, Allergic reactions, Siddha medicine, Histamines,

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Introduction

Allergic reactions are a common health issue worldwide, characterized by symptoms such as itching, sneezing, swelling, and rashes. These symptoms are primarily mediated by histamines, which are released by mast cells and basophils in response to allergens (Aldakheel, 2021). The development of numerous allergic illnesses is greatly influenced by histamine and its receptors (H1R–H4R). The primary source of histamine in the body is mast cells, which are versatile tissue-dwelling cells that originate in bone marrow. Through the differential regulation of T helper cells, histamine plays a pivotal role in the pathogenesis of various allergy disorders,

including atopic dermatitis, allergic rhinitis, and allergic asthma (Thangam *et al.*, 2018). The management of allergic reactions often involves the use of antihistamines, which block the action of histamine at its receptors, thereby alleviating symptoms (Farzam *et al.*, 2024).

Muthuchippi Parpam is a traditional Siddha medicine known for its wide range of therapeutic benefits, including its use in managing allergic conditions. The Siddha system of medicine is one of the oldest holistic medical systems which has been practiced in India for thousands of years and utilizes a variety of natural substances for treatment. *Muthuchippi Parpam* is prepared from the shell of the pearl oyster (*Pinctada fucata*) through a meticulous process of purification and calcination, resulting in a fine, bioactive powder (Thiyagarajan, 2013; Abarna and Manjari, 2024). Recent research exhibited that oyster shell has anti microbial, anti-inflammatory, anti fibrotic, anti-osteoporotic and lipogenic activity (Ulagesan *et al.*, 2022). Despite its long-standing use in traditional medicine, scientific evidence supporting the antihistamine activity of *Muthuchippi Parpam* is limited. This study aims to bridge this gap by systematically evaluating the antihistamine properties of *Muthuchippi Parpam* using *ex vivo* methods. By elucidating its mechanism of action and efficacy, the study aims to validate its traditional use and explore its potential as a natural alternative to synthetic antihistamines.

This study focuses on the ability of *Muthuchippi Parpam* to inhibit histamine-induced contractions in isolated chick ileum (*ex vivo*). The outcomes of this research are expected to provide valuable insights into the therapeutic potential of *Muthuchippi Parpam* and its possible integration into modern allergy management protocols.

Materials and Methods

Ingredients of Muthuchippi Parpam:

1. *Pinctada fucata*
2. *Aloe vera*
3. *Alternanthera sessilis*

All the ingredients are collected and the preparation of *Muthuchippi Parpam* was done employing textual reference (Veeraperumal Pillai, 1999).

Antihistamine activity of Muthuchippi Parpam:

The ileum of a chick was procured from a local slaughterhouse, where the ileocaecal junction was recognized by lifting the caecum portion of the intestine. 2 to 3 cm section of the ileum was cut, extracted, and put in a watch glass with physiological saline solution promptly. Adequate measures were implemented to prevent disruption to the stomach muscle. A bath volume of approximately 25 ml was kept, and the tissue was given 30 min to acclimate before the test drug *Muthuchippi Parpam* (10 µg/ml - 80 µg/ml) was added. Ileal smooth muscle contractions were first induced by histamine and were captured on a kymograph employing a frontal writing lever. To record the responses properly, a contact time of 30 sec and a 5 min time cycle were maintained. Following the measurement of the normal response, the test drug *Muthuchippi Parpam* was incubated with the ileal preparation. The concentration-response curve of histamine was then observed, and the height of the response before and after the test drug incubation was measured to determine the antagonist effect of the test drug (Thavalakshmi *et al.*, 2022; Karthika *et al.*, 2023).

Results and Discussion

The data obtained from the current experiment showed that the height of response of the concentration response curve of histamine before incubation of test drug *Muthuchippi Parpam* ranged from 14 mm to 27 mm (Table 1; Figs. 1,2). Following incubation with test drug *Muthuchippi Parpam*, it ranges from 10 mm to 20 mm. There was a positive diminution in the height of the response curve.

Muthuchippi Parpam is derived from marine origin pearl oyster shell which is meticulously prepared employing incineration process. Pearl

Table 1: Effect of *Muthuchippi Parpam* on response of isolated chick ileum preparation

Dose in µg	Initial Response in mm (Before Incubation)	Final response in mm (After incubation with Test drug MP)
10	14	10
20	19	12
40	23	17
80	27	20

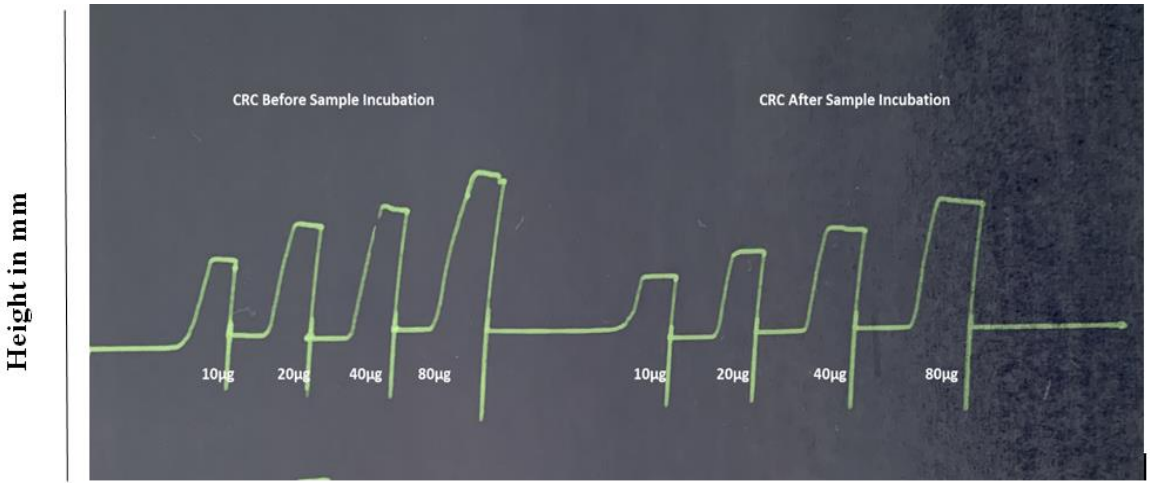

Fig. 1: Concentration response curve of histamine in absence and presence of the sample MP on Isolated chick ileum in optimized condition.

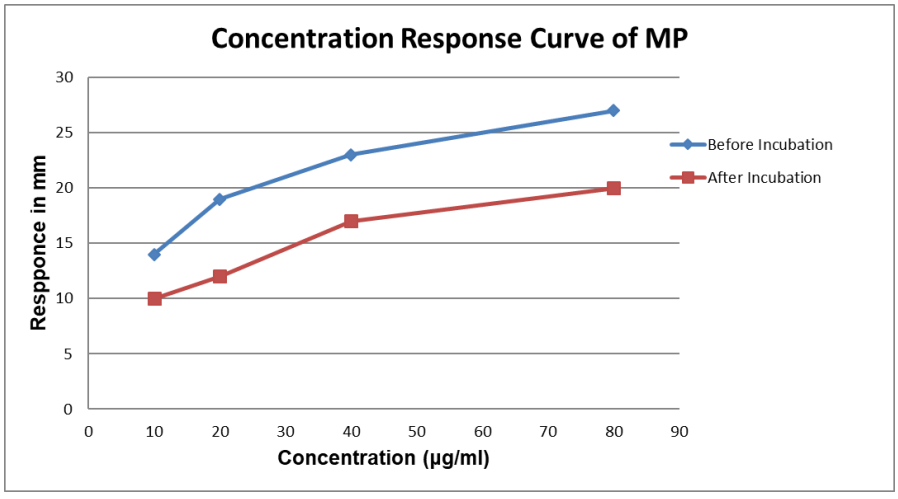

Fig. 2: Concentration response curve of histamine in before and after incubation with the sample MP on Isolated chick ileum in optimized condition.

oyster shell majorly consists of calcium carbonate in the form of aragonite (Upadhyay *et al.*, 2016) which is transformed to calcite during calcination (Abarna *et al.*, 2024).. The present study evaluated the antihistamine activity of *Muthuchippi Parpam* using an *ex vivo* model involving histamine-induced contractions in isolated chick ileum. The ileum is made up of smooth muscles which contain a higher amount of histamine H1 receptors (H_1R). Therefore, to obtain precise results chick ileum has been chosen for the present study (Wang *et al.*, 2024). Histamine H1 receptors are super family

containing G protein coupled receptors (GPCRs), which are considered as "cellular switches" that toggle between an inactive and active state, maintaining a balance (Church and Church, 2013). Our findings demonstrate a dose-dependent inhibition of histamine-induced contractions by *Muthuchippi Parpam*, supporting its potential as an effective antihistamine agent.

At a concentration of 10 µg, *Muthuchippi Parpam* reduced the histamine-induced contraction from 14 mm before incubation to 10 mm after incubation, indicating a 28.6% inhibition (Table 1). Increasing the concentration to 20 µg resulted in a more pronounced reduction, with the contraction size decreasing from 19 mm to 12 mm, corresponding to a 36.8% inhibition. At 40 µg, the contraction was reduced from 23 mm to 17 mm, showing a 26.1% inhibition. The highest concentration tested, 80 µg, exhibited the contraction from 27 mm to 20 mm, which represents a 25.9% inhibition. The greatest inhibition was observed at 20 µg accounting to 36.8% inhibition. These results suggest that *Muthuchippi Parpam* exhibits significant antihistamine activity. The decreasing contraction sizes post-incubation at all tested concentrations indicate that the preparation effectively interferes with histamine-induced smooth muscle contractions. However, it is noteworthy that the percentage inhibition did not increase linearly with the dose. This may suggest a threshold effect or saturation point beyond which higher concentrations do not proportionally increase efficacy, highlighting the need for further investigation to optimize dosage.

Contemporary antihistamine drugs are designed to counteract the effects of histamine, a compound involved in allergic reactions. These medicines are broadly classified as – (i) First generation antihistamines; and (ii) Second generation antihistamines. These drugs functions by blocking the H1 receptors, preventing histamine from exerting its effects on tissues, thus alleviating symptoms of itching, swelling and rashes (Farzam *et al.*, 2024).The antihistamine effect observed in this study aligns with the traditional use of *Muthuchippi Parpam* in managing allergic conditions. The results are particularly promising, as they suggest that even at relatively low concentrations, *Muthuchippi Parpam* can significantly mitigate histamine-induced reactions. One limitation of the study is the focus on *ex vivo* analysis, which, while informative, may not fully replicate the complexity of *in vivo* allergic responses. Future studies should include *in vivo* models to confirm these findings and to explore the pharmacokinetics and safety profile of *Muthuchippi Parpam* in a physiological context. Additionally, investigating the specific mecha-nisms by which *Muthuchippi Parpam* exerts its antihistamine effects could provide deeper insights into its therapeutic potential.

Conclusion

This study provides preliminary evidence supporting the antihistamine activity of *Muthuchippi Parpam*. These findings justify further research to fully elucidate its potential as a natural antihistamine and to explore its clinical applications in allergy management.

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Conflict of Interest

The authors declare no conflicts of interest.

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