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EVALUATION OF ANTI-HISTAMINIC ACTIVITY OF SIDDHA DRUG KARAPPAN MARUNDHU IN MALE GUINEA PIG

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Abstract: This study was initiated to investigate the Antihistaminic activity of Siddha trial drug *KARAPPAN MARUNDHU* in Male guinea pig. *Karappan Marundhu* is used in the treatment of *Varal Karappan* (Atopic Dermatitis). Male guinea pig weighing 350– 400g was kept in fasting condition 18 hours prior to commencement of experiment and given water ad libitum. It was then sacrificed by a blow to the head and exsanguinated as per CPCSEA recommended guidelines. The ileum was dissected and suspended in a 25 ml organ bath with tyrode's solution. The antihistaminic effect of Karappan Marundhu was tested in this bioassay at various concentrations (10, 20 and 40 µg/ml), in terms of their ability to prevent the histamine contractions when they were added to the bath 5 min before histamine and compared with the standard drug Chlorpheniramine maleate (10µg/ml). Responses to histamine were recorded as changes in height from baseline and expressed as percent of maximum response of the histamine. The CRC was constructed with a 20 min-rest between each. The test drug Karappan Marundhu ($P<0.05$) was found to be effective in their antagonism against histamine at 20 and 40 µg/ml when compared with that of the standard antagonistic drug. It is manifest that the Karappan Marundhu had shown marked antihistaminic activity in isolated tissue of guinea pig ileum.

Keywords: Karappan Marundhu, Siddha, Antihistaminic, Varal Karappan, Atopic Dermatitis.

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INTRODUCTION

Atopic dermatitis is characterized by superficial inflammatory edema of the epidermis associated with vesicle formation. Itching varies from mild to severe paroxysms which may even interfere with work and sleep. It can differ in severity, frequency and duration among individuals. Alarmingly, the prevalence of childhood Atopic Dermatitis has almost tripled since the early 1970's. Additionally, the past 10 years there is rapid increase in the prevalence of Atopic Dermatitis, which researchers now suggest are likely impacted by environmental factors. Global estimates, state 12-25% of children worldwide have Atopic Dermatitis.[1] Globally eczema affected are approximately 230 million people as of 2010 (3.5% of the population).[2] The lifetime clinician-recorded prevalence of eczema has been seen to peak in infancy, with female predominance of eczema presentations occurring during the reproductive period of 15–49 years.[3]

In siddha system of medicine it is described as Karappan. There are 18 types of Karappan and one among them is Varal Karappan which simulates most of the characteristic features of Atopic Dermatits. Varal Karappan is more predominant in children from 3-12 years of age. This skin disease was described by various Siddhars in detail about the general etiology, signs & symptoms and prognosis on the basis of three Thosha and Envagai thervugal, one of the causes of Karappan was consumption of non- vegetarian foods, intake of maize, pearl millet, foxtail millet, little millet and certain tuberous root [4]

AD can be usually controlled with corticosteroids, topical immuno modulators, moisturizers, topical calcineurin inhibitors, anti-histamines, and oral cyclosporines. It can produce adverse effects like skin thinning, possible hypothalamo pituitary-adrenal axis suppression, growth retardation in children and malignancies are caused due to prolonged use of immuno modulators[5]. Because of their side effects a newer effective drug with lesser side effects is necessary. In Siddha system of medicine many herbal drugs are non toxic, low cost, easily available, with their effectiveness in the treatment of AD mentioned in various Siddha literature. One of such medicine was Karappan Marundhu mentioned in the siddha text Agasthiar 2000. Karappan Marundhu is indicated for all types of Karappan. This drug mainly constitute Perumara Pattai (Sterculia foeitida), Kadugurohini (Picorrhiza kurroh), Sengathaari (Capparis seipiara), Karunseeragam (Nigella sativa), Sangan Vaer (Azima tetracantha), Poovarasam poo (thespesia populnea), Aadutheendapaalai (Aristolachia bracteolata), Gingelly oil (Seasamum indicum). All these drugs are individually indicated for karappan in siddha texts. Moreover it has mostly anti-inflammatory effect, antibacterial activity, antimicrobial activity, antioxidant, and antihistamine activity. Clinically the drug Karappan Marundhu had good results in treating the children with Varal Karappan.

MATERIALS AND METHODS:

Preparation of Karappan Marundhu:

Ingredients:

- Perumara Pattai (Sterculia foeitida)
- Chukku (Zingiber officinale)
- Seeragam (Cuminum cyminum)
- Kadugurohini (Picorrhiza kurroh)
- Chitrarathai (Alpinia galanga)
- Kandangathiri (Solanum surratense)
- Sengathaari (Capparis seipiara)
- Karunseeragam (Nigella sativa)
- Sangan Vaer (Azima tetracantha)

Preparation:

All the above drugs are collected in equal quantity and dried in sun shade. Then it is powdered finely.

ADJUVANT**:** Water

INDICATIONS: All types of Karappan.

EVALUTION OF ANTI-HISTAMINIC

Animal selection:

Male guinea pig weighing 350– 400g was kept in fasting condition 18 hours prior to commencement of experiment and given water *ad libitum*. It was housed under standard laboratory conditions of temperature (25 ± 2°C) and 12/12 hr light/dark cycle and then sacrificed by a blow to the head and exsanguinated as per CPCSEA recommended guidelines. The experimental procedures described were approved by the Institutional Animal Ethics Committee of Vels University, Pallavaram, Chennai- 117 (Approval no – XIV/VELS/PCOL/23/2000/CPCSEA/IAEC/20.11.2014)

ISOLATED GUINEA PIG ILEUM PREPARATION

Procedure:

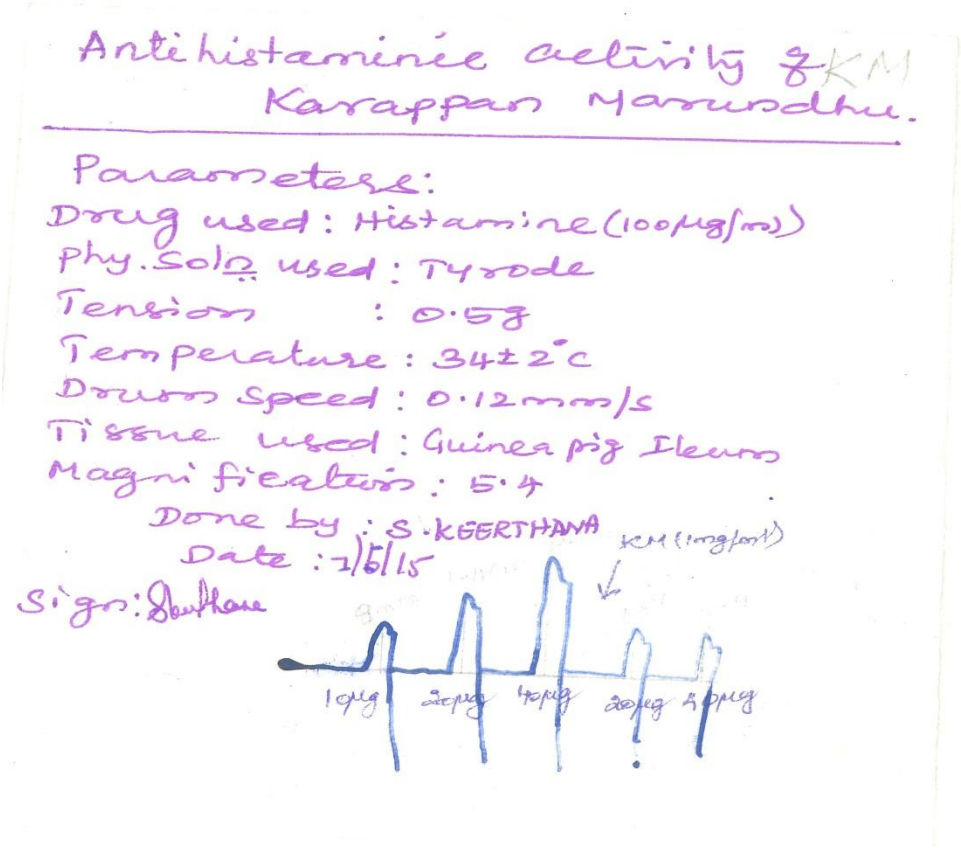
Guinea pig was sacrificed and a segment from ileum (2 cm) was dissected from the terminal ileum and mounted in an organ bath containing Tyrode solution (10 ml) between two stainless steel hooks under 0.5 to 1 g initial tension. The lower hook was fixed at the bottom of the organ bath and upper one was connected to an isotonic transducer. The Tyrode solution composition (pH 7.4) was (concentration in gm/lit.) NaCl 8.0, KCl0.2, CaCl2 0.2, MgCl2 0.1, NaHCO3 1.0, NaH2PO4 0.05, and Glucose1.0 gm/liter. It was continuously aerated and maintained at 37 ± 0.5ºC The equilibrium period was 60 min and the bath solution was refreshed every 15 min. After equilibrium period, a dose response curve for histamine in variant molar concentrations, by maintaining 45 min time cycle.

The antihistaminic effect of Karappan Marundhu was tested in this bioassay at various concentrations (10, 20 and 40 µg/ml), in terms of their ability to prevent the histamine contractions when they were added to the bath 5 min before histamine and compared with the standard drug Chlorpheniramine maleate (10µg/ml). Responses to histamine were recorded as changes in height from baseline and expressed as percent of maximum response of the histamine. The CRC was constructed with a 20 min-rest between each. The mean maximal response obtained from the first concentration–response curve was taken as the 100% response.

Table-1: Effect of Karappan Marundhu on isolated Guinea pig ileum preparation

S. No	Dose of Histamine (µg/ml)	Maximum response in cms	
		Histamine alone	Histamine+Karappan Marundhu (1mg/ml)
1	10	0.8±0.04	----
2	20	1.4±0.08	0.9±0.05*
3	40	2.1±0.10	0.9±0.04*

Values are expressed in mean ± SEM, *p< 0.05 compared with histamine induced contraction (21mm as 100%); n=3.



Statistical analysis

Results were expressed as mean±SEM. The data was analyzed by one way ANOVA followed by Dunnet's multiple comparison test for isolated ileum preparation. $P<0.05$ and $P<0.001$ were considered to be statistically significant.

RESULTS AND DISCUSSION

Histamine is one of the inflammogens that contributes to acute inflammation and increase of vascular permeability. It is reported earlier that the drug like phenylbutazone has the capacity to reduce the histamine concentration by decreasing the vascular permeability[6].

There are two generations in antihistamine, the first generation is also known as antihistamine1 (AH1). AH1 is lipophilic classic that can penetrate the blood brain barrier, causing sedation. Meanwhile, second-and third-generation AH has a better pharmacological profile. Both are more selective on the peripheral receptors and can also reduce lipophilicity, so that adverse

effects on the CNS are more minimal. AH of this new generation affect the release of mediators from mast cells by inhibiting calcium ion influx across the mast cells / basophils membrane or inhibit the release of intracellular calcium ions in cells. These drugs inhibit the allergic reaction by acting on leukotrienes and prostaglandins, or by generating an anti-platelet activating factor.[6,7]

Mast cell infiltration is estimated to play an important role in the pathogenesis of atopic dermatitis. In the atopic dermatitis there is an increased number of mast cells degranulation, more active and visible lesions licenification. The purpose of atopic eczema treatment is to relieve pruritus, suppress inflammation and improve skin texture. Histamine is pruritogen and concentration increased in some patients. Decrease in pruritus is often obtained with the use of H1 receptor antagonists which acts in atopic dermatitis because of its effect on the accumulation eosinophil. Atopic dermatitis can be divided into two immunological phenotypes according to disease conditions. TH2 immune phenotypes acts in acute exacerbations and dominant role in the chronic is TH1. TH1 and TH2 are mediated by immune cytokines IL-12 and IL-4. Here the effect of antihistamine is on the stimulation of production cytokines.

Antihistaminic activity of Karappan Marundhu was tested at various concentrations of 10 - 40 µg/ml, and Concentration-response curves were plotted to check their ability to reverse the activity of Histamine on prior (5 min) contact with the ileum. When evaluated against Histamine, the test drug Karappan Marundhu at 20 and 40 µg/ml significantly ($P<0.05$) antagonized the contraction of guinea pig ileum, in a competitive and concentration dependent manner. Fig.1 represents the contractile response elicited by Histamine on guinea pig ileum in presence and absence of the Karappan Marundhu.

Test drug Karappan Marundhu showed moderately significant antagonism ($P<0.05$) only at 40 µg/ml concentration when compared to control and the % maximal response wasn't decrease at lower concentrations of 10 and 20 µg/ml. Thus the exposure of guinea pig isolated ilem to Karappan Marundhu (20 and 40 µg/ml) for a period of 5 min produced a parallel, rightward shift of the Histamine concentration-response curve as is evident from the Fig.1.

CONCLUSION

In conclusion, the test drug Karappan Marundhu ($P<0.05$) was found to be moderately effective in their antagonism against histamine at 20 and 40 µg/ml when compared with that of the standard antagonistic drug. From the present findings, it is manifest that the Karappan Marundhu had shown marked antihistaminic activity in isolated tissue of guinea pig ileum.

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