



EVALUATION OF ANTI-HISTAMINE POTENTIAL OF SIDDHA FORMULATION VASANTHA KUSMAKARAM TABLET USING ISOLATED CHICK ILEUM PREPARATION

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ABSTRACT

Acute upper respiratory infections, including common cold, is one of the most prevalent infectious diseases in humans. Histamine a known autacoid play tremendous role in emphasizing the symptoms associated with allergy and cold which mainly mediated the inflammation, hyper secretion, dry cough etc. For the management of common cold and cough, antihistamines are used for their anticholinergic effects (i.e., drying up secretions), but in some patients, these anticholinergic effects can manifest as tachycardia, agitation and blurry vision. Typically, antihistamines are considered CNS depressants, causing drowsiness. In young children, however, a paradoxical effect, usually excitability, can be observed. Hence it is need of the hour to explore

medicine from alternate source that has rich anti histamine potential and with less sedation. In recent years; traditional therapies have gained in popularity for medical and economic reasons, in both developing and industrialized countries. Siddha system of medicine follows traditional healing physiology which was derived by ancient siddha physician called siddhars who are the pioneers in identification of drugs and elucidated the pharmacology of each component. Siddha medicine also works behind the synergy of componential formulation one such medicine is *Vasantha Kusmakaram* tablet (VKT) which has twelve versatile ingredients

which has tendency to synergies the action of each other in treating allergy and cold related symptoms. The main aim of the present investigation is to evaluate the anti-histamine potential of siddha formulation VKT using isolated chick ileum preparation. The results obtained from the present research have shown that treatment with VKT has significant reduction in height of the response induced by histamine in chick ileum preparation. Hence it was concluded that the formulation VKT has possess significant anti-histamine property and these pharmacological action may be possess by some of the bio active components which may be responsible for this property.

KEYWORDS: Allergy, Common cold, Histamine, Siddha system, Vasantha Kusmakaram, Anti-histamine.

1. INTRODUCTION

Histamine is a major mediator in allergic diseases, and has multiple effects that are mediated by specific surface receptors on target cells. Four types of histamine receptors have now been recognized pharmacologically and the first three are located in the gut. The ability of histamine receptor antagonists to inhibit mast cell degranulation suggests that they might be developed as a group of mast cell stabilizers.^[1]

Histamine plays an important role in human physiology, influencing immunoregulation of the acute and chronic inflammatory response through 4 different types of receptors, called H1, H2, H3, and H4. Drugs classified in the first generation of antihistamines (sometimes called “classical” antihistamines) act non-selectively. Apart from all histaminic receptors they also block muscarinic, adrenergic (or adrenoreceptors) and dopaminergic receptors, causing cardiovascular, urinary and gastrointestinal adverse reactions. High lipophilicity and consequently easy crossing of the blood-brain barrier additionally intensify the most dangerous adverse events from the central nervous system, including drowsiness, decreased concentration, vigilance and psychomotor efficiency as well as reduced ability to learn and memorize, which is not related to sedation. Allergic diseases are the most common chronic conditions lasting throughout the patient’s life. They not only cause significant deterioration in the quality of life of patients but also lead to significant absenteeism and reduced productivity, resulting in very high costs for society. Effective and safe treatment of allergic diseases is therefore one of the main challenges for public health and should be carried out by all the specialists in family medicine, internists and paediatricians in collaboration with allergists, otorhinolaryngologists and dermatologists. Antihistamines are most commonly

used in the treatment of allergies.^[2] Antihistamines are used in the management of allergic conditions. They are useful for treating the itching that results from the release of histamine. The early so-called 'first generation' antihistamines, such as promethazine, caused sedation.^[3]

Herbal supplements are widely used for the treatment of asthma should have anti-inflammatory, immunomodulatory, antihistaminic, smooth-muscle relaxants and allergic activity.^[4] Antioxidant supplements are effective in reducing bronchoconstriction severity by inhibiting pro-inflammatory events as a result of neutralizing the effects of excess reactive oxygen species and reactive nitrogen species.^[5] Current asthma therapy lack satisfactory success due to adverse effect, hence patients are seeking complementary and alternative medicine to treat their asthma.^[6]

Siddha medicinal preparation is formulated by greater intellectuals who are practiced and documented each formulation along with method of preparation, dosage, administration and procedure of detoxifying the metals if present. The total physiology of siddha basically derived by 18 siddhar's who classified fundamental elemental system of siddha treatment methodology. Present research work aimed at investing the anti-histamine potential of siddha formulation VKT using isolated chick ileum preparation.

2. MATERIALS AND METHODS

2.1. Ingredients

The formulation *Vasantha Kusmakaram* tablet comprises of the following ingredients

1. Lingam - *Mercuric Sulphide*
2. Vengaram - *Borax*
3. Lavangam - *Myrtus caryophyllus*
4. Thippili - *Piper Longum*
5. Kostam - *Saussurea lappa*
6. Akkirakaram - *Anacyclus pyrethram*
7. Adhimathuram - *Glycyrrhiza glabra*
8. Korosanai - *Purified Ox bile*
9. Kunguma Poo - *Crocus sativus*
10. Pachai Karpooram - *Camphora Officinarum*
11. Ginger - *Zingiber Officinale*
12. Cow's milk - Quantity sufficient

2.2. Preparation of *Vasantha Kusmakaram* Tablet^[7]

Each ingredient was purified well as per literature. Followed by this each ingredients were powdered in kalvam with Ginger juice for 2 days, and then with cow's milk for 2 days. Finally each tablet of 100mg were made and allowed for shade dry.

2.3. Anti-Histamine evaluation using Isolated chick ileum^[8]

Chick ileum was purchased from local slaughter house in which the caecum part of the gut was lifted to identify the ileocaecal junction. About 2- 3cm of the ileum portion was cut and removed and immediately placed it in the watch glass containing physiological salt solution. Sufficient care was taken to avoid the damage to the gut muscle. Bath volume of about 25 ml was maintained, and the tissue was allowed to equilibrate for 30 min before adding test drug. Initial response on histamine induces the contraction in the ileal smooth muscles which were recorded on Kymograph by using frontal writing lever. Contact time of 30 sec, and 5 min time cycle was kept for proper recording of the responses. After measuring normal response the ileal preparation were incubated with test drug at the concentration of 500 μ g (0.5ml) for brief period of time and the concentration response curved of histamine was then proceeded the height of response before and after incubation of test drug was measured for calculating the antagonist effect of the test drug.

3. RESULTS

3.1. Effect of VKT on response of isolated chick ileum preparation

It was observed from the data's obtained from the present investigation that the height of response of concentration response curve of histamine before incubation with test drug ranges from 22mm to 49 mm. There was a promising decrease in the height of the response curve after incubation with test drug VKT ranges from 7mm to 43 mm. As show in table 1, figure 1&2.

Table. 1: Effect of VKT on response of isolated chick ileum preparation.

Dose in mcg	Initial Response in mm (Before Incubation)	Final response in mm (After incubation with Test drug VK)
10	22 mm	7 mm
20	26 mm	12 mm
40	35 mm	14 mm
80	41 mm	34 mm
160	47 mm	37 mm
320	49 mm	43 mm

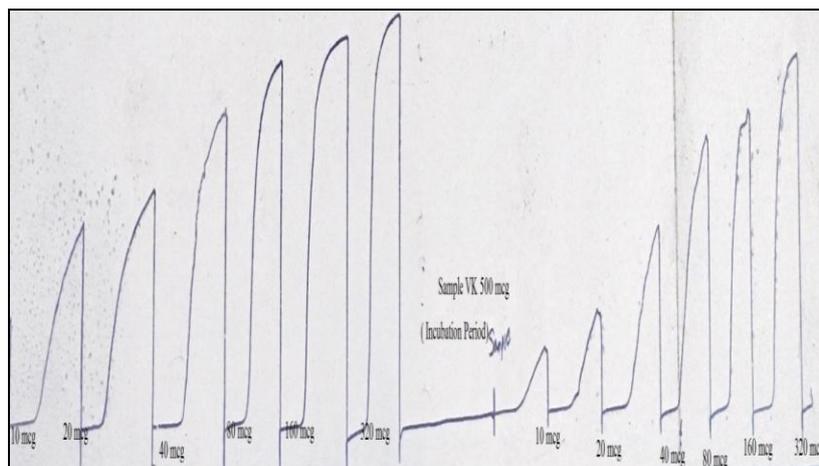


Figure. 1: Concentration response curve of histamine in absence and presence of sample VKT on Isolated chick ileum in optimized condition.

Concentration response curve of Histamine in absence and presence of sample VK tablet on Isolated chick ileum in optimized condition

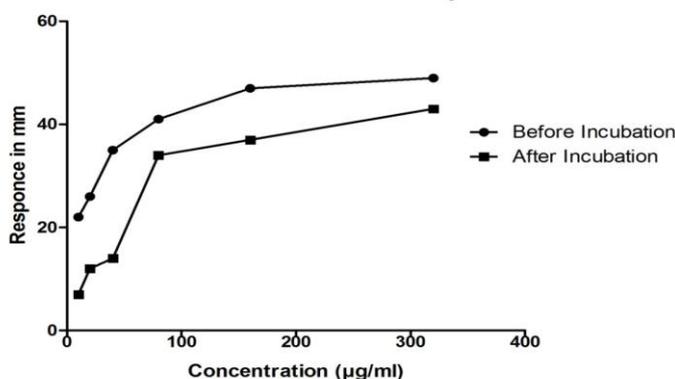


Figure. 2: Response curve of histamine in absence and presence of sample VKT.

4. DISCUSSION

The allergic process is believed to consist of two phases: early and late. The early phase reaction is mainly induced by histamine released from mast cells. Histamine is a potent vasoactive agent, bronchial smooth muscle constrictor, and stimulant of nociceptive itch nerves. In addition to its known effects on glands, vessels and sensory nerves, recent data have provided further evidence of histamine's proinflammatory actions.^[9] Histamine binding specific cell receptors produces clinical allergic symptoms. This mediator also activates neutrophils and eosinophils as well as being a chemoattractant for these cells.^[10] Histamine increases IL-8 level and evokes leukocyte rolling on endothelial cells. Thus histamine participates in both early and late-phase allergic responses.

Histamine is a primary amine synthesized from histidine in the Golgi apparatus, from where it is transported to the granule for storage in ionic association with the acidic residues of the glycosaminoglycans side chains of heparin and with proteinases. The histamine content of mast cells dispersed from human lung and skin is similar at 2-5 pg/cell, and the histamine stored ranges from 10 to 12 µg/g in both tissues. Following mast cell activation, histamine is rapidly dissociated from the granule matrix by exchange with sodium ions in the extracellular environment.

Since last two decades, inflammation has been known as the main pathophysiological characteristics of allergy. Mast cells are major participants of allergic reactions, and their activation may be all that is sufficient and necessary for the rapid development of microvascular leakage and tissue edema in sensitized subjects exposed to allergen. Mast cell is a key source of potent mediators of allergic inflammation including histamine, neutral proteinases, proteoglycans, prostaglandin D₂, leukotriene C₄ and certain cytokines.^[11] Among them, histamine is the first mediator implicated in the pathophysiological changes of asthma when it was found to mimic several features of the disease. Antihistamines are commonly known to have depressant effects on the central nervous system, although occasional paradoxical stimulant effects had been reported, particularly among children. These include tremor, insomnia, irritability, hallucinations and seizure.^[12,13]

The number of animals used in research has increased with the advancement of research and development in medical technology. Every year, millions of experimental animals are used all over the world. The pain, distress and death experienced by the animals during scientific experiments have been a debating issue for a long time. Besides the major concern of ethics, there are few more disadvantages of animal experimentation like requirement of skilled manpower, time consuming protocols and high cost. Various alternatives to animal testing were proposed to overcome the drawbacks associated with animal experiments and avoid the unethical procedures.^[14]

The laboratory animals have to be sacrificed just for a piece of tissue. However, chick ileum is a tissue that is available easily, and animals need not be killed additionally for experimental purpose. The advantages of using chick ileum preparation are that it is economical, very easy to mount in organ bath, gives good response, without sacrificing the experimental animals.^[15] As per literature evidence and studies on chicken small intestine revealed the presence of tachykinin, histaminic, motile receptors. Biological testing is a cheap and specific prelude to

identify the nature of receptors and quantifying the unknown substance. In chick ileum M muscarinic receptors were reported.^[16] Spiral ileal strips from fowl sensitized with albumin, contract many times more with ACh than with histamine and 5-HT.^[17] Chick ileum maintains good stability with reproducibility. It was observed from the data's obtained from the present investigation that the height of response of concentration response curve of histamine before incubation with test drug ranges from 22mm to 49 mm. There was a promising decrease in the height of the response curve after incubation with test drug VKT ranges from 7mm to 43 mm. From this it may be considered that traditional formulations like VKT has rich potential of halting the progression of allergy and cold related symptoms by its versatile anti-histamine property.

5. CONCLUSION

Untreated allergy symptoms, such as sneezing in allergic rhinitis or pruritus in urticaria, can distract attention in patients driving. Clinical manifestations of nasal allergy may cause sedation and altering of cognitive functions. Ocular itching and increased lacrimation in allergic conjunctivitis can affect the proper use of visual capacities. Conventional antihistamines are heterogeneous groups of compounds with various side effects. Use of anti-histaminergic agents is not without risks. As reported by the Centre for Disease Control (CDC). Hence usage of medications like VKT from siddha system of traditional medicines provides good symptomatic relief and offers greater healing in conditions such as allergy, itching, inflammation by its significant anti-histamine property.

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