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SCREENING OF ANTI-HISTAMINE POTENTIAL OF TRADITIONAL SIDDHA FORMULATION KANNAIKU ATTHI NEI BY IN-VITRO CHICK ILEUM ASSAY

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ABSTRACT

Childhood bronchial asthma varies widely from country to country. At the age of six to seven years, the prevalence ranges from 4 to 32%. The same range holds good for ages 13 and 14. UK has the highest prevalence of severe Bronchial Asthma in the world. It has also increased the number of preventable hospital emergency visits and admissions. Apart from being the leading cause of hospitalization for children, it is one of the most important chronic conditions causing elementary school absenteeism. Antihistamines are most commonly used in the treatment of asthma. Several dozen drugs are available on the pharmaceutical market, and their generic forms are advertised widely as very effective drugs for the treatment of bronchial asthma. Adverse effects of these conventional antihistamines includes headache, fatigue, drowsiness, insomnia and rash. Sedating antihistamines have been associated with a lowered seizure threshold. Kannaiku Atthi Nei (KAN) is potential siddha formulation indicated for the treatment of bronchial asthma in literature whereas till now there is no documentary evidence substantiate the claim. Hence the present study aimed at screening the anti-histamine potential of KAN using isolated chick ileum assay. 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 12 mm to 36 mm. There was a promising decrease in the height of the response curve after incubation with test drug KAN ranges from 8 mm to 23 mm. Further it was observed that the formulation KAN shift the dose response curve to right which promises the anti-histamine property of this novel drug, still proper clinical validation is recommend before clinical utilisation of the drug.

KEY WORDS: ***Bronchial asthma, Siddha, Kannaiku Atthi Nei, Anti-histamine, Isolated chick ileum assay***

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1. Introduction

Asthma is one of the most common chronic diseases worldwide. The global prevalence of asthma, using a definition of clinical asthma or treated asthma, is estimated to be about 4.5% [1].Using this prevalence figure, there are about 315 million people estimated to be suffering from asthma worldwide. Using a less rigorous definition for diagnosis of asthma, the global prevalence is approximately 8.6% with a burden of 623 million asthmatic patients [2].There has been an increase in prevalence of asthma over time, similar to other allergic disorders. Thus, an additional 100 million people worldwide are likely to develop asthma, by 2025 [3].

The bronchoconstriction of smooth muscle mediated via H1 receptors is one of the most well-known biological actions of histamine in the respiratory system. It was reported long before that histamine evoked a contraction of human bronchi, and bronchoconstriction was recognized first as one of the biological actions of histamine [4]. While histamine contracts bronchial smooth muscles as strongly as muscarinic M1 receptor agonists, histamine contracts pulmonary peripheral tissue samples more strongly than M1 receptor agonists. This result seemed to suggest the higher sensitivity of peripheral airways to histamine, although it was possible that the contraction of vascular smooth muscles was involved in the contraction of the pulmonary peripheral tissue samples because the sample contained vessels [5].The response of pulmonary arteries to histamine is biphasic induced by vascular contraction via H1 receptors and vascular dilation via H2 receptors [6]. Histamine induces plasma leakage from postcapillary venules by affecting the bronchial microcirculatory system. Histamine increases the secretion of mucous glycoprotein from the human airway in vitro. This action is inhibited by the H2 receptor antagonist (H2RA), cimetidine, not H1 receptor antagonists (H1RAs). Histamine also accelerates the chloride ion transport of airway epithelial cells, which is closely associated with water transfer in the airway [7].

Anti-histamine are the ultimate drug of choice for the clinical management of bronchial asthma. Although very rare, idiosyncratic hypersensitivity reactions have been described for each of the antihistamines [8]. Other reported adverse effects are headache, fatigue, drowsiness, insomnia and rash. Sedating antihistamines have been associated with a lowered seizure threshold. Reports of seizures in patients taking less sedating antihistamines have been received by medicine safety authorities, but the causal link with the antihistamines has not been confirmed [9]. Overdoses of newer, less sedating antihistamines may result in tachycardia, drowsiness, agitation, gastrointestinal effects and headache. An ECG is recommended. Overdoses of sedating antihistamines can give rise to dangerous sedation as well as anticholinergic signs. Seizures and cardiac conduction abnormalities may also occur [10].

Herbal drugs are used as medicines in different formulations to treat various ailments since ancient times. Even at present, medicinal plants play a key role in world health. Use of traditional, complementary, and alternative medicine, which mainly uses plant material for their formulations, remains widespread in both developing and developed countries. According to the World Health Organization (WHO), about 65–80% of the world's population which lives in developing countries depends essentially on medicinal plants for their primary healthcare [11]. Due to this wide use of medicinal plants, the WHO has recommended the initiation of studies to identify and characterize new herbal preparations from traditionally known plants and the development of new effective therapeutic agents, especially in the areas where there is a lack of modern drugs, such as for chronic diseases [12]. Kannaiku Atthi Nei (KAN) is potential siddha formulation indicated for the treatment of bronchial asthma in literature whereas till now there is no documentary evidence substantiate the claim. Hence the present study aimed at screening the anti-histamine potential of KAN using isolated chick ileum assay.

2. Materials and Methods

2.1.Anti-Histamine evaluation using isolated chick ileum [13]

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 (2ml) 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 Siddha drug KAN on Dose response curve of isolated chick ileum preparation

Isolated chick ileum comprises of versatile bioactive receptors of which histamine prioritise the top. Due to its simplicity and reliability the outcome of this study attains greater importance. This model gaining importance as it is considered as a porotype of screening the lead components from herbal origin. Both agnostic and antagonist potential of the drug candidates shall be ascertained easily by using this viable tool. 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 12 mm to 36 mm. There was a promising decrease in the height of the response curve after incubation with test drug KAN ranges from 8 mm to 23 mm. As show in table 1, figure 1&2.

Table 1: Effect of KAN on dose response of isolated chick ileum preparation

Dose in mcg	Initial Response in mm (Before Incubation)	Final response in mm (After incubation with Test drug KAN)
10	12	8
20	20	13
40	25	17
80	35	23

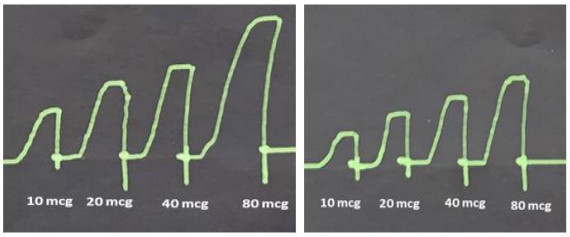

Figure 1: Concentration response curve of histamine in absence and Presence of KAN on Isolated chick ileum in optimized condition

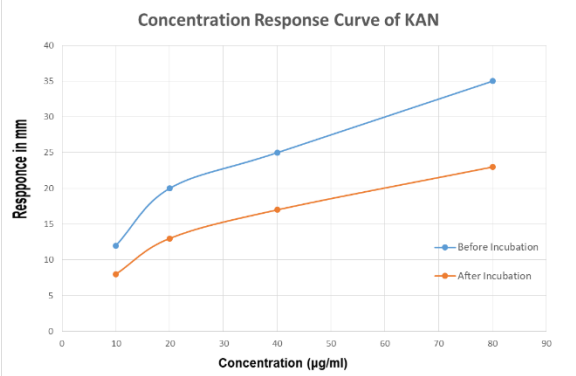

Figure 2: Concentration Dose response curve of KAN

4.Discussion

About 235 million people worldwide have been affected. Many people die from this deadly disease due to its high prevalence rate in many countries. Number of patients has been increasing day by day. Millions of people have died from asthma. The highest incidence is in New Zealand, Australia, and the United Kingdom, and the lowest incidence rate is in China and Malaysia. About 7% of adults and 15% of children have asthma [14].

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 [15]. High lipophilicity and consequently easy crossing of the blood-brain barrier additionally intensify the most dangerous adverse events of commercial anti-histamine class of drugs 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 [16,17]. Therefore, the discovery of compounds selectively acting on H1 receptors.

Siddha is one of the ancient traditional practise emerged from the southern zone of India, ultimate philosophy of siddha has been framed by the siddhar called by their name ancient physician who systematically classify the medicines based on the nature, need and with other characteristic features. According to siddha nomenclature the occurrence of disease could be due to imbalance of fundamental humours like vatham, pitham and kabam. Reversal of equilibrium would substantially heal the disease and benefit the mankind. Majority of the siddha preparation works behind this principle thereby chance of reoccurrence of disease is highly questionable.

Isolated chick ileum assay offers high reliable results to demonstrate the anti-histamine property of wide range of drugs. Response of histamine receptors present over ileal smooth muscle measured in the form of tracing at kymograph. Obvious anti-histamine agent inhibits the length of dose response curve towards the right which denotes antagonistic action. 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 12 mm to 36 mm. There was a promising decrease in the height of the response curve after incubation with test drug KAN ranges from 8 mm to 23 mm. Further it was observed that the formulation KAN shift the dose response curve to right which promises the anti-histamine property of this novel drug.

5. Conclusion

Asthma is an inflammatory disorder of the conducting airways that has a strong association with allergic sensitization. Commercially available antihistamines reported several adverse effects which includes headache, fatigue, drowsiness, insomnia, rash etc. Utilisation of drugs from herbal origin explores the therapeutic potential of alternate medicines. It was observed from the data's obtained from the present investigation that there is a significant decrease in height of concentration response curve of histamine after incubation with siddha formulation Kannaiku Atthi Nei which denotes the anti-histaminic potential.

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