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AntihistaminicActivityofthePaediatricSiddhaFormulationKanaEnnai: An Ex Vivo Study Using a Guinea Pig Model

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KEYWORDS:

Childhood bronchial asthma, Ex vivo antihistaminic activity,Kana Ennai,Paediatric Siddhaformulation, Histaminereceptor blockade.

ABSTRACT:

Childhood bronchial asthma and other allergy-related disorders remain significant health concerns due to the limitedavailabilityofeffectiveandconclusivetreatmentsinpaediatriccare.Thissituationhasincreasedinterest in traditional Siddha formulations for managing such conditions. The present study aimed to evaluate the antihistaminicactivityoftheSiddhapaediatricherbalformulationKanaEnnai(KE)usinganex-vivoguineapig modelofbronchialhyperresponsiveness.Inthisexperimentalstudy,guineapigswereeuthanizedwithketamine, and1-cm ilealsegments were mounted in a 30-mLorgan bath containing aeratedTyrodesolution maintained at 37°C.Contractileresponseswereinducedbycumulativeadditionofhistamineatconcentrationsof5,10,20,40, and 80 µg until submaximal contractions were achieved. After treatment with Kana Ennai (KE), the ileal responsestothesamehistamineconcentrationswererecordedandcompared.TheresultsdemonstratedthatKana Ennai (0.2%) significantly reduced histamine-induced contractions and effectively blocked hyper-responsive histamine receptors in ileal smooth muscle, as evidenced by changes in the histamine concentration–response curve.ThesefindingssuggestthatKanaEnnaipossessesnotable antihistaminicactivityandtherapeuticpotential in the management of bronchial asthma. Further experimental investigations and clinical trials are required to confirm its efficacy and elucidate its mechanism in histamine receptor blockade.

Abbreviations:

KE: Kana Ennai; CRC for concentration response curve; NaCl stands for sodium chloride; KCl for potassium chloride;CaCl2forcalciumchloride;MgCl2formagnesiumchloride;H2Ofordihydrogenmonoxide;NaHCO3 for sodium bicarbonate; NaH2PO4 for monosodium phosphate or sodium dihydrogen phosphate;

1. Introduction

The prevalence of allergies and asthma has increased despite recent improvementsinthe generalhealthof the population [1]. In addition to bronchial constriction, swelling, and increased mucus secretion brought on by exposure to stimuli including dust, pollen, animal fur, smoke,andairpollution,asthmaischaracterizedby recurring episodes of air route obstruction. Asthma comes in two primary kinds. Allergies and/or allergic illnesses(suchallergicrhinitisandatopicdermatitis)are frequentlylinkedtoearly-onset asthma,whichbeginsin childhood or adolescence [2]. In addition to causing continuous inflammation in the respiratory tract, childhood bronchial asthma is an inflammatory disease oftheairwaysthatischaracterizedbyrecurringboutsof

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wheezing, dyspnea, chest tightness, and coughing, especiallyatnightorearlyinthemorning[3].Theairway and pulmonary tissue have been shown to contain four differenttypesofhistaminereceptors,includingH1,H2, H3, and H4[4-7]. One of the most well-known physiologiceffectsofhistamineintherespiratorysystem is the bronchoconstriction of smooth muscle, which is mediatedbyH1receptors[8].Thebody'sprimarysource ofhistamineismastcells,whicharemultipurposetissue-dwelling cells generated from bone marrow [9]. The function of lymphocytes, immunoglobulins, mast cells, anddifferentautacoidsintheetiopathogenesisofallergic diseaseshasbeenextensivelystudiedduringthepastfew decades [10].The Indian traditional medical system (AYUSH)recordsanumberofnaturalformulationsthat have shown promise as treatments for bronchial asthma and allergy disorders [11].The data gathered indicates that the trial medication's constituents have anti-inflammatory, anti-histaminic, immunomodulatory, and anti-asthmatic qualities [12-18]. Therefore, it was decided to evaluate this trial medication experimentally in order to determine its antihistaminic effect [19-20].

2. MaterialsandMethods

According to the classical Siddha text *ChikitsaratnaDeepam*, "Kana Ennai" (KE) is a traditional polyherbal pediatric formulation prepared basedondocumentedtextualevidenceandiscommonly recommended for the management of *Kana Soodu* (childhood bronchial asthma).

Ingredients

Table 1.Ingredients of the Study Medicine Kana Ennai

S. NO	COMMON NAME	BOTANICAL NAME	QTY.
1.	Manathakkalisaaru	*Solanum nigrumL.*	87.5ml
2.	Vengayarasam	*Alliumcepa L.*	87.5ml
3.	Vilvailaikozhundhinrasam	*Aeglemarmelos L.*	87.5ml
4.	Vendhayam	*Trigonellafoenum-graecum L.*	44grams
5.	Chitramannakuennai	Castoroil	700ml

Identification, Confirmation and Collections of raw drugs

Before the preparation of the trial medicine, all the raw drugs were collected and authenticated by Dr. R. Duraisami, M.Pharm., Ph.D., Head, Department of Pharmacognosy, Nandha College of Pharmacy, Erode (Ref. No.: NCP/General/195/2026).

Figure 1.*Solanum nigrum L.*

Fig 2. Juice of *Solanum nigrum* L.

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Figure 3. *Aegle marmelos L.*

Figure 4. Juice of. *Aegle marmelos L.*

Figure 5.*Trigonella foenum- graecum L.*

Figure 6. Paste of. *Trigonella foenum graecum L.*

Figure 7. Castor oil

Figure 8. *Allium cepa L.*

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Figure 9.Boiling study medicine

Figure 10.Wax particle forming consistency

Figure 11. Study medicine – Kana Ennai

Purificationofingredients

Alltheherbalingredientswerethoroughlycleanedusing normal (potable) water to remove dirt and impurities, except castor oil.

MethodofDrugPreparation:

As per the Siddha classical text *ChikitsaratnaDeepam*, after purification of all the ingredients, the fenugreek seedsweresoakedovernightandgroundthoroughly.The pastewasthenblendedwellwithcastoroilandtheother juices listed above. The mixture was heated until the required consistency (waxparticleformationstage) was achieved, after which it was carefully filtered.

Indications: Kana Soodu (Childhood Bronchial Asthma).

Experimental Animals for *Ex vivo* Anti- Histaminic Activity of (KE)

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Thestudy employedhealthyadult guineapigsweighing between 300 and 350 grams. The animal came from the Kerala Veterinary and Animal Science University's animal house in Mannuthy, Kerala. After arriving, the animalwasputinapolypropylenecagewithdriedgrass bedding at the JKKMMRF'S Annai JKK Sampoorani Ammal College of Pharmacy animal house, Komarapalayam, Namakkal, Tamil Nadu for acclimation. The temperature and relative humidity of the animals' housing were 24 ± 2oC and 30–70%, respectively. There was a light: dark cycle of 12:12. Every animal was fed regular commercial pelleted rat chaw (Hindustan Lever Ltd., Mumbai) and had free access to water.

EthicalClearanceofthisResearch Study

The Institutional Animal Ethics Committee (1158/PO/Re/S/07/CPCSEA)examinedallexperimental techniques and protocols utilized in this work to ensure they complied with IAEC guidelines.

Anti-histaminicactivityof *KE*

TreatmentProtocol

Guinea pigs were used to evaluate antihistaminic activity. Adult male guinea pigs weighing 300–350 g were fasted overnight prior to the experiment. The animals were euthanized by an overdose of injectable ketamine. The abdomen was opened, and the terminal ileum was excised. A 1-cm segment of the ileum, taken 10–15cmproximaltotheileocecaljunction,wasisolated and mounted according to the method described by Carvalho*etal.*(2009).Theisolatedileumwassuspended ina30-mLorganbathcontainingaeratednormalTyrode solution (composition in mM: NaCl, KCl, $CaCl_2$, $MgCl_2 \cdot H_2O$, $NaHCO_3$, NaH_2PO_4, and glucose; pH 7.4) and maintained at 37 °C. The tissue was allowed to equilibratefor60minutes,withcontinuousaeration.The mechanicalresponsesoftheileumwererecordedusinga frontal writing lever. Cumulative concentration–response curves to histamine were obtained until submaximal contractions were achieved. The test drug (KE) was then incubated with the isolated ileum for 45 minutes[22]. Following incubation, the contractile responses of the ileum to the same concentrations of histamine were recorded in the presence of KE.

Figure 12. Experimental setup of isolated ileum preparation in organ bath

Figure 13. Mounting of ileal tissue in organ bath holder

3. Results

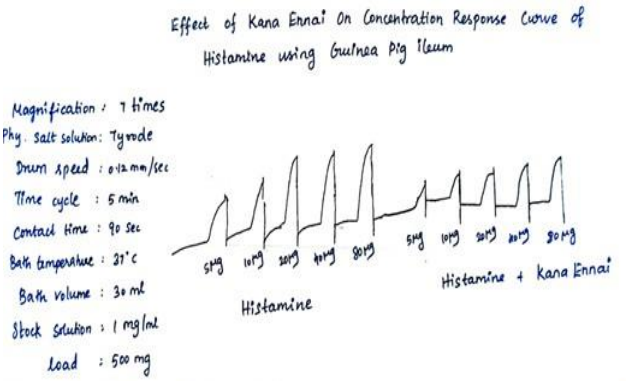

Figure 14. Effect of "Kana Ennai" on concentration response curve of histamine using guinea pig ileum

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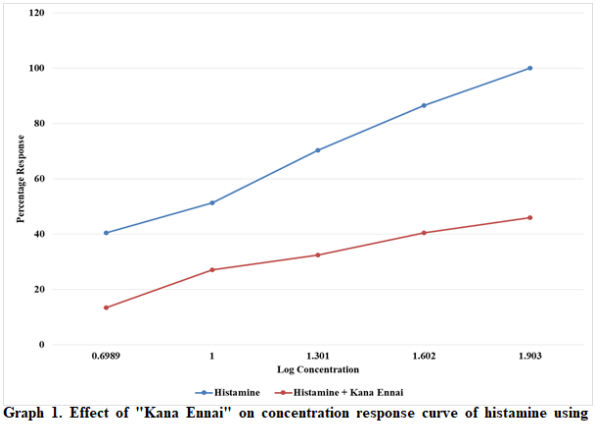
Table 2. Effect of "Kana Ennai" on concentration response curve of histamine using guinea pig ileum

S.no	Concentration of Histamine (µg)	Log Concentration	Histamine		Histamine+ Kana Ennai	
			Response (mm)	Percentage Contraction	Response (mm)	Percentage Contraction
1	5	0.6989	15	40.54	5	13.51
2	10	1.000	19	51.35	10	27.03
3	20	1.3010	26	70.27	12	32.43
4	40	1.6020	32	86.49	15	40.54
5	80	1.9030	37	100	17	45.95



Graph 1. Effect of "Kana Ennai" on concentration response curve of histamine using guinea pig ileum

4. Discussion

Inasthma,multiplemediatorsareproducedandreleased, leading to bronchoconstriction, airway wall restructuring, and airway obstruction. These mediators encompass a broad range of molecules, including histamine, leukotrienes, prostaglandins, cytokines, and chemokines[23].Antigen exposure triggers histamine releasefrommastcellsandbasophils,leadingtosmooth musclecontraction,enhancedvascularpermeability,and increased mucus secretion[24].The histamine-induced contraction of isolated guinea pig ileum via H_1 receptor activationisawell-establishedandreliableexperimental modelforevaluatingantihistaminicandbronchodilatory agents.TheH_1receptorsinguineapigilealsmooth muscle are pharmacologically comparable to those in human bronchial smooth muscle. In both tissues, receptor activation couples to Gαq/11 proteins, stimulates phospholipase C, and increases intracellular Ca^{2+}, leading to smooth muscle contraction. Because of this similarity in receptor behavior and signaling pathways, guinea pig ileum serves as a validated surrogate model for screening potential anti-asthmatic drugs.Selectiveantagonistsplayaroleinasthmatherapy, particularly antihistamines, leukotriene (LT) receptor antagonists,antimuscarinicagents,andendothelin(ET)-1 receptor antagonists [25].*Ex vivo* experiments, especially those utilizing isolated organ bath preparations, are well-established and widely accepted method for assessing ileal contractile responses and gastrointestinal motility [26]. Smooth muscle of study animal expresses H_1 receptors, and their activation by histamine produces a contractile response. This contractile property of the isolated ileum was used to evaluate the antihistaminic potential of the test drug, KanaEnnai(KE).TheresultsarepresentedinFigure14, Graph 1and Table 2. The concentration–response curve (CRC) of histamine alone (5, 10, 20, 40, and 80 µg) in isolated experimental ileum showed a dose-dependent leftward shift, reflecting the responsiveness of H_1 receptors present on the ileal smooth muscle, which resultedinmusclecontraction.Thehighestconcentration of histamine produced a maximal response corresponding to 100% contraction.

5. Conclusion

This research on “Kana Ennai” establishes its antihistaminic property in guinea pig model.The guinea pig ileum contains a high density of H_1 histamine receptors on its smooth muscle, which are functionally and pharmacologically similar to human H_1 receptors. Therefore, responses to histamine and antihistaminic drugscloselyresemblethoseeninhumans.Hence,the medicine “Kana Ennai” may serve as an effective treatmentforKanaSoodu(childhoodbronchialasthma). The Siddha paediatric formulation “Kana Ennai” can be beneficial in managing bronchial asthmatic complications in children, such as shortness of breath, chest tightness, and dyspnoea.Further research is required to clarify the precise medicinal benefits of the trial medicine for children and its role in reducing allergic responses.

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ConflictofInterest

Theauthorsdeclare noconflict of interest.

Author's contribution

VadivelanS-servedasthePrimaryInvestigatorandwas responsible for the conduct of the preclinical study, assessment, treatment planning, and data collection. Sarojini T- contributed to data analysis, data interpretation, manuscript editing, and article drafting. Manikgantan E. M and Vennila K were involved in manuscript review and manual grammar checking. All authors reviewed and approved the final manuscript**.**

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