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Original Research Article

Bronchoprotective effect of *Zingiber officinale* roscoe (Ginger) in guinea pigs

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ABSTRACT

Background: To evaluate the bronchoprotective effect of aqueous extract of *Zingiber officinale* (AZO) in guinea pigs and compare the same with that of standard drugs.
Methods: Guinea pigs of either sex weighing between 350 to 450 Grams were randomly divided into 13 groups, each group containing 6 animals. Bronchospasm was induced by placing guinea pigs in histamine exposition chamber and exposing them to either 0.25% of histamine acid phosphate or 10% acetyl choline through a nebuliser under 40mm Hg pressure. The time for development of asphyxia was noted. After two and half hours, the animals were administered orally with vehicle / drugs as per the following: Gr I- Normal saline 1ml/100 Grams, Gr II- Salbutamol 1.6mg/kg, Gr III- Chlorpheniramine maleate 0.8mg/kg, Gr IV to Gr VI- AZO 200, 400, and 800mg/kg, Gr VII- AZO 200mg/kg and Salbutamol 0.8mg/kg. For acetylcholine-induced Bronchospasm Gr III animals received atropine 2mg/kg and Gr VII was not taken, rest others remaining the same. After 1 hour of treatment, the animals were again exposed to histamine or acetyl choline aerosol. The exposition time for each animal was again noted and mean increase or decrease in exposition time were noted. The data were subjected to stastical analysis by using paired 't' test. Percentage of protection was also calculated.
Results: AZO at all the doses studied (except 200mg/kg), showed highly significant increase in exposition time against histamine-induced bronchospasm. Combination of AZO (200mg/kg) with salbutamol (0.8mg/kg) also produced augmented effect. But against Acetylcholine induced bronchospasm, AZO did not produce any significant protective effect at any of the doses.
Conclusions: AZO produced significant dose dependant bronchoprotection against histamine induced bronchospasm which might be due to antihistaminic action.

Keywords: Bronchoprotective effect, Ginger, Guinea pigs

INTRODUCTION

Ginger (*Zingiber officinale* roscoe), commonly known as 'Ada' or 'Adrak' is a herbaceous perennial plant belonging to the family 'Zingiberaceae' generally found in South East Asia and also is cultivated in many parts of the world including India. Ginger has been used in traditional Indian and Chinese medicine for over 25 centuries.[1,2] The rhizomes and stems of ginger in various forms (fresh root, dried root, tablets, capsules and liquid) and in various routes (oral, topical and intramuscular) have been used for their antiemetic effects in motion sickness, sea sickness, hyperemesis gravidarum, postoperative vomiting and vomiting due to cytotoxic compounds for which there is lack of clear scientific evidence.[3] Ginger has also been used as appetizer, digestant, antiflatulent, carminative, antidiabetic and antimigraine agent.[4] Ginger is distributed throughout India and is widely used in Ayurvedic medicine for its anti-inflammatory, anti-arthritic, analgesic and antiulcer properties.[5] Apart from that ginger is also used for a wide array of other conditions without any scientific evidence of benefit e.g. asthma and depression.[3]

Bronchial asthma is a common disease affecting nearly 7.2% (100 million) world population.[6] It is viewed primarily as an inflammatory disease characterised by increased responsiveness of the tracheobronchial tree leading to bronchial hyper reactivity and bronchospasm. Presently, anti-inflammatory drugs (corticosteroids, cromolyn, nedocromil, zafirlukast and montelukast), bronchodilators (β_2 agonists, theophylline) and anticholinergics (ipratropium) are the mainstay of treatment.[7] But these drugs have their inherent limitations in terms of toxicities and high cost of chronic therapy. Therefore, suitable herbal remedies are sought for scientific validation regarding their bronchoprotective effects.

With this background the present study was undertaken to evaluate the bronchoprotective effect of aqueous extract of *Zingiber officinale* (AZO) in two animal models of asthma i.e. histamine induced, and acetylcholine induced asthma in guinea pigs.

METHODS

Experimental Animals

The study was conducted during March 2018 in Department of Pharmacology, VIMSAR, Burla. The experimental protocol was approved by the Institutional Animal Ethics Committee, VIMSAR, Burla bearing registration number 553/GO/Re/s/02/CPCSEA. Animal care was carried out as per CPCSEA guidelines. A total number of 78 adult Guinea pigs of either sex weighing between 350-450gm were used in the study. They were divided into VI to VII groups containing 6 animals each group. During the whole period of experiment, they were kept in separate polypropylene cages with normal laboratory diet and water ad libitum.

Drugs and Chemicals

AZO was obtained from Indian Herbs Research Supply Co. Ltd, Saharanpur, UP. Salbutamol ampoules from Cipla Laboratories and chlorpheniramine maleate from Zydus Cadila. Histamine diphosphate, acetyl choline and atropine sulphate were obtained from Himedia Lab Pvt Ltd, Mumbai.

The whole study was conducted in two parts.

- Part I: Effect of AZO against histamine induced bronchospasm in guinea pigs.
- Part II: Effect of AZO against acetyl choline induced bronchospasm in guinea pigs.

Part-I

The method by Anil Kumar et al, 2002 was followed in which bronchospasm was induced in guinea pigs by exposing them to histamine aerosol under standardized conditions.[8,9] The efficacy of the test drug was evaluated by estimating the degree of protection imparted against histamine induced bronchospasm. The animals were placed inside the "Histamine exposition chamber" and a finely atomized mist of 0.25% solution of histamine acid phosphate was blown into the chamber through a nebulizer under 40mm Hg pressure. The sharp fall of animal due to asphyxia was taken as the end-point. The time period from the onset of the exposure to the sharp fall of the animal on its side was designated as the "exposition time". The animals which did not develop the typical features of asphyxia like restlessness, irritation of skin and mucous membrane (sneezing), scratching of ear, deep slow and labored respiration, drawing of the abdominal wall, to and fro movement of the head, appearance of cyanosis, air hunger (animal raising its head in intense inspiratory effort) even after more than three minutes of exposure to histamine were considered resistant or completely protected (C.P) and such animals were excluded from study.

Two and half hour after the initial exposure to histamine aerosol, single dose of the drug/ vehicle was administered to various groups as per the following schedule:

Grouping and drug treatment

- Group I: Control group, received Normal Saline 1ml/100gm.
- Group II: Treated with Salbutamol 1.6mg/kg (Reference standard drug).
- Group III: Treated with Chlorpheniramine maleate 0.8mg/kg.
- Group IV, V and VI: Treated with AZO 200mg/kg, 400mg/kg and 800mg/kg respectively.
- Group VII: Treated with AZO 200mg/kg + Salbutamol 0.8mg/kg.

All the drugs/ vehicle was administered orally. The doses of the test drug were selected after observing the response to it in pilot studies as well as after referring to the literature. The doses of salbutamol and chlorpheniramine maleate were chosen after considering their recommended clinical doses.

After one hour of drug administration the animals were re-exposed to histamine aerosol and the exposition time after vehicle/ drug treatment was noted for each animal.

Statistical analysis

Mean pre-treatment and post-treatment exposition times were calculated group wise and the resulting data were subjected to paired 't' test. P value <0.05 was considered significant.

The percentage of protection imparted by each drug was calculated by applying the formula.

$P = (1 - C/T) \times 100$

Where C = mean exposition time before drug treatment

T = mean exposition time after drug treatment

Part- II

For this part study, the method by Kumar A et al, 2002 and Mitra SK et al, 1999 was adopted in which 10% acetyl choline hydrochloride was used for inducing brocnchospasm in place of histamine.[8,10] Grouping pattern was similar as Part-I study except for Group III, where Atropine 2mg/kg was used in place of chlorpheniramine maleate and Group VII was omitted.

RESULTS

In this study, the Bronchoprotective effect of AZO was evaluated using two animal models of asthma.

Table 1 shows the effects of various drugs/vehicle on mean exposition time in guinea pigs against histamine induced bronchospasm along with the P value and percentage of protection.

Table 1: Effect of drugs / vehicle on the exposition time of guinea pigs after histamine aerosol exposure.

Groups	Treatment (P.O)	Mean exposition time (in secs)		t	P	% age of protection
		Before treatment	After treatment			
I	Normal Saline 1cc/100 gm	101.7±1.47	102.3±2.33^{NS}	0.38	>0.05	0.6
II	Salbutamol 0.8 mg/kg	102.7±2.02	168.3±0.95***	29	<0.001	39
III	Chlorpheniramine maleate 0.8 mg/kg	102.3±1.58	176±2.25***	91.77	<0.001	42
IV	AZO 200 mg	106.7±1.76	109.7±1.08*	2.66	<0.05	2.7
V	AZO 400 mg	106.7±2.46	140.7±1.52***	17	<0.001	24
VI	AZO 800 mg	102.0±1.93	148.3±2.03***	57	<0.001	31
VII	AZO 200 mg + salbutamol (0.8mg/kg)	102.7±1.97	156.0±1.93***	43	<0.001	34

The values are expressed as Mean ± SEM, n = 6 in each group. ^{NS} P > 0.05, *P < 0.05, **P < 0.01 and ***P < 0.001 vs. Before treatment

Table 2: Effect of drugs / vehicle on the exposition time of guinea pigs after acetyl choline aerosol exposure.

Groups	Treatment (P.O)	Mean exposition time (in secs)		t	P	% of Protection
		Before treatment	After treatment			
I	Normal Saline 1cc/100gm	52.17±1.16	52.67 ±1.76 ^{NS}	0.34	>0.05	1
II	Salbutamol 0.8mg/kg	51.67±1.2	71.0 ± 1.52***	17.33	<0.001	27
III	Atropine 2mg/kg	51.33±0.98	85.33±1.52***	17.00	<0.001	40
IV	AZO 200mg	54.67±1.76	55.33±1.9^{NS}	0.29	>0.05	1.2
V	AZO 400mg	54.33±2.6	54.33±1.66 ^{NS}	0	>0.05	0
VI	AZO 800mg	53.0±2.23	57.67±1.66*	3	<0.05	8

The values are expressed as Mean ± SEM, n = 6 in each group. ^{NS} P > 0.05, *P < 0.05, **P < 0.01 and ***P < 0.001 vs. Before treatment

As evident from this table, the standard H_1 antagonist chlorpheniramine maleate and the β_2 agonist bronchodilator salbutamol provided significant protection (P <0.001) against bronchospasm in this model as reflected by an increase in mean exposition time after drug treatment. This is contrast to the effect of normal saline which did not bring about any protection. AZO at all doses except 200mg/kg also provided highly significant protection. However, a combination of AZO 200mg/kg and salbutamol 0.8 mg/kg provided highly significant protection.

Table 2 shows the effects of various drugs/ vehicles on mean exposition time in guinea pigs against acetyl choline induced bronchospasm along with P value and percentage of protection. As evident from this table, atropine and salbutamol offered significant protection (P <0.001) as reflected by increase in mean duration of exposition following acetyl choline challenge. However AZO in all the doses studied did not showed any significant protection (P >0.001).

DISCUSSION

In this study, two different animal models of asthma were used to evaluate the bronchoprotective activities of aqueous ginger extract. Bronchospasm induced by either histamine or acetyl choline in guinea pigs placed inside the histamine aerosol apparatus is an old and established method for screening drugs with potential Bronchoprotective effect.[8]

Against histamine induced bronchospasm, the standard and the test drug produced significant protection except AZO 200 mg/kg which however when combined with salbutamol 0.8 mg/kg also produced significant protection. Against acetyl choline induced bronchospasm, the test drug AZO at all doses did not exhibit any bronchoprotective effect which indicates that AZO might be having H_1

antihistaminic activity but no antimuscarinic activity. Further studies are needed to determine the exact mechanism of action of ginger in bronchospasm induced by a variety of spasmogens. Somchit et al, have reported that the aqueous extract of Zinger zerumbet (wild ginger) possessed anti-inflammatory effect against PGE2- induced hind paw edema in rats.[11] Some other reports have also mentioned about the anti-inflammatory properties of ginger which may be of help in controlling the exaggerated immune and inflammatory response in asthma.[5] Mayo clinic in one of its reports have stated that ginger in a dose of 1-4 gms is effective in reducing asthmatic symptoms without any effect on the stage of disease or spirometry findings.[12]

Aqueous extract of ginger (AZO) produced significant dose dependant bronchoprotection against histamine-induced bronchospasm. However, no effect was exhibited against acetyl choline induced bhonchospasm suggesting that it might be having H_1 antihistaminic action without any antimuscarinic effect. Further study is required to delineate the detailed profile of this action of ginger.

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