ASIAN JOURNAL OF PHARMACY & LIFE SCIENCE

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COMPARATIVE EVALUATION OF SOME PLANT EXTRACTS ON BRONCHOCONSTRICTION IN EXPERIMENTAL ANIMALS

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Abstract:

The present investigation was undertaken to evaluate the comparative bronchodilating activity of extracts of four plants Solanum Xanthocarpum (kantkari) fam. Solanaceae , Adhatoda Vasica (Adusa,Vasaka) fam. Acanthaceae ,Tylophora indica (damabel) fam. Asclepiadaceae and Curcuma Cassia (kali haldi) fam. Zingiberaceae. Bronchodilator activity of all the extracts were studied on the histamine aerosol induced bronchospasm and preconvulsion dyspnoea (PCD) in guinea pigs. Treatment with methanolic extracts of Solanum Xanthocarpum 100mg/kg, Adhatoda Vasica 500mg/kg, Tylophora indica 100mg/kg, Curcuma Caesia 500mg/kg showed significant protection against histamine induced bronchospasm.

Key words: *Bronchoconstriction, Solanum Xanthocarpum, Adhatoda Vasica, Tylophora indica, Curcuma Cassia,*

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Received: 01/02/2011 Accepted: 03/03/2011

Introduction:

Asthma is one of the most common disorders encountered globally in clinical medicine in both children and adults characterized by inflammation of the airway that is central to airway dysfunction. It is known that asthma can be triggered by various factors: allergens, drugs, respiratory infection, dust, cold air, exercise, emotions occupational stimuli, chemicals, automobile pollution, histamine[1] etc. Histological examination of bronchial biopsies and cytology of broncho alveolar lavage fluid (BALF) have demonstrated infiltrating inflammatory cells in tracheobronchial mucosa and airway lumen of patients with asthma, even those with mild disease[2]. The influx of inflammatory cells is accompanied by marked and characteristic pathophysiological changes to the airways, including thickening of the airway wall, which have been implicated in the restriction of airflow and the development of airway hyperresponsiveness[3]. The disease statistics clearly necessitates the increasing need for drugs targeting the mechanisms involved in eosinophil and neutrophil activation and accumulation, for the management of asthma. Glucocorticosteroids are the only drugs currently available that effectively reduce airway inflammation in asthma [4].

As a result, there is high prevalence of usage of complementary and alternative medicines for treatment of this disease[5]. Ayurveda, an ancient system of Indian medicine, has recommended a number of drugs from indigenous plant sources for the treatment of bronchial asthma and allergic disorders[6].

Solanam xanthocarpum Schradt. & Wendl. is an annual herbaceous plant com- prising 90 genera and 2000-3000 species. It is reported useful in Kasa Roga (cough) and also in Tamakwasa (bronchial asthma) [7]. *Adhatoda vasica*(L.)Nees is a well known plant drug known in Ayurvedic and Unani medicine. It has been used for the treatment of varioue disease and disorders, particularly for the respiratory tract ailments[8]. *Tylophora indica* is an extensively used Indian traditional medicine to cure various human ailments, and acts as a folk remedy for the treatment of bronchial asthma, inflammation, bronchitis, allergies, rheumatism and dermatitis. It also seems to be a good remedy in traditional medicine as anti psoriasis, seborrheic dermatidis, anaphylactic, leucopenia[9]. *Curcuma caesia* Roxb. (Zingiberaceae) is commonly known as 'Black turmeric'. In India it grows in West Bengal, Madhya Pradesh, Orissa, Bihar, North-East and Uttar Pradesh and is widely used by ethnic communities for various ailments. Rhizomes of the plant are used in cosmetics. In West Bengal it has an important place in traditional system of medicine and is also used as a substitute for turmeric in fresh stage, it is also used to treat bronchitis, asthma cancer, epilepsy, fever, wound, sprains,bruises, impotency, fertility, menstrual disorders, toothache, vomiting[10] etc.All these plants are traditionally used for the treatment of asthma . However, no scientific studies are carried out to investigate comparative bronchodilator effect of all the four plants. In present study methanolic extract of all the four plants were evaluated in experimental guinea pigs by using *in-vivo* model.

Materials and Methods:

The plant Curcuma *caesia* was collected from the forest region of Dindori district of Madhya Pradesh. *Adhatoda vasica*, *Solanum xanthocarpum*, *Tylophora asthmatica* were collected from Government Ashtang Ayurvedic college Indore (M.P.).All the plants were

authenticated in the botany department of government Holkar science college Indore (M.P.) India by H.O.D. Dr. Sanjay Vyas and Voucher specimen (No. 413/03/2008, 413/05/2008, 413/04/2008, 413/02/2008) has been deposited in the department.

Preparation of Extract: *Curcuma caesia* was dried powdered and extracted with methanol using soxhlet apparatus. *Adhatoda vasica*, *Solanum xanthocarpum* and *Tylophora asthmatica* were defatted with petroleum ether and extracted with methanol using soxhlet apparatus. The extracts obtained were dried using roatary evaporator.

Chemicals: Methanol, Petroleum ether and Histamine were purchased from Sigma-Aldrich Chemical Co., USA. Chlorpheniramine maleate standard is procured from Lloyed Pharmaceuticals, Indore.

Animals: Guinea pigs (300-400g) of either sex were procured from Government Veterinary College Mhow (M.P.) India. The animals were housed for 2 weeks prior to the experiment for acclimatization in the animal house of college of Pharmacy IPS Academy ,Indore (M.P.). Animals were maintained under controlled conditions of temperature 26 ± 2°C, relative humidity 44-56%, and photo-schedule (12 h light and 12 h dark).Animals were provided with standard diet (Amrut feeds, Mumbai, India) and water ad libitum. The food was withdrawn 18 h, before the start of the experiment. Institutional Animal Ethics Committee approved th e experimental protocol (37/2009/CPCSEA). The pharmacological work was carried out as per norms of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

Evaluation of bronchodilator activity: Overnight fasted Guinea pigs were divided into six histamine (0.2%, aerosol), STD received chlorpheniramine maleate (2 mg/kg, i.p.), group 3,4,5 and 6 received methanolic extracts of *Adhatoda vasica* 500mg/kg, *Solanum xanthocarpum* 100mg/kg, *Tylophora asthmatica* 100mg/kg and *Curcuma caesia* 500mg/kg p.o. respectively. Bronchospasm was induced in Guinea pigs by exposing them to histamine aerosol (0.2%) produced by an ultra-sound nebulizer in an aerosol chamber (24×14×24 cm) made of Perspex glass. The time required for appearance of pre-convulsive dyspnoea caused by the histamine was recorded for each animal. Prior to drug treatment, each animal was placed in the histamine chamber and exposed to 0.2 % histamine aerosol. The preconvulsion time (PCT), i.e. the time of aerosol exposure to the onset of dyspnoea leading to the appearance of convulsion, was noted. As soon as the preconvu lsion dysp no ea (PCD) was noted, the animals were removed from the chamber and placed in fresh air to recover. This time for preconvulsive dyspnoea was recorded as basal value. Guinea pigs were then allowed to recover from dyspnoea for 24 hrs.

After 24 hrs, the animals were given p.o. methanolic extracts of *Adhatoda vasica* 500mg/kg, *Solanum xanthocarpum* 100mg/kg, *Tylophora asthmatica* 100mg/kg and *Curcuma caesia* 500mg/kg, and Std. received Chlorpheniramine maleate. These animals were again subjected to histamine aerosol later at an interval of 1 hr, 4 hrs and 24 hrs to determine preconvulsion time (PCT) [11,12].

Statistical Analysis: The results of various studies were expressed as mean ± SEM and analyzed statistically using two ways ANOVA

followed by Bonferroni post hoc-Test to find out the level of significance. Data were considered statistically significant at minimum level of $p < 0.05$. The protection offered by the treatment was calculated by using the following formula

Percentage protection = $(1 - T1/T2) \times 100$

Where, $T1$ = the mean of PCT before administration of test drugs, and $T2$ = the mean of PCT after administration of test drugs at 1 hr, 4 hr and 24 hrs.

Results:

Evaluation of bronchodilator activity

Methanolic extracts of *Adhatoda vasica*, *Solanum xanthocarpum, Tylophora asthmatica*, and *Curcuma caesia* significantly prolonged the latent period of convulsions followed by exposure to histamine aerosol at the dose of 500 mg/kg, 100 mg/kg, 100 mg/kg and 500 mg/kg respectively and showed maximum protection of 38.7%, 30.13%, 43.15% and 34.84% at 4th hour as compared to chlorpheniramine maleate (standard) 2mg/kg, p.o. which offered maximum protection of 72.6% at 4th hour (Table 1 and 2).

Table 1. Effect of various extracts on histamine induced bronchoconstriction in Guinea pigs.

Groups	Latent period of convulsion (Second) Mean ± SEM			
	Before	1 hr.	4hr.	24hr.
Control	123.8±1.71	116±1.00	98±2.30	111.6±2.01
Chlorpheniramine maleate 2mg/kg	127.4±2.50***	359.4±4.37***	452.2±5.61***	236.4±3.65***
Adhatoda vasica 500 mg/kg	127.6±3.37***	193±3.93***	202.2±3.29***	152.8±2.81***
Solanum xanthocarpum 100 mg/kg	124.6±2.65***	172±1.51***	177.2±1.24***	143.2±2.08***
Tylophora asthmatica 100 mg/kg	129.4±2.50***	208.4±2.01***	217.8±2.93***	173.4±2.83***
Curcuma caesia 500 mg/kg	121.8±0.86***	183.6±1.43***	190±1.81***	148±1.58***

n=5; control = histamine (0.2%, aerosol)

Statistical analysis done by using two way ANOVA followed by Bonferroni post hoc-Test.

***$p<0.001$, compared to normal control group.

Table 2. Percent protection against histamine induced bronchoconstriction in Guinea pig.

Groups	% Protection		
	1 hr.	4hr.	24hr.
chlorpheniramine maleate 2mg/kg	52.3	72.6	47.6
Adhatoda vasica 500 mg/kg	35.85	38.77	18.97
Solanum xanthocarpum 100 mg/kg	28.02	30.13	13.54
Tylophora asthmatica 100 mg/kg	40.59	43.15	28.60
Curcuma caesia 500 mg/kg	32.57	34.84	16.35

n=5; control = histamine (0.2%, aerosol)

Statistical analysis done by using two way ANOVA followed by Bonferroni post hoc-Test. ***$p<0.001$, compared to normal control group

Discussion:

Bronchial asthma is commonly characterized by increased airway reactivity to spasmogens. An initial event in asthma appears to be the release of inflammatory mediators like histamine triggered by exposure to allergens that directly cause acute bronchoconstriction[13,14]. In the present study extracts of *Adhatoda vasica*, *Solanum xanthocarpum, Tylophora asthmatica*, and *Curcuma caesia* significantly prolonged the latent period of convulsions followed by exposure to histamine aerosol at the dose of 500 mg/kg, 100 mg/kg, 100 mg/kg and 500 mg/kg respectively and showed maximum protection of 38.7%, 30.13%, 43.15% and 34.84% at 4th hour as compared to chlorpheniramine maleate (standard) 2mg/kg, p.o. which indicating its H1 receptor antagonistic activity and supports the anti asthmatic properties of the plant.

Conclusion:

Histamine induced bronchoconstriction is the traditional immunological model of antigen induced airway obstruction. Histamine when inhaled causes hypoxia and leads to convulsion in Guinea pigs and causes very strong smooth muscle contraction, profound hypotension, and capillary dilation in cardiovascular system. A prominent effect caused by histamine leads to severe bronchoconstriction in the Guinea pigs that causes asphyxia and death. Bronchodilators can delay the occurrence of these symptoms. The results of the study confirmed the bronchodilator properties of the plants, justifying their traditional claims in the treatment of asthma and among all the four plants *Tylophora asthmatica* is having maximum protection against histamine induced bronchospasm.

Acknowledgment

The authors are very much thankful to the mr. Pankaj Dixit for providing the technical support to carry out the study. Thanks are also to Dr. D.K. Jain Principal College of pharmacy, I.P.S.Academy, Indore for providing all necessary facilities to carry out the study.

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