JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

# Evaluation of the Effect of Hydroalcoholic Extracts of Cassia Occidentalis in Histamine Induced Bronchospasm on Guinea Pigs

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**ABSTRACT:**

Evaluation of the effect of hydroalcoholic extracts of Cassia occidentalis in bronchospasm induced by histamine hydrochloride on Guinea pigs. Exposure to an aerosol of 0.1% Histamine hydrochloride in closed chamber was given to induce bronchospasm on Guinea pigs. The effect of oral administration of hydroalcoholic extract of Cassia occidentalis leaves on histamine induced bronchospasm has been studied and is compared with the effect of oral administration of Ketotifen as standard on Guinea pigs. An aerosol of Histamine hydrochloride resulted in bronchospasm as well as decreased pre-convulsion time. Supplementation with hydroalcoholic extract of Cassia occidentalis leaves significantly increased the pre-convulsion time. The results indicate that the leaf of Cassia occidentalis is endowed with bronchospasmolytic activity.

**KEY WORDS:** Cassia occidentalis, histamine, ketotifen, pre-convulsion time, analysis of variance.

**Article history:**

Received 10 July 2015
Revised 25 July 2015
Accepted 14 August 2015
Available online 01 September 2015

**Citation:**

Bangoriya U. V., Tank H. M. Analytical Evaluation of the Effect of Hydroalcoholic Extracts of Cassia Occidentalis in Histamine Induced Bronchospasm on Guinea Pigs. **J Pharm Sci Bioscientific Res**. 2015 5(5):470-474

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## INTRODUCTION:

Respiratory diseases are second to cancer as the causes of death and disability to adults. Acute respiratory infection, tuberculosis and chronic obstructive pulmonary disease rank third, fourth and fifth respectively as per the global health situation.[1]

According to a survey in UK in the year 2008, respiratory diseases occupied 15% among all other diseases. Asthma is the commonest disease in children in economically developed countries and it is also common in adults and it is increasing in prevalence and severity. Around 275 million people around the globe suffer from asthma and this number is rising worldwide, deaths from this condition have reached 18 million annually. The number of deaths from asthma also has risen in the United States. The WHO says about five thousand Americans die from asthma attacks each year. In the early 1980s, the yearly death rate from asthma in the United States was about half of that.

Bronchial asthma is a complex disease with several clinically well-defined pathogenic components, including recurrent reversible airway obstruction, chronic airway inflammation and development of airway hyperresponsiveness.[2] Airway inflammation is the primary problem in asthma. An initial event in asthma appears to be the release of inflammatory mediators (e.g., histamine, tryptase, leukotrienes and

prostaglandins) triggered by exposure to allergens, irritants, cold air or exercise. The mediators are released from bronchial mast cell, alveolar macrophages, T-lymphocytes and epithelial cells. Some mediators directly cause acute bronchoconstriction, termed the "early-phase asthmatic response". The inflammatory mediators also direct the activation of eosinophils and neutrophils, and their migration to the airway, where they cause injury. This is called "late-phase asthmatic response" results in epithelial damage, airway edema, mucus hypersecretion and hyperresponsiveness of bronchial smooth muscle. Varying airflow obstruction leads to recurrent episodes of wheezing, breathlessness, chest tightness, and cough.[3] Based on clinical trial grounds and measurement of IgE, there are 2 major types of asthma. 1) Extrinsic asthma (atopic asthma) in which symptoms develops only on exposure to a specific allergen. Extrinsic asthmatics rarely suffer from status asthmatics and require infrequent medication. 2) Intrinsic asthma (perennial) in which the symptoms are precipitated by infection, frequency of status asthmatics is higher and no allergic aetiology is detectable. Both these types behave differently to anti asthmatics drugs. Mixed features of both the types may be seen in some patients.[4]

The gross pathology of asthmatic airway display lung hyperinflation, smooth muscle hypertrophy, lamina reticularis thickening, mucosal edema, epithelial cell sloughing, cilia cell disruption, and mucus gland hypersecretion. Microscopically, asthma is characterized by presence of increased number of eosinophils, lymphocytes, and plasma cells in the bronchial tissues, bronchial secretion, and mucus. Initially, there is recruitment of leukocytes from the bloodstream to the airway by activated CD4 T-lymphocytes also direct the release of inflammatory mediators from eosinophils, mast cells, and lymphocytes. In addition, the subclass 2-helper T-lymphocytes subset of activated T-lymphocytes produces IL-4, IL-5, and IL-13. IL-4 in conjugation with IL-13 signals the switch from IgM to IgE antibodies. The cross linkage of two IgE antibodies molecules by allergen causes mast cells to degranulate; releasing histamine, leukotrienes, and other mediators that perpetuate the airway inflammation. IL-5 activates the recruitment and activation of eosinophils. The activated mast cells and eosinophils also generate their cytokines that help to perpetuate the inflammation.

Regardless of the triggers of asthma, the repeated cycles of inflammation in the lung with injury to the pulmonary tissues followed by repair may produce long term structural changes ("remodeling") of the airways. [5]

Bronchial asthma is major public health problem worldwide, and the morbidity and mortality of asthma have increased in past few decades. Between 100-150 million people around the global roughly the equivalent of the population of the Russian Federation suffers from asthma and this numbers is rising. Worldwide, death from this condition have reached over 1, 80,000 annually. India has estimated 15-20 million asthmatics. In India, rough estimates indicate a prevalence of between 10-15% in 5-11 years old children. [6] The health burden of asthma is increasing globally at an alarming rate, providing a strong impetus for the development of new therapeutics.

The world health organization (WHO) has recognized herbal medicine as an essential building block for primary health care of vast countries like India and China. India is perhaps the largest producer of medicinal herbs and is rightly called the "botanical garden of the world". There are very few medicinal herbs of commercial importance, which are not collected or cultivated in this country. Medicinal herbs have been in use for thousands of years, in one form or another, under the indigenous system of medicine like Ayurveda, Siddha, and Unani. Since independence in 1947, India has made tremendous progress in agro technology, process technology, standardization, quality control, research and development. Large numbers of herbs are being used for the treatment and prophylaxis of asthma since ancient time, however systemic studies that identify all possible mechanism of each and every herbal antiasthmatic drug are lacking.

Asthma is a disease characterized by redcurrant of reversible airway obstruction with attack of wheeze, shortness of breath and often nocturnal cough. Essential features of asthma are airway inflammation which causes bronchial hyper responsiveness which in turn results in recurrent reversible airway obstruction. There are various causative factors for asthma like allergens, drugs induced asthma, cold air, irritant chemicals etc.

Various allopathic drugs like corticosteroids, anticholinergics, mast cell stabilizers leukotriene antagonists, B2 receptor agonist etc., are in use for the

treatment for asthma. In the most extents, these drugs have been helpful in the symptomatic relief, treatment and prophylaxis of asthma. But the involvement of debilitating side effects is major drawback of these drugs. For example, long-term treatment with corticosteroids leads osteoporosis, skeletal muscle myopathy, obesity etc. [7]

As a result of problems in asthma, there is high prevalence of usage of alternative traditional of medicines for the treatment of asthma. Ayurveda offers a unique insight into comprehensive approach to asthma management through proper care of respiratory tract. More than 400 medicinal plant species have been used ethnologically and traditionally to treat the symptoms of asthmatics, other allergic and autoimmune disorders worldwide. The world health organization (WHO) has recognized herbal medicine as an essential building block for primary health care of vast countries like India and China. India is perhaps the largest producer of medicinal herbs and is rightly called the "botanical garden of the world". There are very few medicinal herbs of commercial importance, which are not collected or cultivated in this country. Medicinal herbs have been in use for thousands of years, in one form or another, under the indigenous system of medicine like Ayurveda, Siddha, and Unani. Since independence in 1947, India has made tremendous progress in agro technology, process technology, standardization, quality control, research and development. Large numbers of herbs are being used for the treatment and prophylaxis of asthma since ancient time, however systemic studies that identify all possible mechanism of each and every herbal antiasthmatic drug are lacking. So many herbal drugs are used in treatment of bronchospasm. Mostly used herbal drugs are *Curcuma longa, C. gigantia, Indigofera tinctoria, Asystasia gangetica, Bryonia laciniosa* etc. Options available today have many limitations including risk of adverse effects, where as herbal world offers many options with safety, efficacy & availability with economical aspects also. *Cassia occidentalis*, commonly known as "Kasundri", is one of the leading drugs used as alternative system of treatments. As per traditional method, it is known for its expectorant activity.

In light of this, the objective of the study is to evaluate the effect of hydroalcoholic extracts of *Cassia occidentalis* in bronchospasm.

## MATERIALS AND METHODOLOGY

### Preparation of extract:

Leaves of *Cassia occidentalis* were collected and properly cleaned and dried under shade to remove excess of moisture. The dried plant material was then subjected to size reduction to coarse powder and passed the powder from sieve no. 40. About 500 gm of air dried powder of leaves of *Cassia occidentalis* were extracted in soxhlet with 20:80 ethanols:water hydroalcoholic mixture in soxhlet apparatus by continuous hot extraction. After each extraction, the solvent was recovered using distillation assembly, and the both extracts were concentrated. The extracts were preserved in air tied container for experiment.

### Animal selection:

Healthy, New Zealand guinea pigs of either sex and Albino wistar rats of either sex were used for this study. They were housed at ambient temperature (22±1°C), relative humidity (55±5%) and 12h/12h light dark cycle. Animals had free access to standard pellet diet and water given *ad libitum*. The protocol of the experiment was approved by the Institutional Animal Ethical Committee (IAEC) as per the guidance of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India.

### Bronchospasm induced by Histamine in guinea pigs[8]

Healthy New Zealand guinea pigs of either sex weighing range of 550-700 g were used and divided into four groups. Each groups containing six animals.

Group I: Disease Control (vehicle)

Group II: Standard (Ketotifen, 1 mg/kg, p.o.)

Group III: Hydroalcoholic extract of *C. occidentalis* leaf (100 mg/kg, p.o.)

Group IV: Hydroalcoholic extract of *C. occidentalis* leaf (200 mg/kg, p.o.)

All test and standard drug were dispersed in 0.5% Sodium CMC, 0.2 ml/kg, p.o. as vehicle. The animals were kept in a closed chamber (30×30×15cm) and exposed to an aerosol of 0.1% Histamine hydrochloride and pre-convulsion time (PCT) (The time of aerosol exposure to the onset of dyspnoea leading to the appearance of

convulsions) was noted. As soon as symptoms like convulsion, animals were removed from the chamber and placed in fresh air to recover. PCT was taken as basal value. Later, all treatments were given orally to all respective groups once daily for 7 days. After 7 days, two hours after the respective drug treatment, animals were exposed to histamine hydrochloride aerosol and PCT was measured by nebulizer pump (Aero space nebulizer). The effect of drug was calculated by the following formula.

% Increase in PCT = [1-T1/T2] x 100,

Where, T1= PCT on day 0,

T2= PCT on day 7.

**Statistical analysis:**

Results were expressed as mean ± SEM. Differences among data were determined using one-way ANOVA followed by Student–Newman–Keul's test (Graphpad Prism software for Windows, Version 4.10.1998). Differences between the data were considered significant at $P < 0.05$.

**RESULTS**

In the present study, administration of 0.1 % histamine to healthy guinea pigs resulted in bronchospasm and seen in the form of Pre-Convulsion Dyspnoea (PCD). % increase in Pre-convulsion time was lower in disease control group. However, supplementation with hydroalcoholic extract of *Cassia occidentalis* leaves significantly ($P < 0.001$) delayed onset of pre-convulsion dyspnoea. Treatment with Ketotifen (1 mg/kg, p.o), as a standard drug; HECL (100 mg/kg and 200 mg/kg, p.o.) given 7 days before aerosol exposure delayed onset of pre-convulsion dyspnoea (PCD) (73.48 ± 0.53 %, 35.71 ± 0.46 % and 49.30 ± 0.24 %) respectively in guinea pigs. These significantly and dose dependently increased the onset of convulsion time in guinea pigs. The bronchodilating effect of test drug (HECL) was comparable to standard control (ketotifen) (1 mg/kg). (Table 1, Figure 1)

**DISCUSSION**

Since bronchodilators, mediator release inhibitors and anti-inflammatory drugs are the different classes of drugs used conventionally in the treatment of bronchial asthma; various animal models and experimental protocols were used in the present study to evaluate anti-asthmatic activity of leaves of *Cassia occidentalis* Linn. Bronchial asthma is characterized by increased airway reactivity to spasmogens. [9] An initial event in asthma appears to be the release of inflammatory mediators (e.g. Histamine, Tryptase, Leukotrienes and prostaglandins). Some of these mediators directly cause acute bronchoconstriction, airway hyperresponsiveness and bronchial airway inflammation. Spasmolytic drugs like beta adrenergic agonists, xanthine derivatives and anticholinergics relax the airway smooth muscles and are used as quick relief medications in acute asthmatic attacks.

**Table 1: Effect of hydroalcoholic extract of *Cassia occidentalis* on Histamine induced bronchospasm in guinea pigs**

| Groups | Dose (mg/kg p.o.) | % Increase in |
|---|---|---|
| **Disease Control** | 0.2 ml | **2.71 ± 0.20** |
| **Standard** | 1 | **73.48 ± 0..53**** |
| **HECL** | 1 0 | **35.71 ± 0.46***** |
| **HECL** | **2 0** | **49.30 ± 0.24***** |

All values represented as Mean ± S.E.M. of six animals.

*** indicates significance at the level of $p < 0.001$.

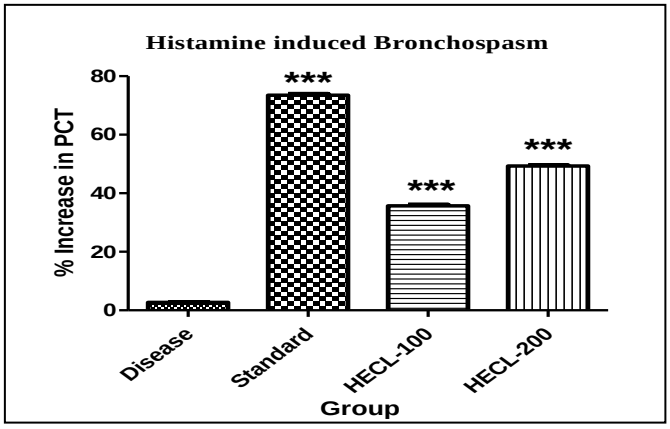


**Figure 1: Effect of hydroalcoholic extract of *Cassia occidentalis* on Histamine induced bronchospasm in guinea pigs**

Guinea pig ileum was used for screening of antihistaminic activity. Stimulation of H1 receptors produces graded dose related contraction of isolated guinea pig ileum.[10]

In present study, significant increase in preconvulsion time was observed due to pretreatment with leaves of *Cassia occidentalis* Linn., when the guinea pigs were exposed to either histamine aerosol. This bronchodilating effect of leaves at high dose was comparable to ketotifen. Spasmolytic effect of *Cassia occidentalis* Linn. leaves was also evaluated by observing the effect of hydroalcoholic extract of leaves (100 and 200 mg/kg) on histamine induced ileum contractions to seek for scientific evidence for beneficial use of leaves in spasm produced by any means. The results showed antagonistic effects of the leaves against the contraction induced by the standard spasmogens. The maximum effects of histamine induced contractions were inhibited in the presence of the leaves extract at 200 mg/kg.

In conclusion, the presented data indicate that administration of the hydroalcoholic extract of *Cassia occidentalis* leaves to Guinea pigs with histamine induced bronchospasm, reduced and prevented the spasm of bronchi, supporting folk information regarding antiasthmatic activity of the plant. The mechanism underlying this effect is still unknown, but is apparently related to dilatation of bronchi. These effects could conclude that *Cassia occidentalis* has an antiasthmatic property.

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