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Research Article

EVALUATION OF ANTI ASTHMATIC ACTIVITY OF
CAPPARIS DECIDUA IN ANIMAL MODELSK Apoorva^{*1}, Ch. Sunitha²Department Of Pharmacology, Princeton College Of Pharmacy In Pocharam, Hyderabad,
Telangana.**Abstract:**

Asthma is a chronic disease that affects approximately 300 million people worldwide. Although wide range of drug is available, the relief provided by them is mainly symptomatic and short lived. Moreover, the side effects of these drugs are also quite disturbing. Hence, a continuous search is on going to identify effective and safe remedies to treat bronchial asthma. Ayurveda is a great Indian tradition and have an important role in discovery of new medicines. There are many natural herbs that can be used for asthma, treatment. *Capparis deciduas* is traditionally used to treat asthma.

Objective: Although these plants possess diverse pharmacological actions, the scientific data on anti-asthmatic actions of this plant has got little attention. An attempt has been made to evaluate antiasthmatic activity of *Capparis deciduas* of aqueous and alcoholic extracts of medicinal plant.

Materials and methods: Different groups of guinea pigs (350-500 g) of either sex were subjected to acetylcholine (n = 5) and histamine-induced (n = 10) airway constriction.

Results: AQECD and ALECD (200 and 300 mg/kg) showed potent bronchodilator activity on histamine-and acetylcholine-induced airway constriction in guinea pigs. These extract has shown the sub-effective dose produced at 100, 200 and 300 mg/kg in all the models. The LD50 of the Aqueous and Alcoholic extracts at a dose of 100, 200 and 300 mg/kg are found to be 2262.7 and 1131.4 by oral route. These LD50 values fall within the practically non-toxic range.

Discussion and conclusion: The present study for the first time indicates anti-asthmatic, acute, sub-acute studies of *Capparis deciduas* medicinal plants, confirming their traditional claims. The anti-asthmatic action of *Capparis deciduas* could be due to the inhibition of the synthesis, release or action of histamine and acetylcholine effect.

Keywords: Antiasthmatic, *Capparis deciduas*, Histamine-induced model and Acetylcholine induced model.

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INTRODUCTION:

Asthma is a disease of the human respiratory system in which the airways constrict and become narrow, often in response to a "trigger" such as exposure to an allergen, cold air, exercise, or emotional stress. Asthma affects 7% of the total population and approx 300 million worldwide. During attacks (exacerbations), the smooth muscle cells in the bronchi constrict, and the airways become inflamed and swollen with difficulty in breathing. Asthma causes 4,000 deaths a year in the US alone. Attacks can be prevented by avoiding triggering factors and by drug treatment¹.

There is limited information on field epidemiology of bronchial asthma in Indian adults. The results of the study indicated that from 73605 respondents (37682 men, 35923 women), one or more respiratory symptoms were present in 4.3-10.5% subjects. Asthma was diagnosed in 2.28%, 1.69%, 2.05 and 3.47% respondents respectively at Chandigarh, Delhi, Kanpur, and Bangalore, with overall prevalence of 2.38%. Female sex, advancing age, usual residence in urban area, lower socioeconomic status, history suggestive of atopy, history of asthma in a first degree relative, and all forms of tobacco smoking were shown as responsible ailments of asthma. Prevalence estimates of asthma in adults in this study pointed a high overall national burden of disease².

Asthma is one of the commonest chronic diseases of affluent societies. The striking increase in prevalence of asthma over recent decades in affluent societies and the rarity of this disease in less affluent populations confirms the importance of environmental and other factors in the cause of asthma, although which environmental and other factors are responsible is still not clear. The studies showed that genetic factors are also important in determining individual susceptibility to asthma. The results of genetic studies suggest that there are many genes with moderate effects rather than a few major genes. Asthmatic airways show inflammation with CD4⁺ helper cells, mast cells, and eosinophils,

characterizing the inflammatory response. Inhaled corticosteroids remain the cornerstone of treatment with the addition of long-acting β -agonists as the next step if symptoms continue. Leukotriene antagonists, the only new drugs to reach the market in the past decade, have modest effects. A better understanding of the mechanisms underlying asthma and the genetic and environmental factors that predispose individuals to asthma will play a key role in understanding better preventative strategies and new therapeutic approaches³.

It has been estimated that about 6000 articles are published every year about asthma in various indexed journals. The increasing prevalence of asthma has led to extensive research into its cause, pathophysiology, and management³.

A few patients have asthma as part of a wider problem such as allergic broncho pulmonary aspergillosis⁴, Churg-Strauss syndrome (Conron & Beynon, 2000) and aspirin-induced asthma⁶. Table 1.1 shows the main features of these disorders.

Historical background

The modern school of thought regarding asthma as a disease is so powerful that it is difficult to imagine asthma, as it was once conceptualized. During the seventeenth century, Once English physicians Thomas Willis and Sir John Floyer began arguing that asthma was different from other breathing disorders and is the same from person to person. They mentioned that asthma, as a specific form of disordered breathing, must be treated differently from other forms of breathlessness cases. By the late nineteenth century, physicians believed that asthma was a disease which had a specific set of causes, clinical consequences, and requirements for treatment, despite the diversity of individual experiences as shown in Table 1.1. Because of the spectrum of severity within asthma, some people with asthma only rarely experience symptoms, usually in response to triggers, where as other more severe cases may have marked airflow obstruction at all times¹.

Table 1.1. Classification of asthma¹

Severity	Symptom Frequency	Symptoms at night	Peak expiratory flow rate or FEV ₁ of predicted	Variability of peak expiratory flow rate or FEV ₁
Intermittent	<once a week	≤ twice per month	≥80% predicted	<20%
Mild Persistent	>once per week but <once per day	>twice per month	≥80% predicted	20-30%
Moderate persistent	Daily	>once per week	60-80% predicted	>30%
Severe	Daily	Frequent	<60% predicted	>30%

Asthma exists in two states: the steady-state of chronic asthma, and the acute state of an asthma exacerbation. The symptoms are different

depending on what state the patient is in. Common symptoms of asthma in a steady-state include: nighttime coughing, shortness of breath with

exertion but no dyspnea at rest, a chronic 'throat-clearing' type cough, and complaints of a tight feeling in the chest. Severity often correlates to an increase in intensity of symptoms. Symptoms can worsen gradually and rather insidiously, up to the point of an acute exacerbation of asthma. It is a common misconception that wheezing is common in patients with asthma-some never wheeze, and their disease may be confused with another Chronic Obstructive Pulmonary Disease (COPD) such as emphysema or chronic bronchitis. An acute exacerbation of asthma is commonly referred to as an asthma attack. The cardinal symptoms of an attack are shortness of breath (dyspnea), wheezing, and chest tightness⁷. Some patients present primarily with coughing, and in the late stages of an attack, air motion may be so impaired that no wheezing may be heard. When present the cough may sometimes produce clear sputum. The onset may be sudden, with a sense of constriction in the chest, breathing becomes difficult, and wheezing occurs (primarily upon expiration, but can be in both respiratory phases). Asthma is classified according to the frequency of symptoms, Forced Expiratory Volume (FEV1) and peak expiratory flow rate (PEFR)⁸. Though symptoms may be very severe during an acute exacerbation, between attacks a patient may show few or even no signs of the disease⁹.

Epidemiology

Asthma has no standard definition. Attempts to define asthma have generally resulted in descriptive statements invoking notions of variable airflow obstruction over short periods of time, sometimes in association with markers of airway hyper-responsiveness and cellular pathology of the airway¹⁰.

Asthma is diagnosed clinically on the basis of symptoms of wheeze, dyspnea, and cough, and by objective evidence of variable airflow obstruction. Allergic asthma can present for the first time at any age, but incidence is highest in childhood¹¹. Asthma in childhood frequently remits during adolescence but can recur in adult life¹². Asthma in adults tends to persist for life and is probably associated with an accelerated decline in lung function¹³. Deaths from asthma are now uncommon, especially in children and young adults; in the past they have occurred in epidemics thought to have been caused by use of high dose formulations of relatively unselective β -agonist drugs.¹⁴

Asthma is an airway disease that can be classified physiologically as a variable and partially reversible obstruction to air flow, and pathologically with overdeveloped mucus glands, airway thickening due to scarring and inflammation, and bronchoconstriction, the

narrowing of the airways in the lungs due to the tightening of surrounding smooth muscle. Bronchial inflammation also causes narrowing due to edema and swelling caused by an immune response to allergens¹.

1.3 Bronchoconstriction

During an asthma episode, inflamed airways react to environmental triggers such as smoke, dust, or pollen. The airways narrow and produce excess mucus, making it difficult to breathe. In essence, asthma is the result of an immune response in the bronchial airways. The airways of asthma patients are "hypersensitive" to certain triggers, also known as 'stimuli' (see below). (It is usually classified as type I hypersensitivity). In response to exposure to these triggers, the bronchi (large airways) contract into spasm (an "asthma attack"). Inflammation soon follows, leading to a further narrowing of the airways and excessive mucus production, which leads to coughing and other breathing difficulties. Bronchospasm may resolve spontaneously in 1–2 hours, or in about 50% of subjects, may become part of a 'late' response, where this initial insult is followed 3–12 hours later with further bronchoconstriction and inflammation. The normal caliber of the bronchus is maintained by a balanced functioning of these systems, which both operate reflexively. The parasympathetic reflex loop consists of afferent nerve endings which originate under the inner lining of the bronchus. Whenever these afferent nerve endings are stimulated (for example, by dust, cold air or fumes) impulses travel to the brain-stem vagal center, then down the vagal efferent pathway to again reach the bronchial small airways. Acetylcholine is released from the efferent nerve endings. This acetylcholine results in the excessive formation of inositol 1, 4, 5-trisphosphate (IP3) in bronchial smooth muscle cells which leads to muscle shortening and this initiates bronchoconstriction³.

1.4 Triggers of asthma (Stimulus that aggravate asthma response)

- ❖ Allergens from nature typically inhaled, which include waste from common household pests, the house dust mite and cockroach, as well as grass pollen, mold spores, and pet epithelial cells¹⁵.
- ❖ Indoor air pollution from volatile organic compounds, including perfumes and perfumed products. Examples include soap, dishwashing liquid, laundry detergent, fabric softener, paper tissues, paper towels, toilet paper, shampoo, hairspray, hair gel, cosmetics, facial cream, sun cream, deodorant, cologne, shaving cream, aftershave lotion, air

freshener and candles, and products such as oilbased paint¹⁵

- ❖ Association between some medications, including aspirin¹⁶, β -adrenergic antagonists (β -blockers), and food allergies such as milk, peanuts, and eggs with asthma have been shown. However, not all people with food or other allergies have asthma¹⁵
- ❖ Use of fossil fuel related allergenic air pollution, such as ozone, nitrogen dioxide, and sulfur dioxide, which is thought to be one of the major reasons for the high prevalence of asthma in urban areas⁷.
- ❖ Various industrial compounds and other chemicals, notably sulfites; chlorinated swimming pools generate chloramines-monochloramine, dichloramine and trichloramine in the air around them, which are known to induce asthma¹⁷.
- ❖ Early childhood infections, especially viral upper respiratory tract infections. Children who suffer from frequent respiratory infections prior to the age of six are at higher risk of developing asthma, particularly if they have a parent with the condition. However, persons of any age can have asthma triggered by colds and other respiratory infections even though their normal stimuli might be from another category (e.g. pollen) and absent at the time of infection. In many cases, significant asthma may not even occur until the respiratory infection is in its waning stage, and the person is seemingly improving⁷. In children, the most common triggers are viral illnesses such as those that cause the common cold.
- ❖ Exercise or intense use of respiratory system in one or other way can also stimulate asthma attack. These are thought to be primarily in response to the exposure of the airway epithelium to cold, dry air.
- ❖ Hormonal changes in adolescent girls and adult women associated with their menstrual cycle can lead to a worsening of asthma. Some women also experience a worsening of their asthma during pregnancy, whereas others find no significant changes, and in other women their asthma diminished during their pregnancy⁷.
- ❖ There is growing evidence that psychological stress is a trigger. It can modulate the immune system, causing an increased inflammatory response to allergens and pollutants. Cold weather

can make it harder for patients to breathe. Whether high altitude helps or worsens asthma is debatable and may vary from person to person¹⁸.

1.5 Bronchial inflammation

The mechanisms behind allergic asthma-i.e., asthma resulting from an immune response to inhaled allergens - are the best understood of the causal factors. In both people with asthma and people who are free of the disease, inhaled allergens that find their way to the inner airways are ingested by a type of cell known as antigen-presenting cells (APCs). APCs then "present" pieces of the allergen to other immune system cells. In most people, these other immune cells (T0 cells) "check" and usually ignore the allergen molecules. In asthma patients, however, these cells transform into a different type of cell (Th2), for reasons that are not well understood. The resultant Th2 cells activate an important arm of the immune system, known as the humoral immune system. The humoral immune system produces antibodies against the inhaled allergen. Later, when a patient inhales the same allergen, these antibodies "recognize" it and activate a humoral response. Inflammation results: chemicals are produced that cause the wall of the airway to thicken, cells which produce scarring to proliferate and contribute to further 'airway remodeling', causes mucus producing cells to grow larger and produce more and thicker mucus, and the cell-mediated arm of the immune system is activated. Inflamed airways are more hyper-reactive, and will be more prone to bronchospasm. The "hygiene hypothesis" postulates that an imbalance in the regulation of these Th2 cell types in early life leads to a long-term domination of the cells involved in allergic responses over those involved in fighting infection. The suggestion is that for a child being exposed to microbes early in life, taking fewer antibiotics, living in a large family, and growing up in the country stimulate the Th1 response and reduce the odds of developing asthma¹⁹.

1.6 Factors that provoke asthma

The factors that commonly provoke asthma are allergens, upper respiratory tract infection, exercise, perfume and fumes, and changes in temperature and humidity. Some agents provoke asthma less frequently, but are important to restrict their use. These include drugs (aspirin and other nonsteroidal anti-inflammatory drugs, β -blockers), food additives (e.g. metabisulphite and tartrazine), and some food and drinks (e.g. peanuts, alcohol)²⁰ and Cola²¹. Some substances found in the workplace cause asthma because of specific sensitisation, and occupational asthma accounts for up to 10% of asthma in young adults in Europe²². Occupational asthma is preventable and can lead to

severe irreversible airway obstruction if the patient is not removed from the sensitizing agent. An occupational history should be taken from all patients with asthma and the history should be supplemented, when occupational asthma is suspected, with frequent peak flow measurements during days when the patient is and is not at work. Some of the common occupational substances that provoke asthma, although more than 200 sensitizing agents have been identified²³. It is now well-established that environmental factors play a major part in the cause of asthma and allergy; family studies showed that a strong component of asthma risk is genetically determined. In the developed countries genetic factors are the major detectable determinants of individual disease risk whereas in the developing countries, the emergence of asthma probably reflects the strong effect of environmental exposures associated with economic development⁷.

1.7 Pathophysiology of asthma

The fundamental problem in asthma appears to be immunological: young children in the early stages of asthma show signs of excessive inflammation in their airways. Epidemiological findings give clues as to the pathogenesis: the incidence of asthma seems to be increasing worldwide, and asthma is now very much more common in affluent countries.

In 1968 Andor Szentivanyi first described *The Beta Adrenergic Theory of Asthma*; in which blockage of the β_2 receptors of pulmonary smooth muscle cells, causes asthma²⁴. Szentivanyi's *Beta Adrenergic Theory* is a citation classic²⁵ using the Science Citation Index and has been cited more times than any other article in the history of the Journal of Allergy and Clinical Immunology, a renowned journal dedicated to allergy and immunology. In 1995, Szentivanyi and colleagues demonstrated that Ig E blocks β_2 receptors²⁴. Since, overproduction of Ig E is central to all atopic diseases, this was a watershed moment in the world of allergy²⁶.

The pathology of asthma is characterized by various changes in the airways including mucus plugging, shedding of epithelial cells, thickening of the basement membrane, engorgement of the vessels, and angiogenesis, inflammatory cell infiltration, and smooth muscle hypertrophy and hyperplasia²⁷. The pathogenesis of asthma can be broadly subdivided into inflammatory and remodeling components.

1.8 Diagnosis and assessment

Ascertainment of whether asthma is present is usually straightforward, and is based on a characteristic history and variability in lung function. In young children it can take some time to

ascertain whether the child has persistent asthma rather than wheezy bronchitis²⁸. In older patients, distinguishing severe chronic asthma from COPD can be difficult and the two disorders sometimes merge in those who have smoked cigarettes. Asthma can also be diagnosed incorrectly, especially in patients with inappropriate hyperventilation, dysfunction of the vocal cords, or obstruction of the upper airway. Diagnosis of asthma still relies on demonstration of variability (measurement of asthma severity) in lung function over time or improvement after a bronchodilator, prednisolone, or high-dose inhaled corticosteroid. Such variability can be measured with spirometry in the clinic or by regular peak flow measurements at home. Demonstration of bronchoconstriction after vigorous exercise can be useful in young people, whereas an increase in blood eosinophils could point to asthma in older patients. Other features associated with asthma, such as non-specific bronchial hyperresponsiveness to agents such as methacholine, are not specific enough to be a useful diagnostic test. The essential treatment for asthma includes oxygen, nebulised β_2 agonists, and oral or intravenous corticosteroids to patients.

1.9 Management

A patient might have poorly controlled asthma due to poor management, severe asthma, or both. Poor compliance with treatment, especially inhaled corticosteroids, continues to be an important cause of poor asthma control and much effort is needed to ensure that patients understand why prophylactic treatment needs to be taken regularly and the dangers of poor compliance. Several developments have contributed to better asthma management including development of guidelines (The British Guidelines on Asthma Management, 1997), better use of peak-flow meters, and recognition of the need to improve patient education. Patients with asthma should be advised strongly not to smoke and to lose weight, if overweight, since these measures improve asthma control. Inactivated influenza vaccine is recommended and is safe in patients with asthma (The American Lung Association Asthma Clinical Research Centers, 2001). Avoidance of allergens can be helpful for patients with specific allergen sensitivities. Complementary approaches to treatment, such as Yoga, help some patients, but overall, the effect seems to be small²⁹.

1.10 Pharmacotherapy

Drugs should be given by inhalation when possible so that the same beneficial effect can be achieved with a much smaller dose, thus causing lower systemic drug concentrations and fewer systemic adverse effects. Over the past two decades, many groups have tried to develop new

types of drug for asthma, but only the leukotriene modifiers are on the market.

Most asthma guidelines include a stepwise approach to asthma treatment, which ranges from β -agonists alone for very mild intermittent asthma to oral corticosteroids for severe chronic asthma. A schematic hierarchy of the drugs considered most appropriate for different levels of asthma severity is

shown in Figure 1.1. Treatment should be determined by symptoms, exacerbations, and lung function. There is some controversy about inhaled corticosteroids, which are very effective at suppressing inflammation in asthma. Symptoms and airway obstruction usually reappear when the drugs are discontinued.

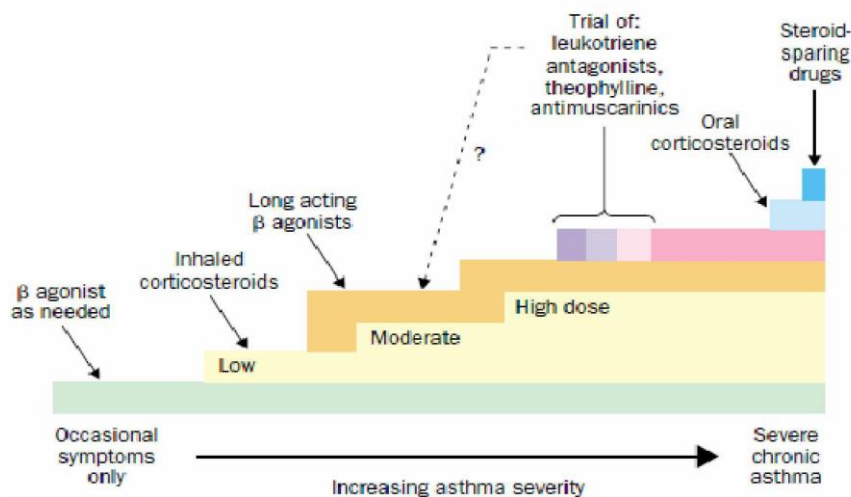


Figure 1.1. Treatment hierarchy used to add further drugs as asthma becomes increasingly severe

1.10.1 Inhaled corticosteroids

Inhaled corticosteroids are the cornerstone of treatment for asthma. They are especially helpful in patients with mild or moderate asthma, improving lung function, and reducing symptoms and exacerbations and they have been shown to reduce readmissions for asthma³¹ and asthma deaths³⁰. Inhaled corticosteroids are recommended for all patients requiring more than one puff a day from their β -agonist inhaler.

However, there are two limitations of inhaled corticosteroids. First, although small doses of an inhaled corticosteroid are very effective, the added benefit from higher doses is limited. Doubling³¹ or quadrupling³² the dose of an inhaled corticosteroid can improve asthma control, but it is usually better to add in a long-acting β -agonist. Second, long-term high doses of inhaled corticosteroids can cause systemic adverse effects, including reduced bone mineral density which is likely to predispose patients to osteoporotic fractures as they get older, and an increase in cataracts³⁴ and glaucoma³⁵.

Since inhaled corticosteroids reduce the need for oral corticosteroids, which have many more adverse effects, the goal of treatment is to give the minimum dose of inhaled corticosteroid to maintain good control. Most patients with asthma can be managed on a low dose, which will produce maximum or near maximum benefit with minimum risk of long-term adverse effect.

6. MATERIALS AND METHODS:

1 Collection, identification and authentication of plant materials

The leaves of *Capparis deciduas* were collected. The collected plant samples were deposited in the Department of Pharmacology, Suralabs, Dilsukhnagar, India for future reference

7.2 Drugs and Chemicals

Histamine dihydrochloride, acetylcholine chloride, atropine sulfate, mepyramine meclate, carrageenan were purchased from Sigma (St. Louis, MO, USA). Histamine solution was freshly prepared in normal saline (NaCl, 8.5 g/l). All the other drugs were of analytical grade and they were dissolved in distilled water and desired concentration was prepared.

Extraction

Leaves of *Capparis deciduas* were washed with distilled water to remove dirt and soil, and shade dried. Routine pharmacognostic studies including macroscopic and microscopic observations were carried out to confirm the identity of the materials.

The dried material of each plant was coarsely powdered (500 g) and defatted with aqueous (60-80°C), and then extracted separately with alcohol (95% v/v) in Soxhlet apparatus (Figure 4.5). The

extracts were filtered, and concentrated by distilling off the solvents and evaporated to dryness using water bath to get crude ethanol extract. The yield values for aqueous extract of *Capparis deciduas* and alcoholic extract of *Capparis deciduas* were 20.48% and 10.96% w/w,

respectively. Now these extracts were subjected to phytochemical screening and screened for possible pharmacological actions. For the pharmacological

tests, the extracts were suspended in double distilled water containing carboxy methyl cellulose (CMC, 0.5% w/v).



Figure 4.5 Soxhlet apparatus for the extraction of different plant Extracts

Experimental animals

Antiasthmatic studies were conducted on guinea pigs (350-500 g) of either sex fed on commercial pellet diet (Amrut, Pranav Agro Industries Ltd, India). They were group housed in polypropylene cages (640 x 410 x 250 mm high) under standard conditions of temperature ($22 \pm 20^\circ\text{C}$), relative humidity ($60 \pm 5\%$). They were divided in groups of ten animals each. The saline fed group served as control and one group was treated with a standard drug.

Before experimentation, the animals were kept on fast for 24 h but water was given *ad libitum*. Animals receiving different doses of plant extracts were also observed for any alteration in their general behavior.

They were provided with standard rodent pellet diet (Amrut, Pranav Agro Industries Ltd, Baroda, Gujarat, India) and tap water *ad libitum* except the food was withdrawn 18–24 h before the experiment. All the experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC). All the experiments and the care of the laboratory animals were according to current ethical guidelines by the Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA).

7.6 Habituation to animals

Guinea pigs were habituated to handling by holding them and injecting vehicle through oral/i.p. routes

to minimize non-specific stress and to simulate the actual protocol conditions. Handling also consisted of weighing and restraining animals on platform for 1 min, and gently massaging on dorsal site as was done in the actual protocols. The same platform was used during drug administration. Moreover, the animals were familiarized with the diet in their home cage-environment and laboratory environments before subjecting them to the tests. All the experiments commenced 24 hours following the final habituation and were conducted according to the protocols mentioned below.

7.7 Acute toxicity test (Determination of LD50)

The acute toxicity tests (LD50) for the different plant extracts were determined according to the procedure described by Lorke (1983). The crude aqueous and alcoholic extracts were used for the test. Guinea pigs (300–350 g) of either sex were used. This method involved an initial dose finding procedure, in which the animals were divided into three groups of three animals per group. Doses of 10, 100, and 1000 mg/kg were administered orally, one dose for each group. The treated animals were monitored for 24 h for mortality and general behavior.

From the result of the above step, four different doses of 200, 400, 800, and 1600 mg/kg were chosen and administered (p.o.) respectively to four groups of one guinea pig per group. The treated animals were again monitored for 24 h. The LD50 was then calculated as the geometric mean of the

lowest dose showing death and the highest dose showing no death.

Preparation of plant extracts

7.5.1 Preparation of Aqueous Extract:

Fresh leaves of *Capparis deciduas* were collected and washed under tap water. The leaves extract used was prepared by taking 20gms of finely cut leaves into 250ml beaker containing 200ml of water. The contents were mixed well and then the mixture was boiled up to 80-100°C for 4-5hrs. Further the extract was filtered with whatmann filter paper. The filtrate was boiled until the concentrated residue is formed. The concentrated product was sealed in sample covers and stored under room temperature and used for further experiment to check the activities.

7.5.2 Preparation of Alcoholic Extract:

Fresh leaves of *Capparis deciduas* were collected and washed under tap water. The leaves extract used was prepared by taking 20gms of finely cut leaves into 250ml beaker containing 200ml of alcohol. The contents were mixed well and then the mixture was boiled up to 50-60°C for 4-5hrs. Further the extract was filtered with whatmann filter paper. The filtrate was boiled until the concentrated residue is formed. The concentrated product was sealed in sample covers and stored under room temperature and used for further experiment to check the activities.

7.12 Phytochemical screening of aqueous and ethanolic extracts of *Capparis deciduas*

Aqueous and Alcoholic extracts were chemically tested to know the presence of different primary, and secondary metabolites present in them as per the following scheme:

7.12.1 Tests for sterol/steroids

7.12.1.1 Salkowski test

Few mg of the sample was taken in 2 ml of chloroform and 2 ml of concentrated sulphuric acid and shaken. The development of red color in the chloroform layer indicates the presence of sterols/steroids.

7.12.2 Test for terpenoids

7.12.2.1 Liebermann–Burchard test

Few mg of the sample was dissolved in 1 ml of chloroform and few drops of acetic anhydride. Concentrated sulphuric acid was added by the side of the test tube. Production of purple color indicates the presence of triterpenoids and blue–green color indicates the presence of sterols.

7.12.3 Test for alkaloids

Few mg of the sample was taken in 5 ml of 1.5% v/v hydrochloric acid and filtered. The filtrate was then tested using following reagents:

7.12.3.1 Dragendorff's reagent

It is a solution of potassium bismuth iodide. It was prepared by dissolving bismuth nitrate (8 gm) in

nitric acid (20 ml), and separately dissolving potassium iodide (27.2 gm) in water (50 ml), mixing the two solutions, and making up the volume to 100 ml. Above Dragendorff's reagent was sprayed on Whatman No. 1 filter paper then the paper was dried. The test filtrate after basification with dilute ammonia was extracted with chloroform and the chloroform extract was applied on the filter paper, impregnated with Dragendorff's reagent, with the help of a capillary tube. Development of an orange red color on the paper indicated the presence of alkaloids.

7.12.3.2 Mayer's Reagent

1.36 gm of mercuric chloride, and 3 gm of potassium iodide were dissolved in water to make 100 ml. To a little of each extract taken in dilute hydrochloric acid in a watch glass, few drops of the reagent was added, formation of cream colored precipitate shows the presence of alkaloid.

7.12.3.3 Hager's reagent

It is a saturated solution of picric acid in water. When the test filtrate was treated with this reagent, yellow precipitate was obtained indicating the presence of alkaloids.

7.12.3.4 Wagner's Reagent

It is a solution of potassium triiodide in water which was prepared by dissolving 1.3 gm iodine in a solution of potassium iodide (2 gm) in water to make 100 ml. Formation of brown precipitate after addition of this reagent in extract indicates the presence of alkaloids.

7.12.4 Test for tannins

Sample was taken separately in water, warmed, and filtered. Tests were carried out with the filtrate using following reagents:

7.12.4.1 Ferric chloride test

A 5% w/v solution of ferric chloride in 90% alcohol was prepared. Few drops of this solution were added to a little of the above filtrate. Dark green or deep blue color shows the presence of tannins.

7.12.4.2 Lead acetate test

A 10% w/v solution of basic lead acetate in distilled water was added to the test filtrate. Precipitate indicates the presence of tannins.

7.12.5 Test for flavonoids

7.12.5.1 Shinoda test

To the sample, 5 ml of 95% ethanol, few drops of HCl, and few magnesium turnings were added. The pink color shows the presence of flavonoids.

7.12.6 Test for carbohydrates

7.12.6.1 Molisch's test

About 0.1 gm of the sample was dissolved in 2 ml of water, and added 2-3 drops of 1% ethanolic solution of alpha naphthol, and then carefully poured 2 ml of concentrated sulphuric acid down the side of the test tube so that it forms a heavy

layer at the bottom. A deep violet color is produced if carbohydrates are present.

7.12.6.2 Fehling's test

1 ml of Fehling's A and 1 ml of Fehling's B solutions were mixed and boiled for 1 minute. Equal volume of sample was then added, heated in boiling water bath for 5-10 minutes. First a yellow then brick red color shows the presence of carbohydrates.

7.12.6.3 Benedict's test

Equal volumes of the reagent, and sample were added. Mixture was then boiled for five minutes. Depending on the reducing sugar present a range of colors develops.

7.12.7 Test for proteins

7.12.7.1 Biuret test

To the sample 4% NaOH, and few drops of 1% CuSO₄ were added. Violet or pink color indicates the presence of proteins.

7.12.7.2 Xanthoproteic test

Sample was mixed with 1 ml of concentrated sulphuric acid, formation of precipitate shows positive test.

7.12.7.3 Millon's test

3 ml of sample was mixed with Millon's reagent, formation of precipitate indicates the presence of proteins.

7.12.8 Test for saponins

7.12.8.1 Foam test

A few mg of the sample was shaken vigorously with water. Honeycomb like foam indicates the presence of saponins.

7.12.8.2 Hemolytic test

Sample was added to one drop of blood placed on glass slide. Hemolytic zone indicated the presence of saponins.

7.12.9 Test for anthraquinone glycosides

7.12.9.1 Borntrager's test

To 3 ml of the sample, dilute sulphuric acid was added, boiled, and filtered. To the filtrate equal volume of chloroform was added, and shaken. After separating the organic layer, ammonia was added. Turning pink of ammoniacal layer indicates the presence of said glycosides.

7.12.10 Test for cardiac glycosides

7.12.10.1 Keller-Kiliani test

The sample was dissolved in acetic acid containing trace amounts of ferric chloride. It was then transferred to the surface of concentrated sulphuric acid. A reddish brown ring will be formed at the junction, and the color slowly changes to blue.

7.12.10.2 Legal's test

A few drops of pyridine, and sodium nitroprusside were added to the sample, and made alkaline. A pink or red color is obtained.

7.10 Screening for antiasthmatic activity

7.10.1 Histamine-induced bronchospasm in guinea pigs (Armitage et al., 1961)

The guinea pigs fasted for 24 h were exposed to an atomised fine mist of 2% histamine dihydrochloride aerosol (dissolved in normal saline) using nebulizer at a pressure of 300 mm Hg in the histamine chamber (24 x 14 x 24 cm, made of perplex glass) (Figure 4.7). Guinea pigs exposed to histamine aerosol showed progressive signs of difficulty in breathing leading to convulsions, asphyxia, and death. The time until signs of convulsion appeared is called pre-convulsion time (PCT/PCD). By observation experience was gained so that the preconvulsion time can be judged accurately. As soon as PCD commenced, animals were removed from the chamber and placed in fresh air to recover. In the present experiments the criterion used was time for onset of dyspnea and percent protection was calculated.

RESULTS:

8. Extraction

Dried leaf powder of *Capparis deciduas* (500 gm) were extracted with water and alcohol (95% w/v) to get concentrated aqueous and alcoholic extract. The yields of extracts were as follows: AQECD (20.48% w/w), ALECD (11.45% w/w).

5.2 Acute toxicity test (Determination of LD50)

The LD₅₀ of the AQECD and ALECD was calculated to be 2262.7 and 1131.4mg/kg by oral route. During the acute toxicity study, animals were observed for gross behavioral and morphological changes (respiratory distress, immobility, convulsion, loss of righting reflex etc.). Based on the results of acute study, doses were then selected. The plant extracts did not produce any significant changes in the normal behavior of the animals, and no toxic symptoms were seen at the dose levels studied.

5.3 Phytochemical screening of different plant extracts

Table ----- depicts results of screening of different plant extracts for various phytochemical constituents. AQECD showed the presence of alkaloids, proteins, anthraquinone glycosides, flavonoids, saponins, sterols, tannins, and carbohydrates. ALECD was found to contain alkaloids, flavonoids, saponins, steroids, and tannins.

Compounds	Name Of The Test	Leaf Extracts
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		Aqueous	Alcoholic
Alkaloids	Dragendroff's test	+	-
	Mayer's test	-	+
	Wagner's test	-	-
	Borntrager's test	+	+
Anthraquinone	Modified Borntrager's test	-	-
	Molisch's test	-	+
Carbohydrates	Anthrone reagent test	+	+
	Benedict's reagent test	+	+
Cardiac Glycosides	Kellar Kilani test	-	-
	Potassium hydroxide test	-	-
Flavonoids	Shinoda test	+	-
	Ammonia test	-	+
Glycosides	Benodict's test	+	-
	Fehling's test	-	-
Phenols	Ferric chloride test	-	-
	Phosphomolybdic acid test	-	-
Phlobatannins	Hydrochloric acid test	-	-
	Xanthoprotein test	-	-
	Biurete test	-	-
Proteins	Million's reagent test	+	-
Quinines	Sodium hydroxide test	-	-
Reducing sugar	Benedict's reagent test	-	-
Resins	Turbidity test	+	+
Saponins	Foam test	+	+
Steroids/Terpenoids	Salkowski test	+	+
	Lieberman-Burchard test	-	-
Tannins	Bramer's test	+	+

'+' found to be present, '-' found to be absent

5.4 Histamine-induced bronchospasm in guinea pigs

The results are summarised in Tables ----. Histamine aerosol produced bronchoconstriction in all control group animals. All control animals showed convulsion during the first 3 min of the experiment. The aqueous and alcoholic extracts were significantly protected animals ($P < 0.01$) from histamine-induced bronchoconstriction. Prior treatment of AQECD (200, and 300 mg/kg, i.p.) offered significant protection to guinea-pigs against histamine aerosol-induced bronchospasm ($P < 0.01$). ALECD at the doses 200, and 300 mg/kg,

i.p. significantly protected guinea-pigs against histamine aerosol-induced bronchospasm ($P < 0.01$). Mepyramine (a standard anti-histaminic drug, 8 mg/kg, i.p.) significantly protected 90% of animals from asphyxia ($P < 0.001$). However, prior treatment with AQECD (100 mg/kg), and ALECD (100 mg/kg) could not offer protection from the development of asphyxia produced by histamine aerosol.

Effect of aqueous and alcoholic extracts of *Capparis deciduas* leaves on acetylcholine-aerosol-induced bronchospasm in guinea pigs

Treatment	Dose (mg/kg, i.p.)	Protection (%)
Control	Saline, 1ml/kg	-
Mepyramine	8	90
AQECD	100	60
	200	80
	300	85
ALECD	100	64
	200	80
	300	80

*Values are mean $\pm$ S.E.M. (n = 5); nsNot significant, ** $P < 0.01$ vs. control; Dunnett's *t*-test after One-way ANOVA.

5.5 Acetylcholine-induced bronchospasm in guinea pigs

The results are summarised in Table ----. Acetylcholine aerosol produced bronchoconstriction in all animals of control group. The aqueous and alcoholic extracts were significantly protected animals ($P < 0.01$) from acetylcholine-induced bronchoconstriction. Prior

treatment of AQECD (200, and 300 mg/kg, i.p.), and ALECD (200 and 300mg/kg, i.p.) has offered significant protection ($P < 0.01$) to guinea-pigs against acetylcholine aerosol-induced bronchospasm. AQECD (100 mg/kg, i.p.), and ALECD (100 mg/kg, i.p.) could not offer protection from the development of asphyxia produced by acetylcholine aerosol. Atropine sulfate (a standard anti-muscarinic drug, 2 mg/kg, i.p.) significantly prolonged pre-convulsion time to 460 ± 4.33 sec ($P < 0.01$) and protected animals from asphyxia.

Treatment	Dose (mg/kg, i.p.)	Preconvulsion time(sec)	Protection (%)
Control	Saline, 1ml/kg	128 $\pm$ 2.72	-
Standard	2	460 $\pm$ 4.33	72.17
AQECD	100	193 $\pm$ 1.38	33.67
	200	287 $\pm$ 2.98	55.4
	300	280 $\pm$ 2.32	54.28
ALECD	100	203 $\pm$ 3.74	36.94
	200	298 $\pm$ 5.03	57.04
	300	295 $\pm$ 5.05	56.61

*Values are mean $\pm$ S.E.M. (n = 5); nsNot significant, ** $P < 0.01$ vs. control; Dunnett's *t*-test after One-way ANOVA.

DISCUSSION:

In this study, an attempt has been made to evaluate antiasthmatic activity of *Capparis deciduas* in the experimental animals. The results of the study indicated that antiasthmatic effect has shown significant protection of *Capparis deciduas* against Histamine and Acetyl Choline induced in rodents.

The acute toxicity was determined by the method of Lorke (1983), which utilizes less number of mice and provides a 24-h LD₅₀ value, which is adequate for most practical purposes. The LD₅₀ values for AQECD were found to be 2262.7 mg/kg, p.o. The LD₅₀ values ALECD were found to be 1131.4 mg/kg. These LD₅₀ values fall within the practically non-toxic range (Loomis, 1978). Based on these results, doses of 100, 200, 300 mg/kg of different plant extracts were selected for various animal models. The antiasthmatic action was evaluated by sub-effective doses of *Capparis deciduas* extracts.

Histamine and acetylcholine antagonists can be conveniently recognized and assayed by their ability to protect guinea pigs against lethal effects of bronchospasm induced by histamine and acetylcholine, respectively (Broadbent & Bain, 1964). The results of the present study showed that prior treatment of aqueous and alcoholic extracts of *Capparis deciduas* protected the animals to a significant extent from the development of asphyxia produced by both the spasmogens. This is indicative of antihistaminic and anticholinergic

activities of the *Capparis deciduas*. Interestingly, the effect was significantly higher in both aqueous and alcoholic plant extracts when compared to control.

In the present study, guinea pigs were used because of the extreme sensitivity of their airways to the primary mediators of bronchoconstriction, including histamine and leukotrienes, and their ability to be sensitized to foreign proteins. Moreover, the resemblance of pulmonary responses and anaphylactic sensitization to histamine challenge in both guinea pigs and humans made this species the model of choice. Although there is no perfect model of asthma which simulates asthmatic patients, guinea pig airways react to histamine, acetylcholine, leukotrienes, and other bronchoconstrictors in a manner similar to that seen in humans (Popa et al., 1973; Agrawal et al., 1991). Another similarity between the guinea pig model and asthmatic patients is that enhanced bronchoconstriction occurs in both species following sensitization, in response to α -adrenergic antagonists (Matsumoto et al., 1994). Thus, the guinea pig model resembles the human allergic pathology in several aspects, especially in terms of mediator release.

The role of histamine and acetylcholine in asthma is well established (Nelson, 2003). In the early stage of asthma, release of inflammatory mediators like histamine, tryptase, acetylcholine, leukotrienes, and prostaglandins are triggered by exposure to

allergens, irritants, cold air or exercise (Bosquet et al., 2000). Some of these mediators directly cause acute bronchoconstriction. Spasmolytic drugs like α -adrenergic agonists, xanthine derivatives, and anticholinergics are used as quick relief medications in such acute asthmatic attacks (Horwitz & Busse, 1995).

In the present study, we have used histamine and acetylcholine as spasmogens in the form of aerosols to cause immediate bronchoconstriction in guinea pigs. Mepyramine (8 mg/kg, i.p.) and atropine sulphate (2 mg/kg, i.p.) were used as reference standard against histamine and acetylcholine-induced bronchospasm respectively (Shah & Parmar, 2003). The *Capparis deciduas* have shown significant bronchoprotection against both the types of spasmogens as compared to control. AQECD and ALECD showed significantly protection from histamine-induced bronchoconstriction and anticholinergic action in the acetylcholine-induced bronchoconstriction. Ayurveda has recommended a number of plants for the treatment of asthma and other allergic disorders and has been successful in controlling the disease as well (Zhimmeth & Tashkin, 2000). Large numbers of medicinal plant preparations have been reported to possess bronchodilatory effects; some of these include *Adhatoda vasica* (Amin & Mehta, 1959), *Benincasa hispida* (Kumar & Ramu, 2002), *Capparis deciduas* (Tripathi & Das, 1977), *Cissampelos sympodialis* (Thomas et al., 1997), and *Sarcostemma brevistigma* (Saraf & Patwardhan, 1988). Phytoconstituents like alkaloids and flavonoids are attributed to possess bronchodilatory activity (Amin & Mehta, 1959; Saraf & Patwardhan, 1988). Qualitative phytochemical investigation of ethanolic extracts which are present as ingredients in the aqueous and alcoholic extracts of *Capparis deciduas*, have shown presence of these constituents. Therefore, the results of present investigation suggested that, leaves extracts have significant bronchodilatory activity.

CONCLUSION:

Among several respiratory diseases affecting man, bronchial asthma is the most common disabling syndrome. The therapy of asthma usually employs steroids or disease modifying drugs. The long-term use of these, however, may not limit the disease progression. All of these drugs have side effects and the search for a novel anti-asthmatic drug continues. There is a need to identify effective and safe remedies to treat bronchial asthma (Govindan et al., 1999). The herbal medicines are rich for the treatment of asthma, selected plant might prove to be the most potent for the treatment of asthma and the side effects of the allopathic treatment can be reduced.

For this purpose, *Capparis deciduas* have been used as ayurvedic medicine to cure asthma and other disease.

The present study demonstrates the potent mast cell stabilizing activity, anti-histaminic activity, anticholinergic activity of leaves of *Capparis deciduas* medicinal plants in different models of asthma thereby indicating the possibility of developing a herbal drugs as cheaper, safer and potent anti-asthmatic therapeutic agent. The AQECD and ALECD have produced protective effect against asphyxia. The selected plant species have been used in the traditional systems of medicine for treating various ailments. Importantly, there was no scientific evidence for the anti-asthmatic activity of these plants.

The present study validates traditional claims of these plants. Although the results from this study are quite promising for the use of *Capparis deciduas* as a medicinal agent for asthma, several limitations exist in the current literature. Further studies are suggested to establish the antiasthmatic activity by conducting clinical trials and also to isolate and characterize the active principle/s responsible for the action.

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