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EVALUATION OF ANTIASTHMATIC ACTIVITY OF ETHANOLIC EXTRACT OF BARK OF *CAPPARIS DECIDUA*

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ABSTRACT

Ethno-pharmacological significance: *Capparis deciduas* family (Capparidaceae) is eminent for curing a variety of ailments such as toothpain, cough, fever and rheumatism.
Aim of the study: The present study was to evaluate anti-asthmatic activity of ethanolic extract of *Capparis decidua* bark in various animal models.
Materials and methods: Animals were housed together of in four cages and separates for male and females. The animals were maintained under standard environment condition and temperature at 22^{0}C and 30-70% RH. The animals were fasted for 3-4 hr with drinking water and slandered palliated diet.
Results: In the groups of mice, pretreated with ethanolic extract of fruits of *Capparis Decidua* at dose of 100 and 200mg/kg p.o, there was significant (p<0.01) inhibition of milk-induced Leucocytosis as compared to the control.
Conclusion: In the present study the ethanolic extracts of bark of *Capparis Decidua* was evaluated for the management of asthma. Ethanolic extract of fruits of *Capparis Decidua* may possesses antiasthmatic activity which may be due to antihistaminic activity, broncho dilating activity, adaptogenic activity, mast cell stabilizing activity, anti-inflammatory activity (inhibition of antigen antibody reaction) and anti-oxidant activity. Thus, *Capparis Decidua* fruits may be used in the management of asthma.
Keywords: Anti-asthmatic, Ethanolic extract, Extraction, Phytochemical Investigation, Toxicity Studies.

INTRODUCTION

Asthma is a chronic inflammatory respiratory disease characterized by periodic attacks of wheezing, shortness of breath, and a tight feeling in the chest. A cough producing sticky mucus is symptomatic. The symptoms often appear to be caused by the body's reaction to a trigger such as an allergen (commonly pollen, house dust and animal dander), certain drugs, an irritant (such as cigarette smoke or workplace chemicals), exercise, or emotional stress. Asthma is a problem in the airways due to multiple factors. The main physiologic features of asthma are episodic airway obstruction characterized by expiratory airflow limitation. The dominant pathological feature is airway inflammation, sometimes associated with airway structural changes.(1)

Asthma is a common illness affecting around 5-10% of the total population in our country. Symptoms can appear at any age, but most commonly start in childhood till the age of 10 years and boys are affected twice as often as girls. Triggers are agent which promotes broncho-constriction they may be specific such as antigens acting through immunologic mechanism or non-specific such as exercise, Emotion cold air, aspirin, and non-steroidal anti-inflammatory drugs. Sulphurdioxide, beta blockers and metabisulphite.(2) The word 'Asthma' is derived from the Greek word aazein, meaning 'sharp breath'. Hippocrates was the first to use it in reference to the medical condition, in 450 BC Galen wrote much about asthma, nothing that it was caused by partial or complete bronchial obstruction. In the 17th century, Bernardino ramazzini noted a connection between asthma and organic dust. The use of bronchodilators started in 1901, but it was not until the

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1960s that the inflammatory component of asthma was recognized and anti inflammatory medication was added to the regimens.[3]

Asthma is a disease of airways that is characterized by increasing responsiveness of the trachea-bronchial tree to a variety of stimuli resulting in widespread spasmodic narrowing of air passage which may relieved spontaneously or by therapy. Asthma is a chronic inflammatory lung disease that can cause repeated episodes of cough, wheezing and breathing difficulty. During an acute asthma episode, the airway lining in the lungs becomes inflamed and swollen. In addition, mucus production occurs in the airway and muscles surrounding the airway spasm. Combined, these cause a reduction in air flow. [4]

Common signs and symptoms of an acute asthma episode include Coughing, wheezing - may be absent, breathlessness-while walking or while at rest, respiratory rate increased, chest tightness, chest or abdominal pain, fatigue, feeling out of breath, agitation, increased pulse rate, inability to participate in sports.[5] Over the years, there have been several ways of classifying asthma and of distinguishing one form of the disease from another.[6]

EPIDEMIOLOGY OF ASTHMA:

Allergy is one of the common diseases that affect mankind with diverse manifestations. The prevalence of allergy and asthma has risen in the recent years despite an improvement in the general health of the population.[7]

Asthma is a common disease which varies widely from one country to another. It affects about 3 to 7% of the adult population, being more common in children ages. It is one of the most important chronic diseases in children and is more common in males by a ratio of 2:1, but when they reached puberty, this ratio tends to equalize. In the past twenty years there has been an increase in incidence due in part to environmental pollution and the consequences of this, and partly to the increase in world population According to World Health Organization (WHO) estimates 300 million people suffer from Asthma, 2, 55,000 people died of Asthma in 2005 and over 80% of Asthma deaths are reported from low and lower-middle income countries. Asthma is the most common chronic disease among children. Asthma is a public health problem not just for high-income countries; it occurs in all countries regardless of the level of development. Most asthma-related deaths occur in low- and lower-middle income countries. Asthma is under-diagnosed and under-treated. It creates substantial burden to individuals and families and often restricts individuals' activities for a lifetime.[8]

In India, 57,000 deaths were attributed due to Asthma in 2004 (WHO, 2004) and it was seen as one of the leading cause of morbidity and mortality in rural India.[8] Though effective screening, evaluation, and management strategies for asthma are well established in high income countries, these strategies have not been fully implemented in India as evidence had previously suggested that asthma is not to be treated independently but fitted into the general spectrum of respiratory diseases. Furthermore, even though medicines that treat asthma effectively are available at affordable costs, they rarely reach more than one percent of those who would benefit from it. [9]

GLOBAL BURDEN OF ASTHMA:

Approximately 300 million people worldwide currently have asthma, with estimates suggesting that asthma prevalence increases globally by 50% every decade. With the projected increase in the proportion of the world's urban population from 45% to 59% in 2025, there is likely to be a marked increase in the number of asthmatics worldwide over the next two decades. It is estimated that there may be an additional 100 million persons with Asthma by 2025.[10]

The airways in a person with asthma are very sensitive and reacts too many things, which are referred to as "triggers." Coming into contact with these triggers often produces asthma symptoms. A physiologic hallmark of asthma is reduction in airflow can be demonstrated and by simple spirometry. Ciba symposium (1959) defined bronchial asthma on a physiological basis as a condition with wide spread narrowing of the bronchial airways which changes its severity over short period time either spontaneously or under treatment and is not due to cardiovascular disease.[11]

PREVALENCE OF ASTHMA IN INDIA:

Over 50 million people in central and southern Asia have asthma, and many do not have access to the medications that can control the disease, Due to rapid industrialization and urbanization throughout the region, the prevalence of asthma is predicted to increase rapidly in the coming years. The increase is likely to be particularly dramatic in India, which is projected to become the world's most populous nation by 2050. An absolute 2% increase in the prevalence of asthma in India would result in an additional 20 million people with the disease. 57.5 estimated total deaths (2'000); 5.1 estimated deaths per 100000 population; 277 DALYs (disability adjusted life-year) per 100,000; 6.5 age-standardized deaths per 100,000; constitutes 0.2% of all deaths and 0.5% of National burden of diseases.[12]

PATHOPHSIOLOGY AND PATHOGENESIS OF ASTHMA

In asthma, constriction of the airways occurs due to bronchoconstriction and bronchial inflammation. Bronchoconstriction is 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 allergens. Airflow limitation in asthma is recurrent and caused by a variety of changes in the airway including bronchoconstriction, airway edema, airway hyper-responsiveness, and airway remodeling.[2]

Inflammation has a central role in the Pathophysiology of asthma. As noted in the definition of asthma, airway inflammation involves an interaction of many cell types and multiple mediators with the airways that eventually results in the characteristic pathophysiological features of the disease. The processes by which these interactive events occur and lead to clinical asthma are still under investigation.

Broncho-constriction:

In asthma, the dominant physiological event leading to clinical symptoms is airway narrowing and a subsequent interference with airflow. In acute exacerbations of asthma, bronchial smooth muscle contraction (bronchoconstriction) occurs quickly to narrow the airways in response to exposure to a variety of stimuli including allergens or irritants. Allergen-induced acute broncho-constriction results from an IgE-dependent release of mediators from mast cells that includes histamine, tryptase, leukotrienes, and prostaglandins that directly contract airway smooth muscle. Aspirin, other NSAID and other stimuli (including exercise, cold air, and

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irritants) can also cause acute airflow obstruction in some patients, and evidence indicates that this Non-IgE dependent response also involves mediator release from airway cells.[13, 14]

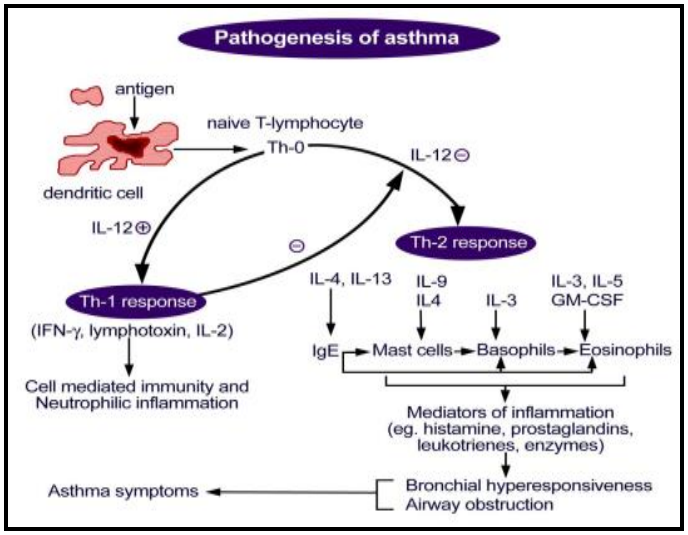

Fig.1: Pathogenenesis of Asthma

INFLAMMATORY MEDIATORS:

Histamine:

Histamine has long been known to be a major mediator of inflammation. Allergen entering the airways may crosslink immunoglobulin E (IgE) on mast cells (or basophils) to release histamine, lipid mediators and cytokines. Antigen is also processed by airway dendritic cells and macrophages for presentation to T-helper cells. [15]

Immunoglobulin E (IgE):

IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic diseases and the development and persistence of inflammation.[15]

AYURVEDIC TREATMENT:

Bronchial Asthma is known as *Tomaka Shvasa* in Ayurveda. It is an allergic condition resulting from the reaction of the body to one or more allergens and is one of the most fatal respiratory diseases. Bronchial asthma is increasing day by day with the increase in level of pollution and the stressful lifestyle followed by people. Asthma is known as Shwaasa roga in Ayurveda. There are five main types of asthma in Ayurveda: tamaka shwaasa roga, urdhwa shwaasa roga, chinna shwaasa roga, maha shwaasa roga and kshudra shwaasa roga. All these kinds of shwaasa roga are due to vitiation of vata and kapha doshas.The main types of vata that are vitiated are the Paraná vata and the udaana vata. Sitopaladi choorna is a very common medicine taken by asthmatic patients. It is to be taken thrice or four times a day, mixed with honey. One alternative to sitopaladi choorna is the pippaladi choorna. Agastya rasayana is another popular medicine which is prepared with Chebulic Myrobalan as its main ingredient. Along with Chyavanprasha, it is commonly prescribed to asthmatic patients.There are some specific ayurvedic preparations that are prescribed in order to reduce the attacks of asthma immediately. These are Shwaasa Kaasa Chintamani rasa, Suwarna Pushpasuga rasa, Kanakasava, etc.[16-19]

INFORMATION ON SELECTED PLANT [16, 17]

Scientific Name and Common Name

Kingdom : Plantae
Phylum : Spermatophyta
Subphylum : Angiospermae
Class : Dicotyledonae
Order : Capparidales
Family : Capparaceae
Genus : Capparis
Species : Capparis decidua

Vernacular Names

Sanskrit → Dirghapattraka
Hindi → Kair
English → Bare Caper,Caper Berry
Bengali → Karil
Gujarati → Kerdo
Marathi → Karil,Kiral
Telugu → Enugadanta
Tamil → Cira-K-Koli
Malyalam → Karimuli
Punjabi → Karinha
Kannada → Chippuri

Fig. 2: *Capparis Decidua Plant*

Chemical Constituents

C. decidua has been found to contain a number of alkaloids, terpenoids, glycosides, and fatty acids. The bark of *C. decidua* has been reported to contain two sitosterols, one diterpene alcohol, two aliphatic constituents and one diterpenic ester.

Spermidine and spermine polyamines, Isocodonocarpine, capparisinine and capparidisine are the important spermidine alkaloids isolated from bark of *C. decidua.* Among other alkaloids, 14-N-acetyl isocodonocarpine, 15-N-acetyl capparisine, cadabicine, stachydrine, capparisine, and codonocarpine have been isolated from bark.

Constituent Percent (wet basis)

Components	
Carbohydrates	59.41%
Fats	7.43
Ash	5.96%
Protein	14.88%
Crude fiber	12.32%

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Uses:

Leaves - Act as appetizer, cardioprotective

Bark - Used against intermittent fever and rheumatism, analgesic diaphoretic, laxative, antihelmenthic, cures cough and asthama

Immature fruit - Cures constipation kills intestinal worms

Flower buds - Renal disinfectant, diuretic, tonic, potherb formation

Root - Purgative activity, Cures bronchial disorders, antidote to scorpion bite

Fruit - Astringent properties, treats dysentery, cholera and intermittent fever

Stem - Used in alveolaris and pyorrhoea, anti-fertility drug, toothache reliever

Seeds - Antibacterial activity, treat urinary purulent discharges

Asthma is a chronic inflammatory respiratory disease characterized by periodic attacks of wheezing, shortness of breath, and a tight feeling in the chest.[20]

The actual goal of the present study was to evaluate anti-asthmatic activity of ethanolic extract of bark of *Capparis decidua* in various animal models.

MATERIALS & METHODS

MATERIALS

Plant Material

The collection of the plant material of *Capparis Decidua* was done in month in the April 2020 from Jodhpur region, Rajasthan. Since the plants will be enriched with phyto constituents during that time.

Housing of animals and Approval of Institutional Animal Ethical committee

Guinea pigs were selected in the range of 300-400gm weight and weights of mice were in between 35-50gm. Isolated Goat trachea was obtained from local slaughter house in Jodhpur.

Animals were housed together of in four cages and separates for male and females. The animals were maintained under standard environment condition and temperature 220C and 30-70 humidity. The animals were fasted 3-4 hr to dosage and drinking water and slandered pelleted diet. All procedures described were reviewed and approved by the institutional committee for ethical use of animals. Prior to study proposal detailing the experimental protocol was submitted to Institutional Animal Ethical Committee of Jodhpur, Rajasthan [Reg. No. 1491/PO/a/11/CPCSEA], with protocol approval reference no. GDMCP/2019-20/255(F).

Instrument:

Soxhlat apparatus Histamine chamber, W.B.C. Counter microscope, Bioassay assembly, surgicals.

METHODS

PRELIMINARY PHYTHOCHEMICAL STUDIES

Standardization of traditional plants is a critical and essential issue to be considered in assuring the therapeutic efficacy, safety and to ratio rationalize their use in the health care. The First step in the standardization of plant material is correct identification of the species concerned.

DRYING

The Fruit of *Capparis Decidua bark* were washed and dried under shade for 10 days.

Grinding of the Plant for extraction

Cleaned and grind with help of iron Mortar-pestle. After proper grinding, the weight of the powder was obtained. These powders were used for extraction.

Solvents order and temperature

Petroleum ether: 60°-80°C

Ethanol: 75°-79°C

General Extraction

An extraction naturally depends on the texture and water content of the plant material being isolated. Extractive values were designed to indicate the percentage of therapeutically important constituents. Successive solvents extraction comprises of treating the moderately coarse powder of the drug, with non polar solvent to polar solvent according to their solubility's Successive solvents extraction was carried out according to the method suggested by Rosenthaler and the extracts obtained were tested for presence of various plant constituents. [16, 19-21]

Selection of Extraction Method

Generally followed three method are employed in the extraction of plant materials-

1. Maceration
2. Percolation
3. Soxhlet extraction

These processes have their own merits and demerits maceration and percolation may be employed in extraction of thermo labile constituents. Soxhlet extraction is rapid and continuous and may be employed in extraction of sparingly soluble constituents due to repeated extraction which cannot be done by either maceration or percolation methods. But soxhlet extraction cannot be used for extraction of thermo labile substance. Due to the various advantages offered by soxhlet extraction this method was selected for present study.

Procedure of Extraction

The flask with the given solvents is heated to a particular temperature. The vapour produce passes through the siphon into the thimble kept above where it is condensed and tickles down in to the flask again through the thimble dissolving. The process is continued in it. The method is described as the continuous extraction. The process is continued until all the soluble constituents get separated. The extract at the bottom was collected and dried under reduced temperature and pressure. Each time, before the extraction with other solvents, the powered substance is air dried. About 100gm of dried powder was properly packed in Whatmann filter paper and kept in thimble and the sox let apparatus was set up. The extraction of powder was done with different solvents with solvents of increasing polarities like petroleum ether (60-80°c), ethanol. The solvent of increasing using reflex condenser and stored in desiccators. Time required for completing the extraction process with both the solvents were noted and percentage yield were calculated accordingly. [16, 19-21]

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QUALITATIVE CHEMICAL EVALUATION

The extract were prepared and subjected to qualitative tests for the identification of various plant constituents. [16, 19-24]

DETECTION OF CARBOHYDRATES:

Small quantities of the extract were dissolved separately in distilled water and filtered. The filtrate was subjected to

a) Molisch's Test
b) Fehling's Test
c) Benedict's Test

Molisch Test:

To the filtrate, a few drops of 1% alcoholic α-naphthol was added and 2ml of concentrated sulphuric acid was added slowly through the sides of the test tube. A brown ring was formed at the junction of the two layers.

Fehling's test:

Small portion of the extract were treated with equal volume of solution A and B and then heated on water bath.A brick red precipitate was formed.

Bendict's test:

Small portion of the extract were treated with equal volume of Bendict's reagent and heated on a water bath.A greenish yellow precipitate was formed indicating the presence of reducing sugar.

DETECTION OF PROTEIN:

A. Biuret test: Small portion of the Filtrates were treated with 4% NaOH and few drops of 1%$CuSO_4$ solution. A violet or pink colour not formed in both alcoholic and petroleum ether extracts of *Capparis Decidua.*

B. Milton test:

Small portion of the filtrate were treated with 5 ml Millions's reagent. White ppt . Warm Ppt. was not turn to brick red in both alcoholic and petroleum ether extract of *Capparis Decidua*.

TEST FOR ALKALOIDS:

Small amount of the solvents free ethanolic and Petroleum ether extracts were separately stirred with a few ml of dilute HCL and filtered. The filtrates were tested with various alcoholic reagents**.**

Mayer's Test

To the small a few quantities of the extracts, Mayers reagents was added. Presence of cream-coloured precipitate the presence of alkaloids in alcoholic extracts and cream colour not formed in petroleum ether extracts *Capparis Decidua*.

Dragendorff's Test

To small quantity of extracts, Dragendorff's reagent was added. Presence of orange brown colour not formed in petroleum ether extracts of *Capparis Decidua.*

Wagner's Test

To small quantity of the extracts, Wagner's reagent was added. Presence of reddish brown precipitate, indicate the presence of alkaloids in alcoholic plant extracts and absences in petroleum ether extracts of *Capparis Decidua.*

TEST FOR FIXED OILS AND FATS

a) Spot test
b) Saponification test:

a) Spot test:

A small quantity of extract was pressed between two filter papers. Oil stains were observed with the extracts indicating the presence of fixed oils and fats in petroleum ether extracts but absence in alcoholic extracts of *Capparis Decidua.*

b) Saponification test:

Few drops of 0.5N alcoholic potassium hydroxide were added to extract along with a few drops of phenolphthalein. The mixture was heated on water both for one hour. Soap was formed with the extracts the presence of fixed oils and fats in petroleum ether extracts and absence in alcoholic extracts of *Capparis Decidua.*

TEST FOR GLYCOSIDES

A small portion of the extract were hydrolyzed with hydrochloric acid for one hour on a water bath and hydrolysis was subjected to

a) Legal's test
b) Baljet's test
c) Borntrager's test

Legal's test:

To the hydrolysis 1 ml of pyridine and few drops of sodium nitro-pruside solution was added and then made alkaline with sodium hydroxide solution A Pink colour was observed in alcoholic extracts of *Capparis Decidua* andabsence in petroleum ether extracts.

Baljet's Test

To a section of plant extracts sodium picrate solution was added. A yellowish orange colour was observed in alcoholic extracts and absence in petroleum ether extracts of *Capparis Decidua.*

Borntrager's Test

Hydrolysate was treated with chloroform and the chloroform layer was separated. To this, equal quantity of dilute ammonia solution was added.

A pick colour was observed in ammoniacal layer of chloroform and alcoholic extracts showed the presence of glycosides while pink colour not formed in petroleum ether extracts.

PHARMACOLOGICAL EVALUTION

ACUTE ORAL TOXICITY STUDY:

Dose was selected by using acute toxicity study (OECD)**.** The acute toxicity study for ethanolic extract of fruit of *Capparis Decidua* was performed using animals (mice). The animals were fasted overnight prior to the experiment and maintained under standard conditions. To find the LD_{50} of ethanolic extract of fruits of *Capparis Decidua*, five groups of animal, containing five in each group, were given *Capparis Decidua* in the doses of 100, 200,and 400, mg/kg orally. The animals were observed for 5 min every 30 min till 2 h and then at 4, 8 and 24 h after treatment for any behavioral changes/mortality. They were further observed daily for 7 days for mortality. Body weight of the animal was recorded. The other observations include change in skin, eyes, and mucous membranes activity and behavior. [25]

Dose selection

Dose was selected based on acute oral toxicity study done on ethanolic extracts of fruits *Capparis Decidua*. Extracts was found to be safe up to dose level.

Prepration of drug solution

Volume of drug solution was calculated based upon the body weight of the animals. Ethanolic extract of *Capparis Decidua* was soluble in distilled water with the help of Sodium CMC.

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Chlorpheniramine Maleate was dissolved in distilled water. Histamine was dissolved in distilled water.

Volume of drug solution

The volume of drug solution was calculated on the bases of body weight. The volume of drug solution was constant throughout the study in accordance to their body weight.

ANTIASTHMATIC- ACTIVITY (16, 19-24)

PREPARATION OF ISOLATED GOAT TRACHEAL CHAINS:

Isolated Goat trachea was obtained from slaughter house. Trachea was cut into individual rings and tied together in form of a chain. Trachea was suspended in bath of Kreb's solution (composition: NaCl-6.9, KCl-0.35, $CaCl_2$-0.28, $MgSO_4$-0.28, $NaHCO_3$-2.1, KH_2PO_4-0.16 and Glucose-gm/liter), which was continuously aerated and maintained at 37 ± 0.5 ^oC) One end of the tracheal chain was attached to an S-shaped aerator tube and other attached to an isotonic frontal writing lever (magnification 10-12 folds). Tissue was allowed to equilibrate for 45 minutes under a load of 400 mg. A dose response curve for histamine was taken in variant molar concentrations by maintaining 15 min time cycle. After obtaining a dose response curve of histamine on trachea, chlorphenaramine maleate (1 µg/ml) was added to the respective reservoir and same doses of histamine were repeated. On another goat tracheal chain preparation step 1 to 6 was repeated and after obtaining a dose response curve of histamine on trachea, the ethanolic extract of *Capparis Decidua* was added to the respective reservoir and same doses of histamine were repeated Graph of percentage of maximum contractile response on ordinate and negative logarithm of molar concentration of histamine on abscissa was plotted to record dose response curve of histamine, in absence and in presence *Capparis Decidua* and standard.

HISTAMINE INDUCED BRONCHO-CONSTRICTION IN GUINEA PIG: (16, 19-24)

Groups (n=4)	Tretment	Evalution Parameters
I(Control)	Phosphate buffered saline (1ml/kg, p.o.)+ 0.2 % w/v histamine aerosol	Biochemical parameters such as: Appearance of (PCD) Percentage protection offered by drug in the Preconvulsive dyspnea Time (PCT)
II (Std)	Chlorpheniramine maleate (2 mg/kg, i.p.) + 0.2 % histamine aerosol.	
III(CC-100)	Ethanolic extract of *Capparis Decidua* (100 mg/kg) + 0.2 % w/v histamine aerosol.	
IV(CC-200)	Ethanolic extract of *Capparis Decidua* (200mg/kg) + 0.2 % w/v histamine aerosol.	

Fasted guinea pigs were divided into five groups (n=4).

Aerosol of histamine is produces bronchoconstriction in guinea pig. The study regarding involvement of H_1 and H_2 receptors has been done in guinea pigs using respiratory smooth muscle and it was confirmed that there is prominent involvement of H_1 receptors as compared to H_2 receptors which when stimulated worsening the condition of asthma. Histamine when inhaled has been shown to induce bronchoconstriction by direct H_1-receptor activation.

Prior to drug treatment each animal was placed in the histamine chamber and exposed to 0.2 % w/v histamine aerosol. The Pre Convulsive Time (PCT) was defined as the time of exposure to onset of dyspnoea leading to the appearance of Pre Convulsive Dyspnoea (PCD). As soon as the PCD was noted, the animal was removed from the chamber and placed in air. After 24 hours, animals belonging to group I served as control and were administered with phosphate buffer (1ml/kg, p.o.); Animals belonging to group II were administered with Chlorpheniramine maleate (2 mg/kg, i.p.) while group III to V were received respective doses of ethanolic extract of *Capparis Decidua.* These animals were again subjected to histamine aerosol later at interval of 1 hr, 4 hr and 24 hrs of drug administration and PCT was determined again. The protection offered by treatment was calculated by using the following formula parcentage protection = $\mathbf{(1 - T_1/T_2) X 100}$

T_1 =the mean of PCT before administration of test drugs.

T_2 = the mean of PCT after administration of test drugs at 1 hr, 4 hr and 24 hrs

MILK - INDUCED LEUCOCYTOSIS (16, 19-24)

Groups (n =5)	Treatment	Evaluation Parameters
I (Control)	Milk (4 ml/kg s.c.)	
I (Std)	Dexamethasone (50mg/kg) +Milk (4ml/kg s.c.)	Biochemical parameters such as: Difference in number of leukocytes count.
III (CC -100)	Ethanolic extract of *Capparis Decidua* (100 mg/kg) + Milk (4 ml/kg s.c.)	
IV (CC -200)	Ethanolic extract of *Capparis Decidua* (200 mg/kg) + Milk (4 ml/kg s.c.)	

Mice were divided into five groups (n=4).

Animals belonging to group I served as control and was administered with only boiled and cooled milk (4 ml/kg, s.c.) Animals belonging to group II served as standard and were administered with Dexamethasone (50 mg/kg i.p.) while animals belonging to group III to V served as test group and were received respective doses of ethanolic extract of *Capparis Decidua* and 1 hr later boiled and cooled milk (4 ml/kg, s.c.) was administered to the same animals. After 24 hr, blood samples were collected from all

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animals from their retro orbital plexus, under light ether anesthesia. Differential leukocytes counts were recorded in each group 24 hr after milk injection.

Subcutaneous injection of milk at dose of 4 ml/kg produced a significant increase in the leucocytes count after 24 hr of its administration. Animals treated with Dexamethasone at the dose of 50 mg/kg, p.o. has significantly inhibited milk-induced leucocytosis as compared to control.

In the groups of mice, pretreated with ethanolic extract of fruits of *Capparis Decidua* at dose there was significant (inhibition of milk-induced Leucocytosis as compared to control) leukocytes counts were recorded in each group 24 hr after milk injection. Describe in Leucocytosis count show Antialergic activity which may useful in treatment of asthma.

RESULTS & DISCUSSION

RESULTS

Table 1: Percentage Yield of Various Extracts of Fruit of *Capparis Decidua.*

S. No	Solvent used for Extraction	Time required for complete extraction	Color of Extraction	Percentage of yield (w/w)
1	Petroleum ether	40	Dark Green	4.52
2	Ethanol	72	Dark Brown	8.45

PHYTOCHEMICAL INVESTIGATION

Phytochemical investigation of the ethanolic extracts of *Capparis Decidua*. Showed the presence of Carbohydrate, alkaloids, tannins, polyphenol where as phytochemical investigation of the petroleum ether extracts of plant *Capparis Decidua* showed the presence of fixed oils, Fats.

Table 2: Qualitative Chemical Anlysis of ethnolic and petroleum ether extracts of *Capparis Decidua Bark*.

S. No.	Test for Plant Constituents	*Capparis Decidua* Bark
		Ethanolic extract
1.	**Test for Carbohydrate**	
	A. Molish test	+
	B. Fehling's test	+
	C.Benedict's test	+
	D. Barfoed's test	–
2.	**Test for Protein**	
	A. Biuret test	+
	B. Million's test	+
3.	**Test for Alkaloids**	
	A. Mayer's test	+
	B. Dragenoff's test	+
	C. Wagner's test	+
4.	**Test for Fats And Oils**	
	A. Spot test	+
	B. Saponification test:	+
5.	**Test for glycoside**	
	A. Legal test	–
	B. Baljet's test	+
	C. Borntrager's Test	+
6.	**Test for Flavonoids**	
	A. Ferric chloride Tests	-
	B. Shinoda's test	-
7.	**Test for Tannins and Phenolic copounds:**	
	A. Ferric chloride test	+
	B. Reaction with lead acetate	–
8.	**Test for Amino acid**	
	A. Ninhydrin test:	–
	B. Test for tryptophan:	–

Table 3: Effect of ethanolic extracts of bark of *Capparis Decidua* on histamine induced contraction of isolated goat tracheal chain preparation

Sr. No.	Dose of Histamine	-ve Log molar concentration of	% Maximum Contraction		
	(30µg /ml) (ml)	**Histamine**	**Control**	**Test**	**Standard**
1	0.1	6.30	21.20 ± 0.89	16.52 ± 1.02	9.64 ± 0.69
2	0.2	5.91	48.14 ± 1.75	36.91±1.32**	20.80 ± 1.04**
3	0.4	5.52	61.34 ± 2.05	49.33±2.94**	33.78±1.12**
4	0.8	5.18	76.49 ± 1.24	65.66±1.58**	41.99±1.29**
5	1.6	4.89	89.69 ± 2.49	75.48±0.94**	54.25±1.35**
6	3.2	4.49	100 ± 0.00	79.26±2.30**	58.55±2.08**

Data are expressed as Mean± S.E.M. Where, n= 5, Statistical analysis done by using Student's - test. Where, $^{**}p<0.01$, significantly different from control; **Control** = D.R.C of histamine(30µg /ml) in absence of test drugs of *Capparis Decidua*. **Test** = D.R.C histamine (30µg /ml) in presence of *Capparis Decidua*. **Standard** = D.R.C of histamine (30µg /ml) in presence of Chlorpheniramine maleate.

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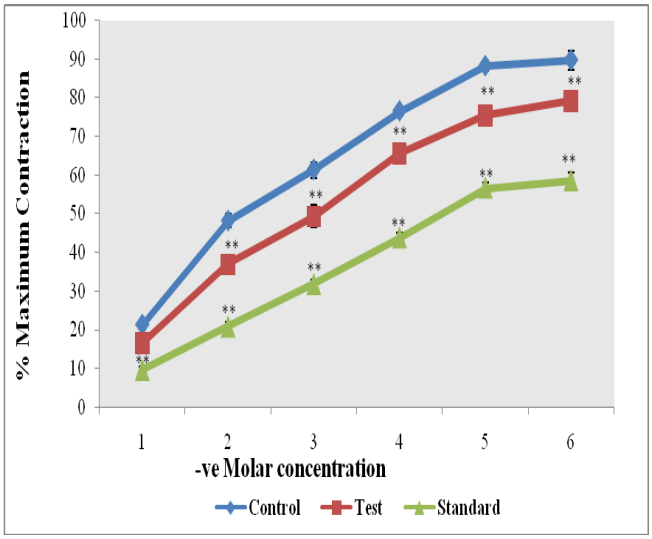

Fig. 3: Effect of ethanolic extracts of bark of *Capparis Decidua* on histamine induced contraction of isolated goat tracheal chain preparation.

Data are expressed as Mean± S.E.M. Where, n= 5,
Statistical analysis done by using Student's-test. Where, $^{**}p<0.01$, significantly different from control
Control =D.R.C of histamine (30µg /ml) in absence of test drugs of *Capparis Decidua.*(100 µg/ml) extracts.
Test = D.R.C histamine (30µg /ml) in presence of *Capparis Decidua*..(100 µg/ml)extracts.
Standard =D.R.C of histamine (30µg/ml) in presence of Chlorphenramine maleate.
(1 µg/ml).

Table 4: Effect of ethanolic extracts of bark of Capparis *Decidua* on percent protection in histamine induced Bronchoconstriction in guinea pigs

Group(n=4)	Preconvulsive dyspnoea (sec.)(mean ±SEM)at			
	Before Treatment	After treatment		
		1hr	3hr	24hr
I(Control)	20.05±1.15	-	-	-
II(Standard)	22.8±1.19	68.5±1.17	88.06±1.23	31.17±1.43
III(CC-100)	19.95±1.05	38.12±1.10	48.86±1.50	29.12±1.80
IV(CC-200)	21.78±1.50	58.86±1.25	72.86±1.61	33.15±1.80

Data are expressed as Mean± S.E.M. Where, n= 5, Statistical analysis done by ANOVA followed by Dunnett's test, where $^{*}p<0.05$, $^{**}p < 0.01$ when group II, III, and IV were compared with group I.

Group- I (Control) = Aerosolized Histamine (0.2 % w/v)
Group-II (Std) = Aerosolized Histamine (0.2 % w/v) + Chlorpheniramine maleate (2 mg/kg, i.p.)
Group-III (*Citrullus colocytnthis*.CC-100) = Aerosolized Histamine (0.2 % w/v) + Ethanolic extract of *Citrullus colocynthis* (100mg/kg, p.o.)
Group-IV(*Citrullus colocytnhis*-CC-200) = Aerosolized Histamine (0.2 % w/v) + Ethanolic extract of *Citrullus colocynthis* (200mg/kg, p.o.)

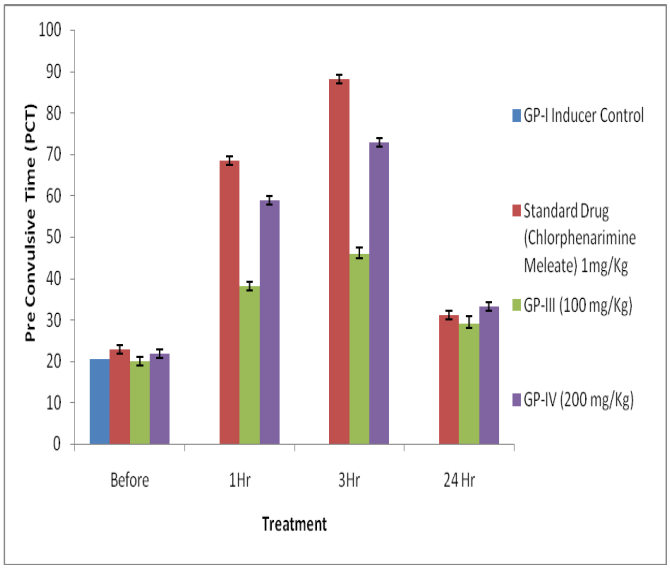

Fig. 4: Effect of ethanolic extracts of bark of *Capparis Decidua*. on percent protection in histamine induced Bronchoconstriction in guinea pigs

Data are expressed as Mean± S.E.M. Where, n= 5,
Statistical analysis done by ANOVA followed by Dunnett's test, where $^{*}p<0.05$, $^{**}p < 0.01$ when group II, III, and IV were compared with group I.
Group- I (Control) = Aerosolized Histamine (0.2 % w/v)
Group-II (Std) = Aerosolized Histamine (0.2 % w/v) + Chlorpheniramine maleate (2 mg/kg, i.p.)
Group-III (*Capparis Decidua*..(CC-100) = Aerosolized Histamine (0.2 % w/v) + Ethanolic extract of *Citrullus colocynthis (*100mg/kg, p.o.)
Group-IV *Capparis Decidua*.- (CC-200) = Aerosolized Histamine (0.2 % w/v) + Ethanolic extract of *Citrullus colocynthis* (200mg/kg, p.o.)

Table 5: Percent protection against histamine induced Bronchoconstriction in guinea pigs:

Group (n=4)	Preconvulsive dyspnea (in sec) (Mean±SEM)				Percent protection (%)		
	Before treatment	After treatment					
		1 hr	3 hr	24 hr	1 hr	3hr	24 hr
I	20.15±1.15	–	–	–	–	–	–
II	22.28±1.19	68.5±1.17	88.06±1.23	31.17±1.43	66.71	74.10	26.85
III	19.75±1.05	38.12±1.10	48.86±1.50	29.12±1.80	47.66	56.49	31.49
IV	21.58±1.50	58.86±1.25	72.86±1.61	33.15±1.80	62.99	70.10	34.29

Group- I (Control) = Aerosolized Histamine (0.2 % w/v)
Group-II (Std) = Aerosolized Histamine (0.2 % w/v) + Chlorpheniramine maleate (2 mg/kg, i.p.)
Group-III (*Capparis Decidua*..(CC-100) = Aerosolized Histamine (0.2 % w/v) + Ethanolic extract of *Citrullus colocynthis* (100mg/kg, p.o.)
Group-IV *Capparis Decidua*.- (CC-200) = Aerosolized Histamine (0.2 % w/v) + Ethanolic extract of *Citrullus colocynthis* (200mg/kg, p.o.)

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MILK INDUCE LEUCOCYTOSIS IN MICE

Table 6: Effect of ethanolic extracts of *Capparis Decidua* on milk induced Leucocytosis

Group (n=4)	Difference in number of Leucocytes (per cu mm)) (Mean ± SEM)
I (Control)	6555.8±5.63
II (Std)	4705.66±5.36
III (CC-100)	5654±6.25
IV (CC-200)	5607±7.70

Data are expressed as Mean± S.E.M. Where, n= 5,
Statistical analysis done by ANOVA followed by Dunnett's test, where *p<0.05, **p < 0.01 when group II, III, IV and V were compared with group I.

When group II, III, IV and V were compared with group I.

Group-I (Control) = Distilled water (10 ml/kg, p.o.) + Milk (4 ml/kg, s.c.)

Group-II (Std) = Dexamethasone (50 mg/kg, p.o.) + Milk (4 ml/kg, s.c.)

Group-III (*Capparis Decidua*.-100)=Ethanolic extracts *of* ***Capparis Decidua.*** (100mg/kg,p.o.) + Milk (4ml/kg.s.c.)

Group-IV(*Capparis Decidua*.-200)=Ethanolic extracts *of* ***Capparis Decidua.*** (200mg/kg,p.o.) + Milk (4ml/kg.s.c.)

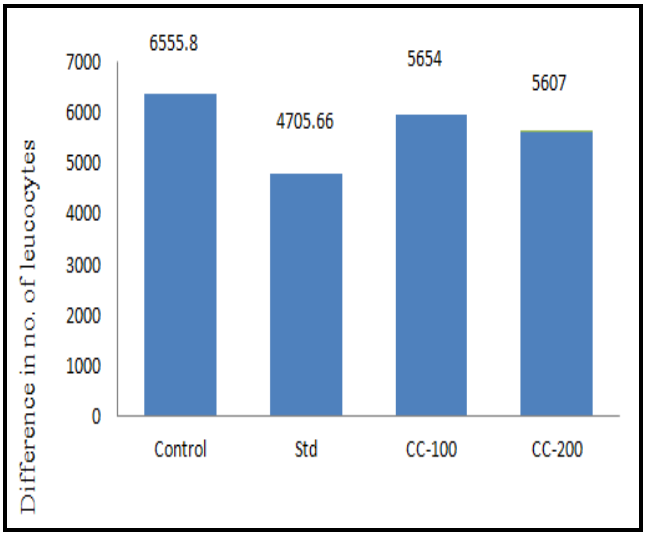

Fig 5: Effect of ethanolic extracts of *Capparis Decidua*. on milk induced Leucocytosis in mice.

Data are expressed as Mean± S.E.M. Where, n= 5,
Statistical analysis done by ANOVA followed by Dunnett's test, where *p<0.05, **p < 0.0001 when group II, III, and IV were compared with group I.
When Group II, III, and Group IV were compared with control

When group II, III, IV and V were compared with group I.

Group-I (Control) = **Distilled** water (10 ml/kg, p.o.) + Milk (4 ml/kg, s.c.)

Group-II (Std) = Dexamethasone (50 mg/kg, p.o.) + Milk (4 ml/kg, s.c.)

Group-III(*CC*-100) = Ethanolic extracts *of* ***Capparis Decidua*.**
(100mg/kg,p.o.) + Milk (4ml/kg.s.c.)

Group-IV(*CC*-200) = Ethanolic extracts *of* ***Capparis Decidua*.**
(200mg/kg,p.o.) + Milk (4ml/kg.s.c.)

DISCUSSION

Asthma is a chronic respiratory disease affecting a large proportion of population throughout the world. Bronchial provocation with allergen induce a prompt early phase immunoglobulin E (IgE)- mediated decrease in the brachial airflow (forced expiratory volume in one second) followed by a late phase IgE-mediated reaction with a decrease in the bronchial airflow for 4-8 hours. Initially asthma is characterized by the presence of increased number of various inflammatory mediators that are eosinophil's, neutrophils, lymphocytes and plasma cells in the bronchial allergens tissues, bronchial secretion and mucus. The cross linkage of IgE molecules by allergens causes mast cells to degranulation, releasing histamine, leukotriene's, and other mediators that perpetuate the airway inflammation.

Ultimately the mediators promote vascular permeability, smooth-muscle contraction and mucus production, which cause symptoms of asthma including airway constriction, coughing, shortness of breath and wheezing.

Large numbers of drugs are used for in the treatment of asthma. The currently used drugs for the treatment of this disease in modern medicine are far from satisfactory as they provide only symptomatic relief, produce several adverse effects and may lose effectiveness on continued use.

Traditionally the fruits are used in treating asthma, and inflammation disorders. *Capparis Decidua* reported activity to have anti-inflammatory activity. Thus, the present study was evaluating the effect of ethanolic extracts of *Capparis Decidua* fruits in pathogenesis of asthma. The result obtained by using various experimental animal model of asthma was discussed as follows.

Isolated goat tracheal chain preparation:

Histamine contracts the trachea-bronchial muscle of guinea pig, goat, horse, dog and man. Goat tracheal chain is easier to handle and also much more sensitive than guinea pig tracheal chain. Spasmogens such as histamine acetylcholine and barium chloride show dose dependent contraction on goat tracheal chain preparation.

Histamine antagonism is modulated by using the relaxing factors and may be due to the suppression of histamine H_1-receptors. The goat tracheal muscle has H_1, M_3 and β_2 receptors.The stimulation of H_1 receptor causes contraction of bronchial smooth muscle.

In the present study, the potential of ethologic extract of *Capparis Decidua* has antagonized the histamine induced contractions on goat tracheal chain preparation which have shown a significant relaxation indicated by right shift of DRC of histamine. In the present study histamine (30µg /ml) produced dose dependent contraction of goat tracheal chain preparation maximum percentage of response versus log molar concentration of histamine.

The modified physiological salt solution containing Chlorpheniramine maleate (1 µg/ml) significantly inhibited (p<0.01) the contractile effect of histamine. The modified physiological salt solution containing ethologic extract of *Capparis Decidua (*100 µg/ml) significantly inhibited (p<0.01) the contractile effect of histamine.

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Hence Chlorpheniramine maleate and ethanolic extract of *Capparis Decidua* (100 µg/ml) shifted the DRC of Histamine towards the right side indicating that there was competitive antagonism between histamine and both the drugs for histaminergic receptors.

Histamine induced Bronchoconstriction in Guinea pig:

Histamine is an important mediator of immediate allergic (type-1) and inflammatory reactions. It causes brochoconstriction by activating H_1 receptors. The trachea is used for the experimental purpose rather than the bronchi since it is easier to dissect and has the same reaction to spasmogenic and spasmolytic drug. The goat tracheal chain is easier to handle and to prepare; it is also much more sensitive than guinea pig tracheal chain. Although, the method is known for its suitability in the study of anti spasmodic drugs in general, emphasis is given on its use in the testing of bronchodilators. This is because of the close anatomical and physiological association, which exists between tracheal and bronchial musculature. Therefore, the dose relative contractile response of different agonist like Ach, histamine, 5-hydroxytryptamine and bradykinin can be observed in isolated goat trachea. Histamine contracts the trachea-bronchial muscles of guinea pig, goat, horse, dog and man. Goat tracheal chain is easier to handle and to prepare; it is also much more sensitive than guinea pig tracheal chain.

Histamine produces highly variables effects on the airways smooth muscles of mammalian species. Histamine antagonism modulated by the relaxing factors involved and may be due to the suppression of histamine H_1 receptors.

The guinea pigs when exposed to 0.2 % histamine aerosol showed signs of preconvulsive dyspnoea leading to convulsions. Chlorpheniramine maleate (2 mg/kg, i.p) prolonged the preconvulsive dyspnoea in 1st, 3th and 24th hr as compared to control.The ethanolic extracts of fruits of *Capparis Decidua* at doses of 100,200mg/kg p.o. significantly prolonged (p<0.01) the preconvulsive dyspnoea at 1st, 3th hr and 24 hr as compared to control.

Prolonged the preconvulsive dyspnoea at 1, 3 and 24th hr as compared to control. While at doses of 100,200mg/kg p.o. Thus shows more protection against dyspnoea as compared to control, following exposure to histamine aerosol.

Chlorpheniramine maleate at the dose of 1mg/kg, i.p significantly protected the guinea pigs against histamine-induced bronchoconstriction at 1st, 3 and 24th hr and % protection was 66.61, 74.10, and 34.29% respectively.

The ethanolic extract of fruits of*Capparis Decidua* at doses of 100mg/kg significantly protected the guinea pigs against histamine-induced bronchoconstriction at 1st hr. and 3 hr and 24th hr and % protection was 47.66, 56.49, and 31.49 respectively. The ethanolic extract of fruits of*Capparis Decidua* at doses of 200mg/kg significantly protected the guinea pigs against histamine-induced bronchoconstriction at 1st hr.3 hr and 24th hr and % protection was 62.99, 70.10, and 34.29 respectively.

Milk- induced Leucocytosis:

Antiasthmatic activity using milk induced leukocytosis model in rat involves relese of various types of mediators in pathology. It was reported that subcutaneous administration of milk produces a marked increase in the leukocytes counts after 24 hours. An important feature of the adaptogens is their capacity to increase organism resistance to various adverse effects of a physical, chemical and biological nature. After parental administration of milk there is increase in total leukocytes count and this stress full condition can be normalized by administration of an adaptogenic drug.

Adaptogens are the medicinal substances that are meant to put an organism into a state of non-specific heightened resistance in order to better resist stress and adaptation to external challenges**.** An important feature of the adaptogens is their capacity to increase organism resistance to various adverse effects of a physical, chemical and biological nature.

Treatment with ethanolic extract of *Capparis Decidua* showed significant decrease in total leukocytecount. This effect may be due to adapatogenic activity of the ethanolic extract of *Caparis Decidua* and thus may contribute in the management of asthma.

Subcutaneous injection of milk at dose of 4 ml/kg produced a significant increase in the leucocytes count after 24 hr of its administration. Animals treated with Dexamethasone at the dose of 50 mg/kg, p.o. has significantly (p<0.01) inhibited milk-induced leucocytosis as compared to control. In the groups of mice, pretreated with ethanolic extract of fruits of *Capparis Decidua* at dose of 140 mg/kg, there was significant (p<0.05) inhibition of milk-induced Leucocytosis as compared to control. In the groups of mice, pretreated with ethanolic extract of fruits of *Capparis Decidua* at dose of 100 and 200mg/kg p.o, there was significant (p<0.01) inhibition of milk-induced Leucocytosis as compared to control.

KK Limbasiya, *et al*., (2012) has studied Evaluation of Anti-asthmatic activity of dried whole plant extraxt of leucas aspera using various experimental animal models. It concludes that the methanolic extract of *Leucas aspera* shown significant effect anti-histaminic, bronchodilatory, anti-inflammatory, mast stabilizing and anti-allergic activity in various anti-asthmatic models.[20] Pravin shelke *et al.,* (2014) has studied Preclinical evaluation and anti-asthmatic activity of *Euphorbia hirata linn*. It concludes that plant exhibit significant dose dependent anti-asthmatic activity in various in-vitro and in-vivo animal model. [23] Dahiya *et. al*., (2019) concluded that a wide range of biologically active phytochemicals lends the plant its diverse pharmacological activities, some of which are antidiabetic, antibacterial, antifungal, anti-aging, antitumor, antinociceptive, antiatherosclerotic, hepatoprotective, antioxidant, Anti-giardial, antihypertensive, hypolipidemic, and anti-inflammatory. Using the in the local communities of *C. Decidua* in rheumatism and gout prevails. [16]

CONCLUSION

In the present study the ethanolic extracts of bark of *Capparis Decidua* was evaluated for the management of asthma. Ethanolic extract of fruits of *Capparis Decidua* may possesses antiasthmatic activity which may be due to antihistaminic activity, broncho dilating activity, adaptogenic activity, mast cell stabilizing activity, anti-inflammatory activity (inhibition of antigen antibody reaction) and anti-oxidant activity.

Thus, *Capparis Decidua* fruits may be used in the management of asthma.

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