



(RESEARCH ARTICLE)



Anti-asthmatic activity of *Tinospora cordifolia* leaves extract against ach and citric acid-induced asthma in rats

Deeparani Urolagin ^{1,*}, Dudekula Sheshbee ², Ansari Aashif Raza Mohd Imtiyaz ¹, Samir Panda ¹ and Arundhati Kashyap ¹

¹ Department of Pharmacology, R R College of Pharmacy, Bangalore, India.

² Department of Pharmacology, Aditya Bangalore Institute of Pharmacy Education and Research, Bangalore, India.

International Journal of Science and Research Archive, 2024, 12(01), 586–595

Publication history: Received on 31 March 2024; revised on 08 May 2024; accepted on 11 May 2024

Article DOI: <https://doi.org/10.30574/ijrsra.2024.12.1.0829>

Abstract

Asthma is one of the common clutters experienced in clinical medication in both grown-ups and children are asthma and it is characterized by irritation of the aviation routes which causes aviation route brokenness. Breathed-in bronchodilators and anti-inflammatory drugs are accessible and compelling and they require long term utilize and are related with side impacts. Typically, why elective and complementary medication is being sort after to anticipate these side impacts. A few restorative plants have anti-inflammatory impact and have demonstrated successful within the treatment of asthma. Citric corrosive, Acetylcholine, Histamine is basically utilized for assessing anti-asthmatic movement of specific sedate. Numerous plants gotten from the normal source play a critical part within the wellbeing care framework. Writing overview on home grown drugs has appeared noteworthy anti-asthmatic movement which has not shown any momentous side impact. The pharmacological component that the phytoconstituents creating the hostile to asthmatic action are not clearly caught on till date. A few herbal formulations have been determined from the Ayurveda, conventional framework of Indian medicine and its extra framework of medication, however to be experimentally approved that they have exhibited pharmacological activity against Asthmatic. As it were less number of logical data of conventional medications is accessible for the treatment of Asthmatic. This survey contains list of restorative plant which have been tried for anti-asthmatic action within the Citric corrosive, Acetylcholine actuated asthmatic in Rodent demonstrate. Rats were divided into 4 groups and given each of them individual intervention based on the activity. *Tinospora cordifolia* leaf extract shows an anti-asthmatic activity in rats. hence, the data given in this inquiry will offer assistance the analysts for the advancement of elective strategies instead of inhalers and verbal anti-asthmatic drugs for the treatment of asthma and COPD which can minimize the complications.

Keywords: Anti-asthma; Bronchodilators; Anti-inflammatory; Inhalers; Phytoconstituents

1. Introduction

Asthma may be a hyper-reactive aviation route illness running a chronic course; it has around the world predominance and may be a common cause of hospitalization in children. It is assessed that right now, 300 million people groups endure from asthma with a plausibility of an extra 100 million likely to endure from the illness over the another 15-20 a long time. Asthma could be a unremitting provocative clutter of the aviation route in which numerous cells and cellular components play a part, in specific, pole cells, eosinophils, T-lymphocytes, macrophages, neutrophils, and epithelial cells. In vulnerable people, this aggravation causes repetitive scenes of wheezing, breathlessness, chest tightness, and hacking, especially at night or within the morning. These episodes are more often than not related with broad but variable wind current obstacle that's reversible either suddenly or with treatment. The irritation too causes an related increment within the existing bronchial responsiveness to a assortment of boosts [1].

* Corresponding author: Deeparani Urolagin

1.1. Etiology

There are two sorts of asthma;

- Unfavorably susceptible or outward
- Peculiar or inborn. Unfavorably susceptible asthma may be a result of an antigen/antibody response on pole cells within the respiratory tract.

This sort is frequently related with a family history of atopy (allergic diseases) such as skin inflammation. Quirky asthma or natural asthma could be a result of neurological awkward nature within the autonomic framework in which the thoughtful and parasympathetic frameworks are not appropriately facilitated. The causes of asthma are numerous counting natural and hereditary components. Atopy is the most grounded hereditary inclination for the advancement of an IgE reaction to common aeroallergens. Most cases of childhood asthma (90%) are unfavorably susceptible; it is alluded to as outward asthma. In this frame of infection, the incendiary response could be a result of an unusual reaction to common aeroallergens and natural allergens. The late incorporate clean vermin, creatures, dust, molds, parasites, cockroaches, fossil powers, solid exhaust, inward breath of aggravations (splashes and paints), cigarette smoke, and presentation to cold and muggy climate. The natural components act as triggers in those people who have incendiary changes in their respiratory entries and are profoundly vulnerable to intense assaults of asthma. The other vital causes of asthma incorporate viral respiratory contaminations, work out (hyperventilation), inveterate sinusitis or rhinitis, gastroesophageal reflux malady (GERD), and drug-induced asthma (headache medicine, NSAIDs,β blockers, cholinergic drugs). In exercise-induced asthma, the contributing variables incorporate presentation to cold or dry climate and natural toxins (sulfur, ozone)[2].

1.1.1. Pathophysiology & clinical management of asthma

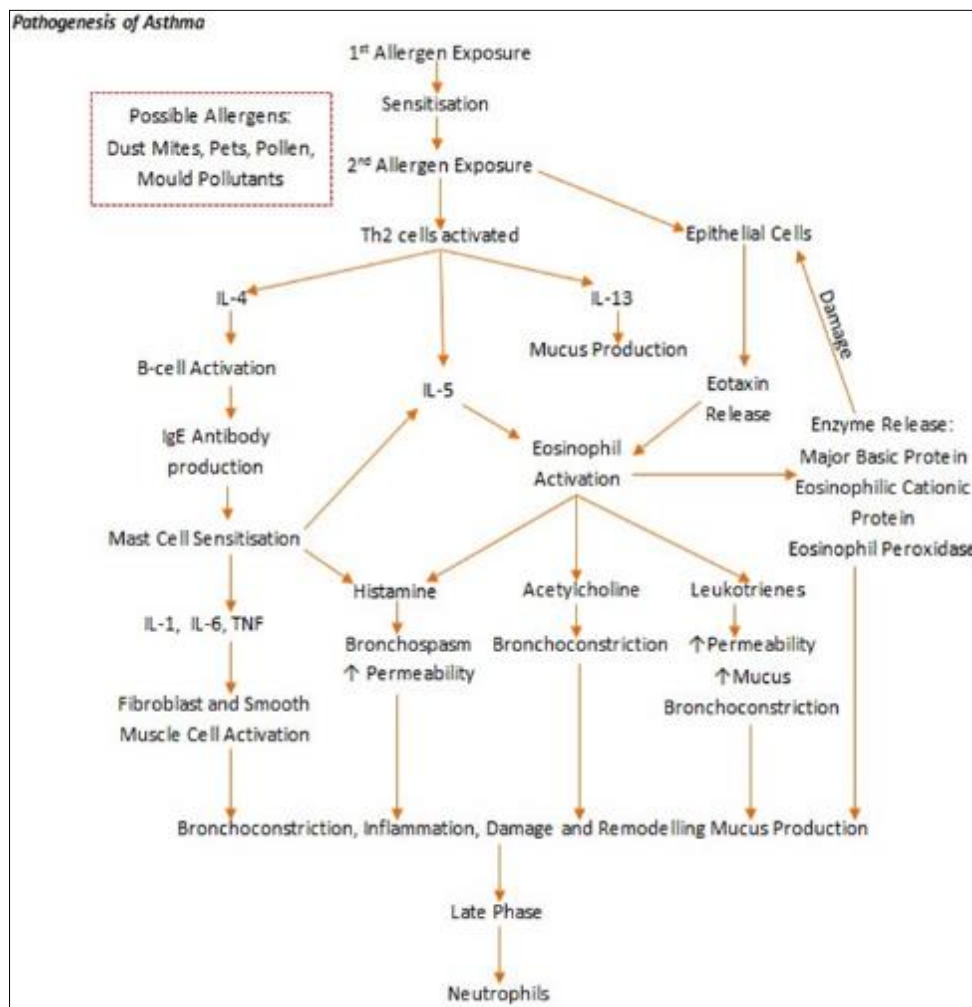


Figure 1 Pathogenesis of Asthma

The persistent provocative response is the characteristic highlight within the pathogenesis of bronchial asthma which comes about in discontinuous wind current obstacle and bronchial hyperresponsiveness. Aviation route hindrance in asthma is due to variables that incorporate bronchospasm edema of the aviation route, expanded bodily fluid discharge, cellular penetration of the aviation route dividers, and harm to the aviation route epithelium. Redundancy of the provocative occasions in asthma can cause irreversible utilitarian changes within the aviation route sections, a prepare called remodeling. The remodeled aviation route sections are tirelessly limit as the infection advances and ended up less and less responsive to sedate treatment. The component of irritation in asthma may be intense, sub-acute, or unremitting.

Bronchial asthma could be a persistent weakening infection related with dreariness and mortality. Reasonable administration of the illness is fundamental depending upon the seriousness of the malady. Treatment of childhood asthma requires extraordinary consideration as children are exceptionally defenseless and display with changing degrees of clinical highlights regularly requiring standard healing center visits. A common rule stipulates that the littlest measurements of the sedate required to enough control the side effects ought to be utilized. Patients with more visit or extreme indications or with disabled lung work ought to be treated with normal prophylactic treatment such as breathed in glucocorticoids, in case fundamental in higher dosages depending on the seriousness of the indications. Long-acting β 2 agonists such as salmeterol and formoterol may be included to help quick control of indications. Leukotriene altering specialists such as montelukast are very accommodating in children for prophylactic utilize to anticipate exacerbations of asthma likely to happen when they are uncovered to known and obscure allergens counting natural allergens. One vital thought for the treatment of asthma is the plausibility of medicate resistance and drug toxicities which may constrain their value and require an alter within the sedate [3].

1.2. Plant profile



Figure 2 Plant picture with Binomial nomenclature (TINOSPORA CORDIFOLIA)

1.3. Distribution

Tinospora cordifolia may be a glabrous, succulent, woody climbing bush local to India. It prospers well inside the tropical district, regularly fulfills a mind blowing stature, and climbs up the trunk of broad trees. The stem of *Tinospora cordifolia* is gray and smooth white, significantly cleft spirally and longitudinally, with the space between spotted with gigantic rosette-like lenticels. The wood is white and porous and the freshly cut surface anticipate a yellow tint when revealed to talk about. Clears out are direct, exstipulate, long petiolate, compatibility, and chordate in shape showing up multicoated reticulate venation. Long thread-like ethereal roots come up from the branches. Sprouts are small and unisexual. Male blooms are in clusters, Six sepals organized in two whorls, female blooms are single, they are obovate, and membranous. Add up to characteristic item is reddish, and bulky with various drupelets on a thick stalk with subterminal fashion scars, scarlet-colored. the Ayurvedic study Guduchi or Amrita is the first basic helpful orchestrate indicated completely different works of the Ayurvedic system of pharmaceutical viz:

Charak, Sushrut & Ashtang Hridaya underneath other distinctive names viz:

Amara, Amritvalli, Chinmarruha, Chinnodebha & Vatsadani, etc, ,other herbal drugs such as *Anogesissus latifolia* and *Ixora coccinea* flowers, *Piper longum* and grape seeds are effective in treating asthma [4,5,6,7].

2. Materials and methods

2.1. Materials

2.1.1. Collection and extraction of plant

Plant choice may be a computerized novel approach to choice strategy or writing data choice procedure (LIST) that connects organic movement, botanical actualities and chemotaxonomical data.. Based on the writing survey, the plant was collected from confirm plant provider and recognized by a botanist. Stems was discuss dried and powdered were carefully discuss dried beneath shade over a period of 7 days, cut to little pieces and powdered (60 work). Powdered stem fabric was defatted utilizing petroleum ether. Defatted plant fabric was extricated within the soxhlet device. Advance extricate with 90% of ethanol and concentrated by utilizing desiccators for the evacuation of the remaining dampness. The ultimate sum of strong buildup was 35% w/w.

CHEMICALS: Ethanol 90%, Petroleum ether, Refined water, Citric corrosive 0.1 mg/Spray, Acetylcholine 0.2 % /Splash. SOLVENTS: Ethyl liquor, Water, CMC (carboxy methyl cellulose).DRUGS: Theophylline 200mg/kg [8].

2.1.2. Preliminary phytochemical studies [9].

The pharmacological and restorative activity of rough drugs is decided by the nature of its constituents. In this way the plant species may be considered as a biosynthetic research facility not as it were for the chemical compounds e.g. carbohydrates, proteins and fats that are utilized as nourishment by people and creatures, but moreover for a size of compounds counting alkaloids, flavonoids, glycosides etc. which apply unequivocal physiological impacts. These chemical compounds are mindful for the specified helpful properties.

Table 1 Preliminary Phytochemical Studies

Sr.no	Constituents	Results Presence(+)/Absence(-)
1	Carbohydrates and glycosides	+
2	Alkaloids	+
3	Phytosterol	+
4	Fixed oils	+
5	Gums and mucilage's	+
6	Proteins and free amino acids	+
7	Phenolic compounds and tannins	+
8	Flavonoids	+

2.2. Methods

2.2.1. Animals

Sound grown-up Wistar rats of either sex between 8 of 12 weeks of age after IAEC endorsement obtained from enrolled creature house. All the rats kept beneath acclimatization for 5 days earlier to gathering and start of try. The creatures were kept in clean and dry plastic cages, with 12 h light:12 h dim cycle at 25+20 c temperature and 45 – 60% relative mugginess. Creatures were given free get to to standard bolster and water and libitum. For exploratory reason the creatures were kept on overnight fasting but permitted free get to to water. The regulation creature morals committee were taken after all through the experimentation [10].

Rats were chosen haphazardly and partitioned into five bunches (Bunches I, II, III and IV) each bunch contain six creatures. All the rats were numbered bunch shrewd and separately. Asthma was initiated by citric corrosive 0.1 mg and acetylcholine 0.2 mg within the frame of splashing in elective days for two weeks. The extricate of *Tinospora cordifolia* and Theophylline was managed by nasal course for two weeks. At the conclusion of the treatment, all of the rats were yielded and Lungs Blood Tests were taken out, settled at that point histopathological considers were taken after.

2.2.2. Acute oral toxicity for AECS [11].

Table 2 Acute Oral Toxicity Studies

TREAT MENT	DOSE Mg/kg	MORT ALITY	SEDA TION	CONVU LSION	URINA TION	BOD Y COL OR CHA NGES	LOCO MOTI ON	BOD Y WEI GHT
AETC	mg/kg	-	-	-	-	-	-	-
AETC	mg/kg	-	-	-	-	-	-	-
AETC	200mg/ kg	-	-	-	-	-	-	-
AETC	1000mg /kg	+	-	-	- mild	-	- mild	-

Based on the mortality result of the sighting study starting dose in the main study is decided and carried out with six animals per dose level (1000mg/kg). Based on the mortality result on 14h day of observation, the doses for the *in vivo* study were selected.

2.3. *In vivo* method

2.3.1. Experimental design

Overnight fasted Rats were isolated into four bunches Inducer control (IC) = Acetylcholine + Citric corrosive (0.2% shower), Standard gather gotten Theophylline (200 mg/kg), and Test bunch -I AETC (100mg/kg) & Test bunch -II (200mg/kg), p.o. Bronchospasm was initiated in rats by uncovering them to Acetylcholine & Citric corrosive (0.2% splash) created by an ultra sound nebulizer in a vaporized chamber (24*14*24 cm) made of Perspex glass. The time required for appearance of pre convulsive dyspnoea caused by the Acetylcholine & Citric corrosive (0.2% splash) was recorded for each creature. Earlier to medicate treatment, each creature was set on Histamine chamber and uncovered to Acetylcholine + Citric corrosive 0.2rosol. The preconvulsive time (PCT), i.e the time of vaporized introduction to the onset of dyspnoea driving to the appearance of shaking, was famous. As before long as the preconvulsion dyspnoea (PCD) was famous, the creatures were expelled from the chamber and set in new discuss to recoup as basal esteem. Rats were at that point permitted to recuperate from dyspnoea for 24 hrs. After 24 hrs, the creatures of STD gotten Theophylline (200 mg/kg), AECS (100mg/kg) (200mg/kg). These creatures were once more subjected to Acetylcholine + Citric corrosive 0.2rosol afterward at an interim of 1hr, 4hrs, and 24 hrs to decide preconvulsion time (PCT). The security advertised by the treatment was calculated by utilizing the taking after equation

$$\text{Percentage protection} = (1 - T1/T2) * 100$$

Where,

T1 = the mean of PCT before administration of test drugs, and

T2 = the mean of PCT after administration of test drugs at 1 hr, 4 hrs, and 24 hrs [12,13,14,15].

The Ach + Citric acid induced asthma in rats, results have expressed on below Table No. All the groups of animals were affected in asthma, which indicated PCD were constantly increased, the bark extract of *Tinospora cordifolia* 100 & 200 mg/kg was dose-dependent manner decreased ($P < 0.001$)** & ($P < 0.001$)** (59.8 + 1.750**↓ & 33 + 1.225**↓). When compared with the control group but positive control have more antiasthmatic activity ($P < 0.001$)** & ($P < 0.0001$)** When compare to each group of aqueous extract of *Tinospora cordifolia* 200 mg/kg have equipotent activity (59.8 + 1.750**↓ & 33 + 1.225**↓). When compared with positive control. The aqueous extract of *Tinospora cordifolia* 200 mg/kg has been expressed more anti-asthmatic action when compared to the 100 mg/kg extract of *Tinospora cordifolia* [16,17,18,19,20].

Table 3 PreConvulsion Dysnopea.

TREATMENT	DOSE	BEFORE	Hr	Hrs	Hrs
Negative control	Ach + Citric acid	18.2 ± 2.3739	19.1± 0.1550	18.4 ± 0.091	18.2 ± 0.210
Positive control	Ach + Citric acid + Theophylline	20.2 ± 0.1250	55.8 ± 1.415	62.3 ± 1.548**	± 1.472**
AETC	mg/kg	18.3 ± 0.1471	± 1.291	± 1.291	22.8 ± 0.478
AETC	mg/kg	18.5 ± 0.2955	58.8 ± 1.750	58.8 ± 1.750**	± 1.225**

2.4. Statistical analysis

All the values were expressed as mean + - SEM. The results were analyzed for statistical significance by using one-way ANOVA followed by Dunnett’s test. P<0.05 was considered significant

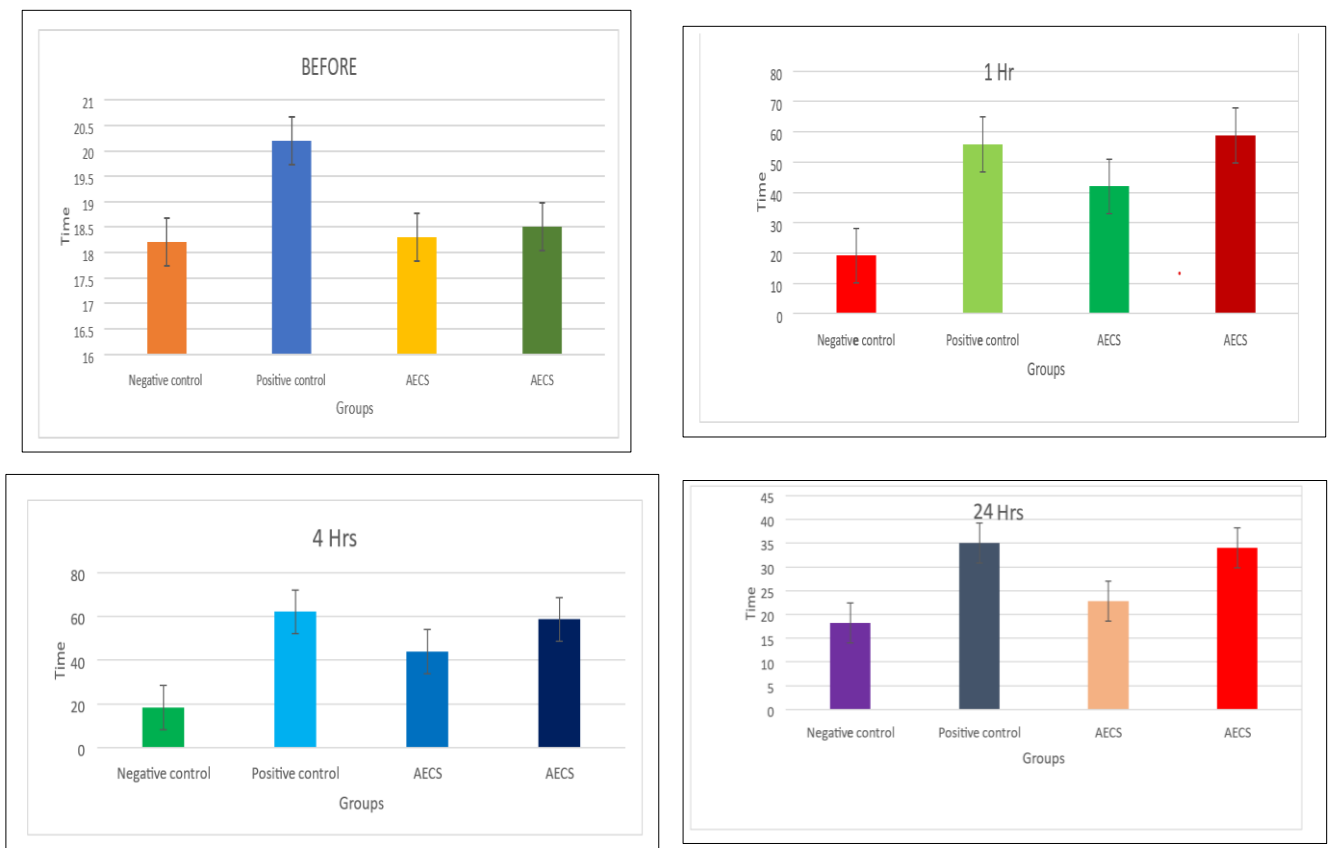


Figure 3 Graphs Represent the Comparison Between All Groups

2.5. Invitro method

2.5.1. Induction of asthma

Asthma was initiated by citric corrosive 0.1 mg and acetylcholine 0.2 mg within the shape of showering in elective days for two weeks. The extricate of Tinospora cordifolia and Theophylline was managed by nasal course for two weeks. At the conclusion of the treatment, all of the rats were yielded and lung blood Tests were taken out, settled at that point histopathological considers were taken after.

2.5.2. Experimental design

24 male grown-up rats were haphazardly partitioned into 4 bunches:

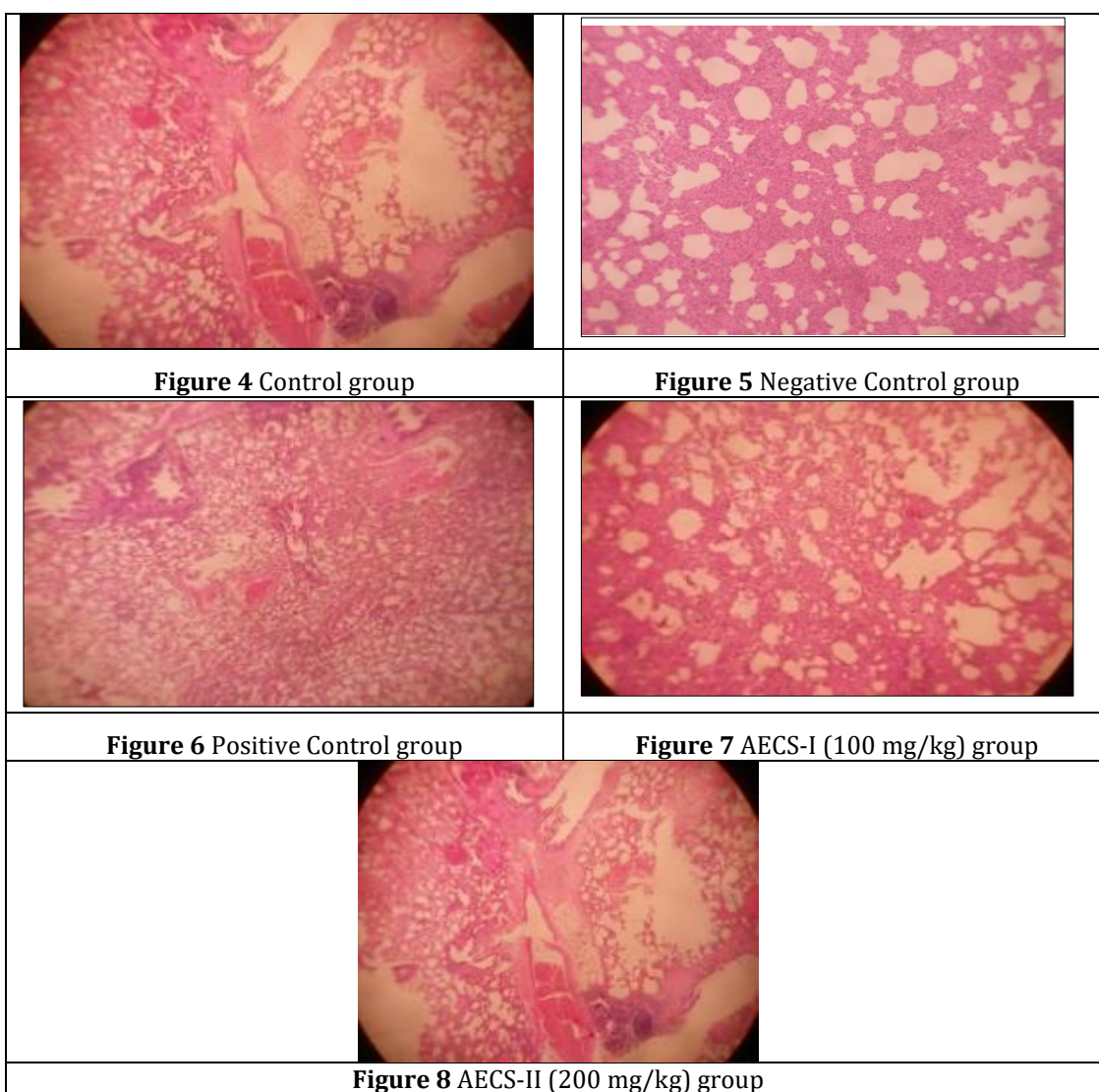
- Asthma gather gotten a ordinary eat less (A)
- Asthma gather treated with Theophylline (200 mg/kg b.w.) (T)
- Asthma gather which gotten AETC (100 mg/kg b.w.) (P1)
- Asthma gather which gotten AETC (200 mg/kg b.w.) (P2)

The impact of bark oil extricate of *Tinospora cordifolia* Eosinophils on demonstrated in Table, which is related to hostile to asthmatic activity. After the Ach + Citric corrosive treatment, on day 15 all the bunches of creature Eosinophils levels were altogether diminished. The Eosinophils levels were altogether dosage subordinate way diminished, after the treatment of Aq. and Non Aq. extricate of *Tinospora cordifolia* 100 & 200 at 15 th day. On day 15th the extricate of *Tinospora cordifolia* treated bunches 200 mg/kg were Eosinophils levels were more essentially diminished when compared with Typical gather.

Table 4 Eosinophils levels

Normal	Negative Control	Positive Control	AECS 100 mg/kg	AECS 200 mg/kg
± 0.333	380.66 ± 0.881	186.33 ± 0.881**	± 0.577	± 0.577**

2.6. Histopathological examination [21,22,23,24].



IMPRESSION: Control Bunch- The alveoli thickness is typical so free of drain. Negative Control gather- The alveolar divider shows up thickened in most of the ranges when compared to the control bunch. Positive Control bunch - Alveolar divider thickness shows up ordinary in both lungs. Negligible thickening of the alveolar dividers when compared to the Control bunch. AECS-I bunch- More thickening of the alveolar dividers when compared to the Control bunch and somewhat less thickening dividers when compared to the Negative control gather. AECS-II bunch- Negligible thickening of the alveolar dividers when compared to the Control gather.

After 14 days test period and the final blood testing, the total Lungs were expelled after relinquishing the creature and were settled in 10% formalin for histopathological examination. Segments were cut and recolored by hematoxylin and eosin (H&E) for histological examination.

3. Result and discussion

Asthma is one of the common disarranges experienced in clinical medication in both grown-ups and children are asthma it is characterized by aggravation of the aviation routes which causes aviation route brokenness Asthma is right now a around the world issue with around 300 million individuals around the globe enduring from it and world passings of around 25000 every year. Breathed in bronchodilators and anti-inflammatory drugs are accessible and viable and they require long term utilize and are related with side impacts. Asthma is one of the common disarranges experienced in clinical medication in both grown-ups and children are asthma and it is characterized by aggravation of the aviation routes which causes aviation route brokenness. Typically why elective and complementary pharmaceutical is being sort after to avoid these side impacts. A few therapeutic plants have anti-inflammatory impact and have demonstrated viable within the treatment of asthma. *Tinospora cordifolia* is one of the foremost imperative restorative plant commonly known as Giloy having a place to the Menispermaceae family may be a deciduous climbing bush portrayed known for its colossal application within the treatment of different maladies such as jaundice, asthma, fever, diabetes, and skin illnesses etc Citric corrosive, Acetylcholine, Histamine is primarily utilized for assessing against asthmatic action of specific sedate. This audit contains list of therapeutic plant which have been tried for hostile to asthmatic movement within the Citric corrosive, Acetylcholine initiated asthmatic in Rodent demonstrate In this way, the data given in this inquire about will offer assistance the analysts for the advancement of an elective strategies instead of inhalers and verbal hostile to asthmatic drugs for the treatment of asthma and COPD which can minimize the complication. Numerous plants gotten from the common source play a noteworthy part within the wellbeing care framework. Writing study on home grown drugs has appeared critical against asthmatic activity which has not appeared any momentous side impact. The pharmacological component which the phyto constituents creating the against asthmatic movement are not clearly caught on till date. The a few home grown definition have inferred from the Ayurveda, traditional system of Indian medication and its extra framework of medication, however to be scientifically validated that they have displayed pharmacological activity against Asthmatic. As it were a smaller number of logical information of conventional solutions is accessible for the treatment of Asthmatic.

4. Conclusion

Asthma is common respiratory malady. The dreariness and the mortality of the infection is expanding and making a worldwide concern. The disorder of bronchial asthma is characterized by wide spread narrowing of the bronchial tree due to withdrawal of the smooth muscle in reaction to numerous boosts coming about within the discharge of chemical go between such as Ach and Citric corrosive. Within the nearness ponder *Tinospora cordifolia* essentially hindered the Ach and Citric corrosive actuated hostile to asthmatic properties of the plant. Ach and Citric corrosive actuated Bronchoconstriction is the conventional immunological show of the antigen actuated discuss way obstacle. Ach and Citric corrosive when breathed in causes hypoxia and leads to writhing in rats and causes exceptionally solid smooth muscle compression, significant hypotension, capillary enlargement in cardio vascular framework a unmistakable impact caused by histamine leads to extreme Bronchoconstriction in rats that causes asphyxia and passing. Bronchodilator can delay the event of these side effects. The comes about of the ponder affirmed the bronchodilator properties of the plant, legitimizing its conventional claim within the treatment of asthma. Drugs viable within the asthma are mostly steroidal conjointly Flavonoids in nature. Phytochemical profile of the plant uncovers the nearness cinnamaldehydes within the shape of Flavonoids. The against asthmatic action appeared by takes off of the plant extricate may be since of the chemical moieties. In any case this claims requests for encourage investigate and thinks about are underway to disconnect and characterize the dynamic standards mindful for the anti-asthmatic movement.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The study involves animal use and got ethical approval from Aditya Bangalore Institute of Pharmacy Education and Research, Bangalore- India. Approval No:72/1611/CPCSEA.

References

- [1] Lippincott's Illustrated Reviews, Pharmacology 14th Edition, South Asian Edition 2010.
- [2] Goodman & Gilman. The pharmacological basis of therapeutics, 10th International edition, McGraw Hill publication, 2001:1687.
- [3] Conceptual Pharmacology by Jagadish Prasad University Press 2010.
- [4] Hishobkar SM*,Urolagin DK ,Ashish C,Sivarupa M.S.Evaluation of Synergistic Antimicrobial Effect of Anogeissus latifolia and glycerrhiza glabra extract. International Journal of Pharmaceutical Sciences 2010;2(2):570-573.
- [5] Deeparani K. Urolagin, S. Jayakumari.*In-vitro* Anti-Cancer Study of *Vitis Viniferae*, *Ixora Coccinea* and *Piper Longum* Ethanolic extracts on Human Breast Carcinoma Cells.Research J. Pharm. and Tech 2018;11(12):5345-5347.
- [6] U. Deeparani, S. Jayakumari.*In vitro* Anti-Cancer Study of *Vitis viniferae*, *Ixora coccinea* and *Piper longum* Extract on Human Prostate Carcinoma Cells.Research J. Pharma and Tech 2019;12(9):4485-88. .
- [7] Deeparani Urolagin.Pharmacological screening on Effect of grape seed extract on wound healing in rats.Annals of Pharma Research 2021;09(12):594-603.
- [8] Bhatt R P & Sabnis S D, Contribution to the Ethnobotany of Khedbrahma region of North Gujarat. Journal of Economic & Taxonomic Botany 1987; 9: 139.
- [9] Anonymous, An Appraisal of Tribal-Folk Medicine, (Central Council for Research in Ayurveda & Siddha, New Delhi) 1999. 25. Vir J; Dar G H; Bhat G M, Taxo-ethnobotanical studies of the rural areas in district Rajouri (Jammu). Journal of Economic & Taxonomic Botany 1984; 5: 831.
- [10] Singh SS., Pandey SC., Srivastava S., Gupta VS., Patro B. Chemistry & medical properties of *Tinospora cordifolia*. Indian Journal of Pharmacology 2003; 35: 83.
- [11] Qudrat-I-Khuda M., Khaleque A., Ray N. Scientific Research (Dacca) 1964; 1: 177.
- [12] Ghosal S., Vishwakarma RA. Tinocordiside: a newly rearranged cadinene sesquiterpene glycoside from *Tinospora cordifolia*. Journal of Natural Product 1997; 60: 839.
- [13] Ghori SS, Fathima I, Qureshi MS, Tehseen F. Evaluation of antiasthmatic activity of *Tinospora cordifolia* root extract against ach and citric acid induced asthmatic rats . Plantarchives.org.cited 2024 Apr 27.
- [14] savita d. Patil, Sameer v. Ahale, Sanjay j. Surana et al., Evaluation of the antiasthmatic and anti anaphylactic activity of *balanites aegyptiaca* (delile), (Balsaminaceae) Asian journal of pharmaceutical and clinical research vol. 4, issue 1, 2011 ISSN - 0974-2441.
- [15] Maurya R; Sukhdev S. Tinocordifolin: A sesquiterpene from *Tinospora cordifolia*. Phytochemistry 1998; 49:1343.
- [16] Kiem PV. Minh CV., Dat NT., Kinh LV. Fitoterapia 2010; 81: 485.
- [17] Beneficial Effect of *Achyranthes Aspera* Linn. In Toluene-Di-Isocyanate Induced Occupational Asthma in Rats Bhoomika R. Goyal, Ramesh K. Goyal and Anita A. Mehta.
- [18] Micropropagation of *Clerodendrum serratum* L. Through Direct and Indirect Organogenesis S.M. Vidya*, V. Krishna 1, B.K. Manjunatha 2 and Pradeepa Plant Tissue Cult. & Biotech. 22(2): 179-185, 2012 (December).
- [19] P. Venkatesh, Pulok K. Mukherjee, Satheesh Kumar N, Neelesh K. Nema,A. Bandyopadhyay, Hiroyuki Fukui, et al., Mast cell stabilization and antihistaminic potentials of *Curculigo orchoides* rhizomes Hiroyuki Mizuguchi Journal of Ethnopharmacology126 (2009) 434–436.
- [20] Gupta RK & Tandon V, An experimental evaluation of the anticonvulsant activity of *V.negundo*, proceeding of 48th annual conference, Dec 17-20, 2002 in CME program in physiology and pharmacology, Lucknow (abstract), In: Indian J Physiol Pharmacol, 2002, 46 (5S), 82.

- [21] The Role of Mast Cells in Citric Acid-Induced Airway Constriction and Cough Yih-Loong Lai, Li-Ling Wu, Tai-Yin Lin, and Chien-He Lin Chinese Journal of Physiology 52(5 Supplement): 332-338, 2009 DOI: 10.4077/CJP.2009.AMH079.
- [22] Benacerraf, B., 1978. A hypothesis to relate the specificity of T lymphocytes and the activity of I region-specific Ir genes in macrophages and B lymphocytes. Journal of Ethnopharmacology 18, 133–141.
- [23] Mast cell stabilizing and antiallergic activity of Abrus precatorius in the management of asthma DJ Taur, RY Patil Asian Pacific Journal of Tropical Medicine (2011)46-49.
- [24] Farah Farokhi, Fereshteh Khaneshi, et al., Histopathologic changes of the lung in asthmatic male rats treated with hydroalcoholic extract of Plantago major and theophylline Received: Sep 2, 2012; Accepted: Nov 25, 2012, Epub ahead of print.
- [25] Priyashree Sunita, S Jha, Shakti Prasad Pattanayak, et al., Bronchodilatory and mast cell stabilizing activity of Cressa cretica. Evaluation through *in vivo* and *in vitro* experimental models. Asian Pacific Journal of Tropical Medicine (2012)180-186.
- [26] OECD; guidelines 425. Acute oral toxicity. Environmental health and safety monograph series on testing and assessment. 2000. p. 24.
- [27] Englert CE, Wirth K, Gehring D, Fürst U, Albus U, Scholz W, Osenkranz B, Schölkens BA. Airway pharmacology of the potassium channel opener, HOE 234, in guinea pigs: *in vitro* and *in vivo* studies. Eur J Pharmacol, 1992; 210: 69–75.