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PHARMACOLOGICAL EVALUATION OF THE ETHANOLIC EXTRACT OF ALPINIA CALCARATA RHIZOMES FOR ANTI-ASTHMATIC ACTIVITY

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Abstract

The present study investigates the anti-asthmatic activity of the ethanolic extract of Alpinia calcarata rhizomes (EEAC) using histamine aerosol-induced bronchoconstriction in guinea pigs and milk-induced leukocytosis and eosinophilia in mice. The rhizomes were collected, authenticated, shade-dried, powdered, and extracted using ethanol through Soxhlet extraction, yielding 17% w/w extract. Preliminary phytochemical screening revealed the presence of flavonoids, tannins, phenols, steroids, proteins, carbohydrates, and cardiac glycosides. Acute toxicity studies, conducted as per OECD guidelines 423, showed no mortality up to 2000 mg/kg, indicating the extract's safety. In vivo studies demonstrated significant protection against histamine-induced bronchospasm, with maximum protection (62.62%) observed at 200 mg/kg, comparable to the standard drug chlorpheniramine maleate. The extract also significantly reduced milk-induced leukocytosis and eosinophilia, indicating anti-inflammatory potential. The anti-asthmatic effects may be attributed to the presence of flavonoids and steroids, known for their bronchodilatory and antioxidant properties. The results validate the traditional use of Alpinia calcarata in asthma management and suggest further studies to isolate and characterize the bioactive compounds responsible for these effects.

Introduction to Herbal Drugs: Embracing Nature's Remedies

Herbal drugs, also known as botanical medicines or phytomedicines, are derived from plants and natural sources that possess therapeutic value. Unlike synthetic drugs, herbal preparations utilize the natural bioactive compounds of plants to promote health and prevent disease. The growing preference for plant-based therapies reflects a global shift toward safer, sustainable, and holistic approaches to healthcare [1-3].

Historical and Cultural Background

The medicinal use of plants dates back to ancient civilizations such as Egypt, China, India, and Greece. Traditional systems like Ayurveda, Traditional Chinese Medicine (TCM), and Indigenous Medicine have relied on herbs for centuries to restore balance and treat illness. Each culture developed its own pharmacopoeia based on local flora-for example, Ayurvedic preparations in India and herbal formulas in China-reflecting the deep interconnection between culture and natural healing [4-5].

Scientific Validation and Global Market

Modern research has greatly advanced the understanding of herbal medicine. Through pharmacological and biochemical studies, scientists have identified the active constituents of many medicinal plants and validated their therapeutic efficacy through clinical trials. Consequently, herbal medicines have gained increasing acceptance in mainstream healthcare.

The global herbal drug market has expanded rapidly, supported by consumer demand for natural and sustainable remedies. Pharmaceutical companies and research institutions continue to develop standardized

extracts and herbal formulations, contributing to both innovation and economic growth [6].

Challenges in Herbal Medicine

Despite its benefits, herbal medicine faces challenges such as variation in plant quality, lack of standardization, and differing regulatory policies across countries. Safety issues, including contamination or adulteration, must also be addressed. Ethical concerns like biopiracy and the misuse of indigenous knowledge require fair recognition and benefit-sharing with traditional communities [7-8].

Table 01: Common Herbal Drugs and Applications [9-10]

Herbal Drug	Botanical Name	Traditional Use	Modern Application
Aloe vera	*Aloe barbadensis*	Wound healing	Used in skin care and digestive supplements
Ginseng	*Panax ginseng*	Energy enhancer	Reduces stress, boosts immunity
Turmeric	*Curcuma longa*	Anti-inflammatory	Supports joint and digestive health
Ginger	*Zingiber officinale*	Digestive aid	Relieves nausea, reduces inflammation
Garlic	*Allium sativum*	Heart health	Manages cholesterol and blood pressure

Asthma and Herbal Support [11-13]

Asthma is a chronic inflammatory disease of the airways marked by wheezing, coughing, and breathlessness. Conventional therapy includes bronchodilators and corticosteroids to reduce inflammation and prevent attacks. Certain herbs also offer supportive roles:

- Boswellia serrata reduces airway inflammation.
- Coleus forskohlii acts as a bronchodilator.
- Glycyrrhiza glabra (Liquorice) soothes cough and aids mucus expulsion.
- Zingiber officinale (Ginger) and Eucalyptus globulus improve breathing and reduce congestion.

  Such herbal remedies complement standard treatment and enhance respiratory function when used responsibl [14].

Plant Profile: Alpinia Calcarata [15]

Alpinia calcarata, known as dwarf cardamom or cardamom ginger, is a perennial herb from the Zingiberaceae family. Native to India and Southeast Asia, it grows in warm, humid climates with fertile soil. Its aromatic rhizome and attractive flowers make it valuable both medicinally and ornamentally. Traditionally, it is used to relieve digestive problems, respiratory discomfort, and inflammation. Studies show that it contains antioxidant, antimicrobial, and anti-inflammatory compounds. However, medical consultation is advised before use, especially for individuals sensitive to ginger-family plants.

Aim and Objective

The growing preference for herbal remedies stems from their perceived safety, efficacy, and fewer side effects compared to synthetic drugs. Alpinia calcarata is an important medicinal plant used in traditional therapy.

Aim

To evaluate the anti-asthmatic activity of the ethanolic extract of Alpinia calcarata rhizomes.

Objective

To assess the anti-asthmatic potential of the ethanolic extract of Alpinia calcarata rhizomes.

Experimental Methodology

Plan of Work

1. Collection and authentication of Alpinia calcarata rhizomes.
2. Preparation of the ethanolic extract from the rhizomes.
3. Preliminary phytochemical screening of the extract to identify active constituents.
4. Acute toxicity studies of the ethanolic extract as per OECD 423 guidelines.
5. Evaluation of anti-asthmatic activity using in vivo models:
6. Histamine aerosol-induced bronchoconstriction in guinea pigs.
7. Milk-induced leukocytosis and eosinophil count.

Materials and Methods

Plant Material

Alpinia calcarata was selected for the study based on its traditional medicinal use. The rhizomes were collected, authenticated, shade-dried, and coarsely powdered.

Chemicals and Reagents

- Carboxymethylcellulose – Spectrum Reagents and Chemicals Pvt. Ltd.
- Histamine – NICE Chemicals Pvt. Ltd.

  Drugs Used
- Chlorpheniramine maleate – Abbott Laboratories Pvt. Ltd.
- Dexamethasone – Zydus Biogem, Cadila Healthcare Ltd.

Instruments

- UV–Visible Spectrophotometer – Jasco International
- Incubator – Rotek Instruments, B&C Industries, W. Vengola
- Centrifuge – Rotek Instruments, B&C Industries, W. Vengola
- Histamine Chamber – Orchid Scientific Innovations India Pvt. Ltd.

Experimental Animals

Swiss albino mice (25–40 g) and guinea pigs (400–600 g) were used. They were maintained under standard

laboratory conditions (25 ± 2 °C; 12 h light/dark cycle) with ad libitum access to food and water. All procedures followed CPCSEA guidelines, Government of India.

Preparation of Plant Extract

The powdered rhizomes of Alpinia calcarata were extracted with ethanol using a Soxhlet apparatus. The extract was concentrated by evaporation and stored under refrigeration for further use.

Preliminary Phytochemical Screening

The ethanolic extract was subjected to standard qualitative tests to identify phytoconstituents:

Carbohydrates: Molisch's test

Proteins/Amino acids: Biuret and Ninhydrin tests

Fats and Oils: Solubility test

Steroids: Salkowski test

Glycosides: Legal's test

Saponins: Foam test

Flavonoids: Shinoda test

Alkaloids: Dragendorff's test

Acute Toxicity Study

Acute toxicity was assessed in mice as per OECD guideline 423. The ethanolic extract was administered orally at doses of 50, 300, and 2000 mg/kg. Animals were observed for behavioral changes and signs of toxicity for 3 hours post-dosing and periodically for 24 hours.

Evaluation of Anti-Asthmatic Activity

1. Histamine Aerosol–Induced Bronchoconstriction in Guinea Pigs

Guinea pigs were exposed to 0.2% w/v histamine aerosol in a histamine chamber. The time until the onset of pre-convulsive dyspnea (PCT) was recorded.

After a 2-day recovery period, animals were divided into four groups (n = 4–5):

Group I: Control (Carboxymethylcellulose)

Group II: Extract 100 mg/kg (p.o.)

Group III: Extract 200 mg/kg (p.o.)

Group IV: Standard (Chlorpheniramine maleate, i.p.)

PCT was measured at 1, 4, and 24 hours post-treatment.

$$\text{Percentage protection} = \frac{E_t a - E_t b}{E_t a} \times 100$$

Where E_ta = PCT after treatment and E_tb = PCT before treatment.

2. Milk-Induced Leukocytosis and Eosinophilia in Mice

Mice were divided into four groups (n = 6):

- Group I: Control (Carboxymethylcellulose)
- Group II & III: Extract 100 and 200 mg/kg (p.o.)
- Group IV: Dexamethasone 50 mg/kg (i.p.)

Thirty minutes post-treatment, all animals received 4 mL/kg of boiled, cooled milk subcutaneously. Blood samples were collected from the retro-orbital plexus before treatment and 24 hours after milk injection. Total leukocyte and eosinophil counts were determined, and changes in counts were calculated to assess anti-asthmatic potential.

Results

Collection and Authentication of Plant Material

Rhizomes of Alpinia calcarata were collected, cleaned, shade-dried, and authenticated by a qualified botanist. The dried rhizomes were coarsely powdered and stored in an airtight container for further analysis.

Extraction of Plant Material

Powdered rhizomes were extracted with ethanol using a Soxhlet apparatus. The obtained extract was concentrated under reduced pressure and stored in a refrigerator until use. The percentage yield of the ethanolic extract was found to be 17% w/w.

Preliminary Phytochemical Screening

The ethanolic extract of Alpinia calcarata rhizomes (EEAC) was subjected to qualitative phytochemical analysis following standard procedures. The extract showed the presence of flavonoids, tannins, phenolic compounds, carbohydrates, proteins, amino acids, steroids, and cardiac glycosides, while alkaloids, saponins, anthraquinone glycosides, cyanogenic glycosides, and fats were absent (Table 02).

Table 02: Phytochemical Screening of Ethanolic Extract of Alpinia calcarata Rhizomes

Sl. No.	Constituents	Result
1	Phenols	+
2	Alkaloids	–
3	Flavonoids	+
4	Tannins	+
5	Carbohydrates	+
6	Saponin glycosides	–
7	Cardiac glycosides	+
8	Anthraquinone glycosides	–
9	Cyanogenic glycosides	–
10	Proteins	+
11	Fats and oils	–
12	Steroids	+
13	Amino acids	+

(+ indicates presence; – indicates absence)

Acute Toxicity Studies

Acute toxicity of the ethanolic extract was performed in Swiss albino mice following OECD guideline 423. The extract was administered orally at doses of 50, 300, and 2000 mg/kg. No mortality or behavioral changes were observed, indicating the extract was safe up to 2000 mg/kg. Hence, doses of 100 mg/kg (1/20th) and 200 mg/kg (1/10th) were selected for pharmacological evaluation.

In Vivo Anti-Asthmatic Activity

Histamine Aerosol–Induced Bronchoconstriction in Guinea Pigs

The anti-asthmatic potential of EEAC was evaluated using histamine aerosol–induced bronchoconstriction in guinea pigs. Animals were exposed to 0.2% w/v histamine aerosol in a histamine chamber, and the time to onset of preconvulsive dyspnea (PCT) was recorded as the basal value.

After two days of recovery, animals were divided into four groups (n = 4–5):

Group I: Control (Carboxymethylcellulose)

Group II: EEAC 100 mg/kg (p.o.)

Group III: EEAC 200 mg/kg (p.o.)

Group IV: Standard (Chlorpheniramine maleate, 1 mg/kg, i.p.)

PCT was recorded at 1, 4, and 24 hours after drug administration. The percentage of protection was calculated as:

$$\text{Percentage Protection} = \frac{E_{ta} - E_{tb}}{E_{ta}} \times 100$$

Where

E_{ta} = preconvulsion time after treatment and E_tb = preconvulsion time before treatment.

The ethanolic extract at 200 mg/kg showed the highest percentage protection (62.62%) at 4 hours, indicating significant bronchodilatory activity comparable to chlorpheniramine maleate.

Table 03: Effect of EEAC on Histamine Aerosol–Induced Bronchoconstriction in Guinea Pigs

Group	Latent Period of Convulsion (min)			
	Before	1 Hour	4 Hours	24 Hours
Control	15.3 ± 0.18	17.36 ± 0.18	17.63 ± 0.18	17.4 ± 0.12
EEAC (100 mg/kg)	15.7 ± 1.01	28.6 ± 0.25	38.4 ± 0.05*	27.2 ± 0.23
EEAC (200 mg/kg)	14.7 ± 0.57	29.5 ± 3.08	39.4 ± 1.04**	27.4 ± 0.35
Standard (CPM 1 mg/kg)	17.5 ± 0.69	59.3 ± 0.03*	67.3 ± 1.01**	35.5 ± 0.45

Values are Mean ± SEM (n = 6). P < 0.05, P < 0.01 compared to control.

Statistical analysis was performed using one-way ANOVA followed by Dunnett's multiple comparison test.*

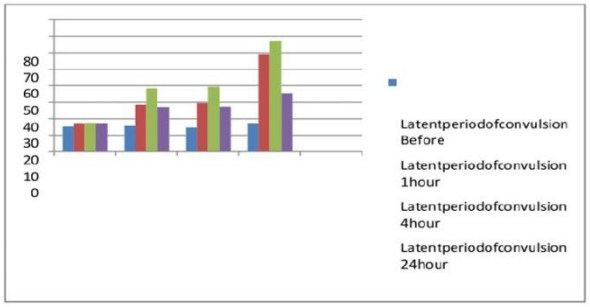

Fig 01: Effect of EEAC on Histamine Aerosol–Induced Bronchoconstriction in Guinea Pigs.

Table 04: Protection of the plant Alpinia calcarata rhizomes against histamine induced bronchoconstriction in guinea pig;

GROUP	% Protection		
	1 hour	4 hours	24 hours
Control	11.86	13.21	12.06
Ethanolic extract (100mg/kg)	45.16	59.06	42.24
Ethanolic extract (200mg/kg)	50.13	62.62	46.31
Standard (CPM) (1mg/kg)	70.53	74.04	50.81

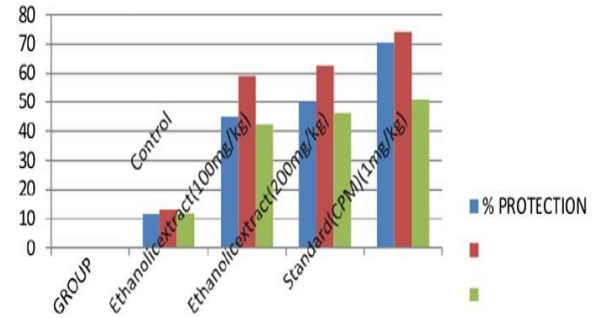

Fig 02: Percentage of Protection of the plant Alpinia calcarata rhizomes against histamine induced bronchoconstriction in guinea pig

Milk-induced leukocytosis

In the control group (5104±9), the highest rise in leukocyte count was noted 24 ours following milk administration. A 200 mg/kg ethanolic extract pretreatment significantly increased the activity of the mice. Leukocyte count (2270±12) was lower in the ethanolic extract of Alpinia calcarata (200 mg/kg) than in the control. In comparison to the control, the plant extract (100 mg/kg) showed less significant activity, whereas the standard medicine (700±10) showed substantial activity.

Table 05: Effect of ethanolic extract of Alpinia calcarata rhizomes on milk induced leukocytosis

GROUP	Difference in no of leukocytes before and after treatment (Cu.mm)
Control	5104±9
Ethanolicextract (100mg/kg)	3570±8
Ethanolicextract (100mg/kg)	2270±12
Standard Dexamethasone (50mg/kg)	700±10

Values are Mean ± S.EM., where n=6 in each group, P<0.05*, P<0.01** (significant) compared withcontrol Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnctt's multiple comparison test.

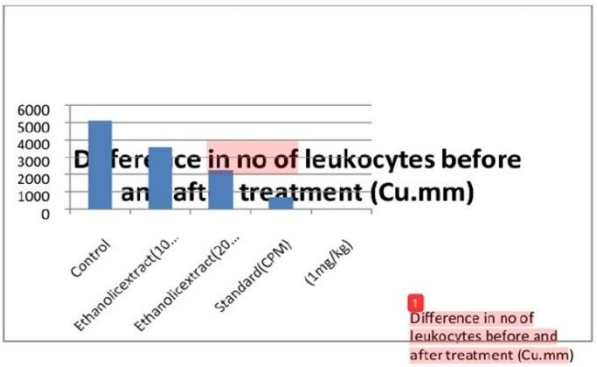

Fig 03: Effect of ethanolic extract of Alpiniacalcarata rhizomes on milk induced leukocytosis

Milk-induced eosinophilia

The difference in eosinophil levels before and after therapy was investigated in this study. The largest increase in the variation in eosinophil counts (128±1.414) was noted in the control group. Alpinia calcarata 200 mg/kg ethanolic extract showed substantial efficacy as evidenced by a smaller difference in eosinophil counts (63±1.434). In a similar vein, the conventional medication showed notable efficacy with a smaller variation in eosinophil levels (48±1.13). Less notable action was shown by the plant's 100 mg/kg ethanolic extract.

Table 05: Effect of ethanolic extract of Alpiniacalcarata rhizomes on milk induced eosinophilia

GROUP	Difference in no of leukocytes before and after treatment (Cu.mm)
Control	128±1.414
Ethanolic extract (100mg/kg)	92±1.48
Ethanolic extract (100mg/kg)	63±1.434
Standard (CPM) Dexamethasone (50mg/kg)	48±1.13

Values are Mean=S.E 48+1.13 induced M., where n=6 in each group, P<0.05*, P<0.01* (significant) compared with control, Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test.

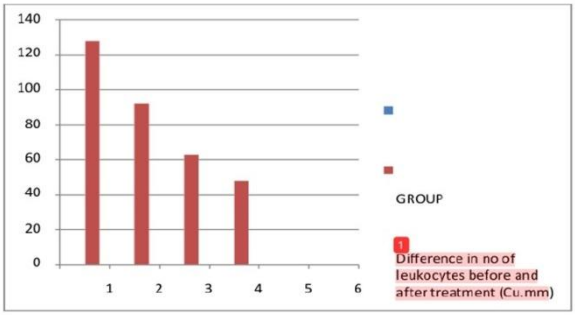

Fig 04: Effect of ethanolic extract of Alpiniacalcarata rhizomes on milk induced eosinophilia

Discussion

Preliminary phytochemical screening of the ethanolic extract of Alpinia calcarata rhizomes revealed the presence of proteins, carbohydrates, cardiac glycosides, flavonoids, tannins, and phenolic compounds. Understanding the phytochemical composition of medicinal plants is vital for identifying bioactive constituents responsible for therapeutic effects. Plants naturally produce two categories of metabolites-primary (e.g., sugars, amino acids, and proteins) and secondary (e.g., alkaloids, flavonoids, terpenoids, and phenolic compounds). Secondary metabolites often contribute to the pharmacological activities of medicinal plants [16].

Among these, phenolic compounds and flavonoids are known for their potent antioxidant, cardioprotective, and anti-inflammatory effects, as well as their ability to modulate cell proliferation and delay aging. Tannins, another class of secondary metabolites, exhibit antimicrobial properties and are being investigated for their role in reducing the risk of cardiovascular disorders. Their antioxidant and free radical scavenging activities further enhance their therapeutic relevance in inflammatory diseases such as asthma [17].

The histamine aerosol–induced bronchoconstriction model in guinea pigs is a well-established paradigm for assessing bronchodilator activity. Histamine, a major inflammatory mediator in asthma, triggers airway hyperresponsiveness, smooth muscle contraction, hypotension, and capillary dilation, resulting in symptoms resembling human asthma. In this study, the ethanolic extract of A. calcarata rhizomes significantly delayed the onset of histamine-induced bronchospasm in guinea pigs. The maximum protection was observed at a dose of 200 mg/kg, which was comparable to the standard antihistaminic drug, chlorpheniramine maleate. This suggests that the extract possesses marked bronchodilator activity, likely mediated through inhibition of histamine

receptors or reduction of inflammatory mediator release [18-19].

Further, the anti-asthmatic activity was supported by the milk-induced leukocytosis and eosinophilia model in mice. Administration of milk resulted in a significant increase in leukocyte and eosinophil counts, indicating an inflammatory response. Treatment with the ethanolic extract markedly reduced both total leukocyte and eosinophil counts, suggesting suppression of inflammatory processes and oxidative stress. Eosinophils play a key role in airway inflammation, hyperreactivity, and mucus hypersecretion in asthma. Therefore, reduction in eosinophil count by the extract indicates attenuation of Type I hypersensitivity reactions and improved airway function [20].

Overall, the results demonstrate that the ethanolic extract of Alpinia calcarata rhizomes exhibits significant anti-asthmatic activity, potentially through a combination of bronchodilatory, anti-inflammatory, and antioxidant mechanisms. The findings validate the traditional use of A. calcarata in the management of respiratory disorders and suggest that its bioactive constituents, particularly flavonoids, tannins, and phenolic compounds, may contribute to the observed pharmacological effects. Further studies on the isolation and characterization of these constituents, along with mechanistic and clinical evaluations, are warranted to substantiate its therapeutic potential in asthma management [21-24].

Conclusion

The findings of the present study demonstrate that the ethanolic extract of Alpinia calcarata rhizomes possesses significant anti-asthmatic activity. The observed effects may be attributed to the plant's potent anti-inflammatory and antioxidant properties. Phytochemical analysis confirmed the presence of flavonoids and steroids, compounds known to exhibit bronchodilatory and anti-inflammatory actions comparable to corticosteroids commonly used in asthma management. These bioactive constituents are likely responsible for the observed pharmacological effects. Overall, the results validate the traditional use of A. calcarata in the treatment of asthma and highlight the need for further studies to isolate, characterize, and elucidate the mechanisms of the active constituents responsible for its anti-asthmatic potential.

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Conflict of Interest

The authors declare no conflict of interest.

Informed Consent and Ethical Statement

Not Applicable

Author Contribution

All authors are contributed equally

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