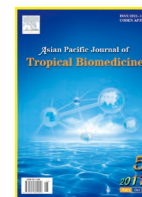




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Some medicinal plants with antiasthmatic potential: a current status

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ABSTRACT

Asthma is a common disease that is rising in prevalence worldwide with the highest prevalence in industrialized countries. Asthma affect about 300 million people worldwide and it has been estimated that a further 100 million will be affected by 2025. Since the ancient times, plants have been exemplary sources of medicine. Current asthma therapy lack satisfactory success due to adverse effect, hence patients are seeking complementary and alternative medicine to treat their asthma. Ayurveda and other Indian literature mention the use of plants in various human ailments. India has about 45 000 plant species and among them several thousand are claimed to possess medicinal properties. Researches conducted in the last few decades on the plants mentioned in ancient literature or used traditionally for asthma have shown antiasthmatic, antihistaminic and antiallergic activity. This review reveals that some plants and their extract have antiasthmatic, antihistaminic, anticholinergic and antiallergic activity.

1. Introduction

Asthma is a complex inflammatory disease causes airway narrowing and associated with changes in the levels of eosinophils, mast cells, lymphocytes, cytokines and other inflammatory cell products. It is well known that patients with asthma have high levels of specific IgE that binds to receptors of mast cells and other inflammatory cells. Interaction between IgE antibody and antigen results in the activation of a series of inflammatory cellular reactions, including the release of mediators such as histamines, prostaglandins and leukotrienes, which subsequently lead to contraction of airway smooth muscle and bronchoconstriction[1–3]. Asthma is a common disease that is rising in prevalence worldwide, with the highest prevalence in industrialized countries. Asthma affect about 300 million people worldwide and it has been estimated that a further 100 million will be affected by 2025[4, 5]. Since 1970s, the global prevalence, morbidity, mortality, and economic

burden of asthma have increased particular in children[6].

Medicinal plant used for the treatment of asthma should have anti-inflammatory, immunomodulatory, antihistaminic, smooth-muscle relaxants and allergic activity[7]. According to Ayurveda anti-asthmatic drug should have properties such as anti-kapha and anti-vata[8]. Antioxidant supplements are effective in reducing bronchoconstriction severity by inhibiting pro-inflammatory events as a result of neutralizing the effects of excess reactive oxygen species and reactive nitrogen species[9]. Current asthma therapy lack satisfactory success due to adverse effect, hence patients are seeking complementary and alternative medicine to treat their asthma [10]. Quercetin is one of the most widely occurring flavonoids ingested in food by humans. Quercetin inhibits mast cell degranulation and subsequent release of histamine.

2. Adverse effects of current treatments used in asthma[11]

2.1. Isoprenaline

Causes tachycardia.

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2.2. Salbutamol

Muscle tremors (dose related), palpitation, restlessness, nervousness, throat irritation and ankle edema.

2.3. Theophylline

Convulsions, shock, arrhythmias, increased muscle tone, tachypnoea, (dose dependent) flushing, hypotension, restlessness, tremors, vomiting, palpitation, diuresis, dyspepsia, insomnia etc.

2.4. Anticholinergics

Dry mouth, difficulty in swallowing and talking, scarlet rash, photophobia, blurring of near (Atropine and its congeners) vision, palpitation, ataxia, delirium, hallucinations, hypotension, weak and rapid pulse, cardiovascular collapse with respiratory depression, convulsions and coma (in severe poisoning).

2.5. Ketotifen

Sedation, dizziness, dry mouth, nausea and weight gain.

2.6. Corticosteroids

Cushing's habitus, fragile skin, purple striae, hyperglycemia, muscular weakness, susceptibility to infection, delayed healing of wounds and surgical incisions, peptic ulceration, osteoporosis, glaucoma, growth retardation, psychiatric disturbances, suppression of hypothalamo–pituitary–adrenal (HPA) axis etc.

As a consequence, the search for effective low–risk, non–drug strategies that provide a valuable adjunctive or alternative treatment in asthma management is clinically attractive and relevant. There is much interest in complementary and alternative medicine, and its use in the management and treatment of asthma is growing at a significant rate^[10]. Present review describes some plants that have been pharmacologically evaluated for those parameters involved in asthma.

3. Some traditional plants with antiasthmatic potential

3.1. *Aerva lanta* Linn (Amaranthaceae)

Aerva lanta (*A. lanta*) is an erect or prostrate herbaceous common wayside weed which is recognized by its white axillary bunches of small woolly flowers. It is abundant on the plains in the warmer parts of India. Ethanol extract of aerial parts of *A. lanata* at 100 μ g/mL in the isolated goat tracheal chain preparation model and 30 and 60 mg/kg doses orally in clonidine–induced catalepsy and mast cell

degranulation in mice possesses antiasthmatic activity^[12].

3.2. *Ageratum conyzoides* L.

Ageratum conyzoides (*A. conyzoides*) is an erect, herbaceous annual plant from the family Asteraceae (Compositae), native to tropical America, but with a distribution range in tropical and subtropical areas around the world. Hydroalcoholic extract of leaves of *A. conyzoides* at doses of 250, 500 and 1 000 mg/kg shows antihistaminic activity by inhibiting clonidine induced catalepsy in mice^[13].

3.3. *Argemone mexicana*

Argemone mexicana (*A. mexicana*) is common everywhere by road–sides and fields in India. It possesses antiallergic and antistress activity of aqueous extracts of *A. mexicana* stem at dose 50 mg/kg, *i.p.* using milk–induced leucocytosis and milk–induced eosinophilia^[14].

3.4. *Asystasia gangetica* T. Adams (Acanthaceae)

Asystasia gangetica (*A. gangetica*) is used in many parts of Nigeria for the management of asthma. Akah, *et al.* evaluated hexane, ethylacetate, and methanol extracts of the leaves of *A. gangetica* for antiasthmatic activity using guinea pig trachea; rat stomach strip; guinea pig ileal preparation and egg albumin–induced acute inflammation. The results indicated that the extracts did not exhibit contractile or relaxant activity in isolated tissue preparations; however, they inhibited the contraction evoked by spasmogens^[15].

3.5. *Bacopa monnieri* L. (Scrophulariaceae)

Bacopa monnieri: Samiulla, *et al.* evaluated petroleum ether, chloroform, methanol and water extracts of *B. monnieri* leaves at doses 10 μ g/mL for mast cell stabilizing activity in rats. The result of investigation observed that all the extract significantly inhibits mast cell degranulation^[16].

3.6. *Cassia sophera* (caesalpinaceae)

Cassia sophera (*C. sophera*) is used in traditionally for treatment of asthma and bronchitis. Chloroform, ethyl acetate and ethanol fractions isolated from ethanol extract of leaves of *C. sophera* possesses significant antiasthmatic activity in carrageenan induced paw edema, histamine induced bronchoconstriction, clonidine and haloperidol induced catalepsy, milk induced leucocytosis, and eosinophilia and passive paw anaphylaxis animal models at doses 250, 500 and 750 mg/kg and this activity may be due to presence of flavonoids^[17].

3.7. *Casuarina equisetifolia* Linn (Casuarinaceae)

Casuarina equisetifolia (*C. equisetifolia*) is evergreen tree; generally attain height up to 50 m, cultivated on Coastal regions from Gujarat to Orissa, some parts of West Bengal and in Andamans. The methanol extract of extracts of wood and bark possesses antihistaminic activity by inhibiting the histamine induced contraction of trachea (10–80 mcg/mL), clonidine induced catalepsy and mast cell degranulation at doses 100 mg/kg^[18].

3.8. *Clerodendrum Serratum* Linn (*Verbenaceae*)

Clerodendrum Serratum (*C. serratum*), known as bharangi in ayurveda, is traditionally useful in treating pain, inflammation, rheumatism, respiratory diseases, and malarial fever. Ethanol extract of roots of *C. serratum* showed antiasthmatic activity using isolated goat tracheal chain preparation, clonidine induced catalepsy; Milk induced leucocytosis and eosinophilia in mice at doses 50,100 and 200 mg/kg^[19].

3.9. *Cnidium monnieri* (*Umbelliferae*)

Cnidium monnieri (*C. monnieri*) in traditional medicine of China has been used for treatment of pain in female genitalia, impotence and suppurative dermatitis as an antipruritogenic agent. Matsuda *et al.* reported antiallergic activity of ethanol extract and Osthol a chromane isolated from ethanol extract of fruits of *C. monnieri* in passive cutaneous anaphylaxis in rats^[20].

3.10. *Crinum glaucum* (*Amaryllidaceae*)

Crinum glaucum (*C. glaucum*) is popular in Yoruba of South West Nigeria. Traditional medicine practitioners reported it as an effective remedy in the relief of cough, asthma and convulsions. The aqueous extract of *C. glaucum* possesses antiallergic activity at dosed 100–400 mg/kg by reduction in area of dye leakage in passive cutaneous anaphylactic reaction, protecting degranulation of mast cell and histamine induced bronchoconstriction in the guinea pig^[21].

3.11. *Curculigo orchioides* Gaertn (*Amaryllidaceae*)

Curculigo orchioides (*C. orchioides*) is a tiny herbal plant widely distributed in India, China, Malaya, and Japan. Alcoholic extract of *C. orchioides* rhizomes at doses (100–400 mg/kg) shows mast cell stabilizing and antihistaminic activity on Compound 48/80–induced mast cell degranulation and systemic anaphylaxis^[22]. It also inhibited histamine–induced contraction in goat trachea, guinea pig ileum and bronchoconstriction in guinea pigs; egg albumin induced passive paw anaphylaxis in rats; milk induced leucocytosis and eosinophilia; clonidine induced catalepsy in mice^[23].

3.12. *Eclipta alba* Linn (*Asteraceae*)

The 50% ethanol extract shows antianaphylactic and antihistaminic activity at doses 250 and 500 mg/kg on compound 48/80–induced degranulation of mast cell, egg albumin induced passive Cutaneous and paw anaphylaxis; bronchoalveolar lavage (BAL) study on guinea pig trachea; and determination of histamine^[24].

3.13. *Euphorbia hirta* (*Euphorbiaceae*)

Popularly known as asthma weed, *Euphorbia hirta* is an herbaceous wild plant which grows in the hotter parts of India. Ethanol extract of whole aerial part of the plant at doses (100–1000 mg/kg) shows antihistaminic and antiallergic activity by inhibiting inhibited the passive cutaneous anaphylaxis and paw anaphylaxis reaction; protection of mast cell from degranulation^[25].

3.14. *Ficus bengalensis* Linn (*Moraceae*)

Ficus bengalensis (*F. bengalensis*) is a very large tree reaching about 30 m high and sending down many aerial roots from the branches. Ethyl acetate, ethanol and aqueous extracts as well as fractions isolated from aqueous extract of *F. bengalensis* bark possesses antihistaminic activity by inhibiting clonidine induced catalepsy in mice at dose 50 mg/kg. These activity may be due to presence of flavonoids^[26,27].

3.15. *Gakani*

Gakani is a polyherbal drug contains *Cenchrus biflorus* Roxb. Gramineae *Ola subscorpioidea* Oliv. (Olaaceae), *Piper guineense* schum Thonn (Piperaceae), *Psorospermum guineense* Hochr. (Hypericaceae), *Securidaca longipedunculata* Tressen (Polygalaceae), *Syzygium aromaticum* (L.) Merr. (Myrtaceae). The anti-asthmatic potential of *Gakani*, a popular herbal drug was investigated using guinea pig tracheal chain; guinea pig ileum preparation; on the rat stomach strip and egg albumin induced hind paw edema. Result indicates that the extract blocked the effects of histamine and isoprenaline on the guinea pig tracheal chain. It shows inhibition contraction of isolated guinea pig ileum and rat stomach strip, caused by histamine and 5–hydroxytryptamine (5–HT). The extract had good anti–inflammatory effect in rats^[28].

3.16. *Hemidesmus indicus* R. Br. (*Asclepiadaceae*)

Hemidesmus indicus (*H. indicus*) is a twining shrub commonly found in India. Bhujbal *et al.* reported antiasthmatic activity of ethanol extract of *H. indicus* roots at doses 25, 50, 100 mg/kg using isolated goat tracheal chain preparation, passive paw anaphylaxis in rat and clonidine–

induced catalepsy in mice^[29].

3.17. *Amburana cearensis* (Fabaceae)

Amburana cearensis (*A. cearensis*) is a medicinal plant common to the Brazilian Northeastern “caatinga” (savannah), and popularly used in respiratory tract diseases including asthma. The flavonoid isokaempferide isolated from Trunk barks of *A. cearensis* shows significant relaxation of KCl induced contraction on guinea pig trachea^[30].

3.18. Plants from Zinziberaceae

Tewtrakul *et al.* reported antiallergic activity of ethanol and water extract of some plants of Zinziberaceae family^[31].

3.19. *Lepidium sativum* Linn (Cruciferae)

Commonly known as Asaliyo, it is an erect, glabrous annual herb cultivated as a salad plant throughout India. The ethanol extract and ethyl acetate, n-butanol and methanol fractions isolated from ethanol extract inhibit bronchospasm induced by histamine and acetylcholine^[32].

3.20. *Mentha spicata* L

The four new flavonoids and three new glycosides isolated from ethyl acetate soluble fractions of *M. spicata* leaves shows antihistaminic activity by inhibiting antigen stimulated rat basophile^[33].

3.21. *Momordica dioica*

Momordica dioica is climbing creeper plant. Its fruits and leaves are traditionally used as medicinal agent of asthma, leprosy, bronchitis, fever, tridosha. Methanol and aqueous extract of pulp possesses antihistaminic activity by inhibiting clonidine induced catalepsy in mice at dose 50 mg/kg; this activity may be due to polar constituents^[34].

3.22. *Mucuna pruriens*

The L-DOPA isolated from methanol extract of seed possesses antihistaminic activity by inhibiting clonidine induced catalepsy and mast cell degranulation in mice at dose 50, 100 and 200 mg/kg^[35].

3.23. *Myrica esculenta* Buch. Ham. (Myricaceae)

Myrica esculenta is commonly known as Kaiphala. It is used for treatment of asthma and bronchitis in ayurvedic system of medicine. Patel *et al.* reported antiallergic and anti-inflammatory activity of ethanol extract of aerial parts using acetic acid induced vascular permeability and allergic pleurisy in mice methods at doses 75 and 150 mg/

kg^[36]. Stem bark of this plant possesses bronchodilator and antianaphylactic activity by inhibiting acetylcholine induced bronchospasm in guinea pigs, egg albumin induced anaphylaxis in guinea pigs at dose 75 mg/kg and by relaxing histamine and acetylcholine induced guinea pig trachea and ileum^[37].

3.24. *Nyctanthes arbortristis*

It is used traditionally in the treatment of asthma. The petroleum ether extract shows antihistaminic activity by inhibiting clonidine-induced catalepsy in mice at dose 50 mg/kg^[38].

3.25. *Olea europea* (Oleaceae)

It is a small evergreen tree, from 12 to 20 feet high, with hoary, rigid branches, and a grayish bark. Aqueous extract of ripe olives possesses antiasthmatic activity by inhibiting clonidine induced peritoneal mast cell degranulation in rats and catalepsy in mice at doses 4 and 8 mg/kg and also by protecting histamine induced contraction of goat trachea and guinea pig ileum at concentration of 100 μ g/mL^[39].

3.26. *Phymatodes scolopendria* (Burm.) Ching (Polypodiaceae)

Phymatodes scolopendria is a crawling fern growing in the sandy areas of the East coast of Madagascar. Ramanitrahambola *et al.* reported bronchodilator activity of 1, 2-benzopyrone (coumarin) isolated from ethanol extract of aerial parts by inhibiting histamine or carbachol pre-contracted guinea pig trachea^[40].

3.27. *Piper betel* Linn

Piper betel is traditionally used to cure cough, cold, pruritis, asthma and rheumatism. Ethanol and aqueous extract of leaves at doses 100 and 200mg/kg possesses antiasthmatic activity on histamine induced bronchoconstriction in guinea pig and histamine induced dose dependent contraction of guinea pig tracheal chain and isolated guinea pig ileum preparation^[41].

3.28. *Striga orobanchioides* Benth (Scrophulariaceae)

Striga orobanchioides is a parasitic plant, lives on the roots of various plants. Ethanol and aqueous extracts of whole plant shows antihistaminic and mast cell stabilizing activity by inhibiting histamine-induced contractions of the guinea-pig ileum at the concentration 2.5–25 μ g/mL in a dose-related manner and inhibiting degranulation of mast cells at dose 100 and 200 mg/kg^[42–49].

3.29. *Sphaeranthus indicus* Kurz (Asteraceae)

Sphaeranthus indicus is a medicinally important plant used as folk medicine. The ethanol extract at the doses of 150, 300 mg/kg and its ethyl acetate extract at the dose of 100, 150 mg/kg and 300 mg/kg showed slightly better protection against sheep serum and Compound 48/80–induced mast cell degranulation than the standard drug ketotifen^[50].

3.30. *Cynodon dactylon* (Poaceae)

Cynodon dactylon is one of the most commonly occurring perennial grass throughout India, commonly known as Dhuh. The petroleum ether, chloroform and methanol extracts of whole plant and fractions isolated from chloroform extract possess antianaphylactic activity but fractions isolated possess more potent activity at doses 10, 25, 50 and 100 mg/kg using compound 48/80–induced mast cell degranulation, determination of level of nitric acid in serum, compound 48/80–induced anaphylaxis^[51].

4. Conclusion

Almost 70 percent of the prescription and OTC (Over the Counter) medicines that are being used for many diseases' treatment is derived from plants and natural sources. Pharmacologists, Medical Doctors, Scientists and pharmaceutical companies study the plants and herbs that are traditionally used for treatment of various diseases. After vigorous study they identify the particular molecule that has therapeutic properties. These molecules do undergo various modifications and mutations in laboratories. And then, it is mass produced in factories and systematically marketed.

For example, *Digitalin* which is a drug used to stimulate the heart. Well, *Digitalin* comes from an herb called foxglove. Another example is the effective anti-clotting agent called *Coumarol*, that comes from a herb sweet clover. Another one is *Reserpine*, which is one of the most popular tranquilizers. It is the first ever modern psychiatric drug. Most of the modern tranquilizers are derived from *Reserpine*. *Reserpine* comes from a herb named snakeroot. In India they used snakeroot for thousands of years to calm people down. Still another example is *Quinine*. It is very efficient in reducing fever, especially malarial fever. This drug comes from the Peruvian bark in South America. Another example is Aspirin which was derived from white willow bark.

Let us see the herbs connection to Asthma. The first ever modern prescription medicine used to treat asthma is ephedrine. It is derived from the Chinese plant known as Ma Huang. Chinese have been using Ma Huang to treat breathing disorders, wheezing etc. for the past 2000 years. The molecule ephedrine was isolated from Ma Huang in 1940 and was widely prescribed since then. Cromolyn Sodium is another popular medicine used for the treatment of asthma. Cromolyn was derived from a plant known as

Khellin (Ammi Visnaga) commonly found in Egypt. It was used as a muscle relaxant by Egyptians for many centuries. Dr. Roger Altouyan (the discoverer of Cromolyn molecule), an asthmatic, tried Khellin on himself and found it to be very beneficial. Today cromolyn sodium is one of the first lines of treatment for asthma. Cromolyn sodium has weaned great number of patients away from harmful corticosteroids. Cromolyn effectively prevents asthma attack before it occurs. Prescription medicines Codeine, atropine, hyoscyamine, digoxin, digitoxin, pilocarpine, and quinidine are all derived from plants. Asthma and Allergy are lifestyle diseases and herbs are extremely effective.

The goals of medicine no matters to which group it belongs, are the same *i.e.* welfare of patients. One can look towards a future of integrated medicine and hope that research in alternative medicine will help to cure asthma safe and effectively rather than managing.

Conflict of interest statement

We declare that we have no conflict of interest.

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