IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
August 2020 Vol.:19, Issue:1
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A Review on Herbal Therapy of Asthma

IJPPR
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An official Publication of Human Journals
ISSN 2349-7203
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Sumayya S[1*], Anusree S[2], Silvia Navis[3], Prasobh G R[4]

1 Final year B pharm student, Sreekrishna College of Pharmacy and Research Centre, Kerala, India.

2 Assistant Professor, Sreekrishna College of Pharmacy and Research Centre, Kerala, India.

3 HOD Department of Pharmacology, Sreekrishna College of Pharmacy and Research Centre, Kerala, India.

4 Principal, Sreekrishna College of Pharmacy and Research Centre, Kerala, India.

Submission: 27 July 2020
Accepted: 02 August 2020
Published: 30 August 2020

Keywords: Herbal remedies, anti-asthmatic, Bronchoconstriction, Immunomodulatory

ABSTRACT

Asthma is a complex inflammatory disease that is rising in prevalence worldwide with the highest prevalence in industrialized countries. Current asthma therapy lacks satisfactory success due to adverse effects, hence patients are seeking complementary and alternative medicine to treat their asthma. 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.

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INTRODUCTION

Asthma is one of the most common chronic inflammatory disorders, associated with reversible airflow obstruction, airway hyperresponsiveness, and airway remodeling. This disease has a significant impact on individuals, their families, and society. It is also affected by 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[1]. 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.

The medicinal plant used for the treatment of asthma should have anti-inflammatory, immunomodulatory, antihistaminic, smooth-muscle relaxants, and allergic activity. According to Ayurveda anti-asthmatic drugs should have properties such as anti-Kapha and anti-Vata.

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[2].

ANTI ASTHMATIC PLANTS

I. ***BACOPA MONNIERI*** (Plantaginaceae)

Bacopa has also been used to treat numerous inflammatory conditions such as asthma, bronchitis, dropsy, and rheumatism. The evaluated petroleum ether, chloroform, methanol and water extracts of *B. monnieri* leaves at doses 10 µg/mL for mast cell stabilizing activity. Finally observed that all the extract significantly inhibits mast cell degranulation.

Bacopa is also used in Ayurvedic medicine to treat inflammatory conditions such as asthma and arthritis Neuroinflammation is mediated by microglial cells, which are the resident macrophages in the CNS Microglia exist in two distinct functional states; the M1 phenotype that produces proinflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-α) and Interleukin 6 (IL-6), and the M2 phenotype that produces the anti-inflammatory cytokine IL-

10 and downregulates the M1 response Chronic inflammation can result from an imbalance between the M1 and M2 subsets *Bacopa* has been shown to have anti-inflammatory effects on macrophages and inhibits the release of IL-6 and TNF-α from monocytes that have been stimulated with lipopolysaccharide (LPS) Many current studies have proven the ability of many extracts of bacopa to inhibit inflammation. the extracts were proved for inhibitory activity against enzymes involved in inflammation and cell death. Bacopa was found to significantly inhibit the release of IL-6 and TNF-α from LPS activated microglia[3].

Bacopa monnieri possesses significant anti-inflammatory activity that may well be relevant to its effectiveness in the healing of various inflammatory conditions in traditional medicine. The ethanol extract selectively inhibited prostaglandin E(2)- induced inflammation. The methanolic and aqueous extract of *Bacopa monnieri* caused a significant reduction in the edema paw volume. However, no such inflammatory reduction was observed in petroleum ether, and hexane extracts. The anti-inflammatory activity of *Bacopa monnieri* is due to the triterpenoid and bacoside present in plants.

II. ***EUPHORBIA HIRTA*** (Plantaginaceae)

It is 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 shows antihistaminic and antiallergic activity by inhibiting inhibited the passive cutaneous anaphylaxis and paw anaphylaxis reaction; protection of mast cell from degranulation.

Quercetin has a wide range of therapeutic properties, like antioxidant, anti-cancer, anti-inflammatory, and anti-allergic activities. Recently, many findings have been made regarding the effects of quercetin on the airway[4].

Mast cells play an important role in the early and late phases of asthma, as they release several mediators, including histamine, leukotrienes, and cytokines, which modulate airway hyperreactivity and inflammation. IgE binds to mast cells and basophils through their high-affinity IgE Fc receptor (FcεRI), and subsequent exposure to antigen induces IgE-sensitized mast cell degranulation. During degranulation, both pre-formed and newly generated mediators are released. These mediators, either alone or in conjunction with Th2 cytokines, increase smooth muscle cell contractility, epithelial cell permeability, and mucus production20. Furthermore, mast cell degranulation triggers the recruitment of macrophages, eosinophils, and basophils to the inflammatory site. Previous findings have shown that

treatment with quercetin inhibits the release of histamine and pro-inflammatory mediators (TNF-α, IL-1β, IL-6, and IL-8) from mast cells stimulated with IgE, likely due to inhibition of NF-kB and p38 mitogen-activated protein kinase (p38 MAPK). Thus, quercetin demonstrates the potential to modulate the early and late phases of asthma[5].

III. ***ASYSTASIA GANGETICA*** (Acanthaceae)

It is commonly known as the Chinese violet, coromandel, or creeping foxglove. In South Africa, this plant may simply be called *Asystasia*.It is evaluated hexane, ethyl acetate, and methanol extracts of the leaves of *A. gangetica* for antiasthmatic activity. The leaf of *Asystasia gangetica* T. Adams (Acanthaceae) is used in many parts of Nigeria for the management of asthma. This study was aimed at investigating the anti-asthmatic property of hexane, ethyl acetate, and methanol extracts of the leaves of *Asystasia gangetica*, obtained by successive soxhlet extraction The extracts relaxed histamine-precontracted tracheal strips in the following degree of potency— ethylacetate extract>hexane extract=methanol extract[6]. The extracts also exhibited anti-inflammatory activity in the order of magnitude methanol extract>hexane extract>ethylacetate extract. phytochemical screening showed the presence of carbohydrates, proteins, alkaloids, tannins, steroidal aglycones saponins, flavonoids, reducing sugars, and triterpenoids, with the methanol extract having the highest number of constituents.

IV. ***ACHYRANTHES ASPERA*** (Amaranthaceae)

Achyranthes aspera is an important medicinal herb found as a weed throughout India. Though almost all of its parts are used in traditional systems of medicines, seeds, roots, and shoots are the most important parts which are used medicinally. Alcoholic extract of the roots of *Achyranthes aspera* was found to exhibit anti-inflammatory activity[7].

V. ***SOLANUM XANTHOCARPUM*** (Solanaceae)

Many studies on the clinical efficacy of *Solanum xanthocarpum* and *Solanum trilobatum* in bronchial asthma proved the significant use of herbs in treatment of asthma. *Solanum xanthocarpum* extract on some of the parameters like smooth muscle relaxation, and antagonism of asthma mediators such as histamine, eosinophils, and protection against mast cell degranulation which seemed to be prominent in the pathophysiology of asthma. *Solanum xanthocarpum* has shown significant antihistaminic activity in histamine-induced contraction

in goat tracheal chain preparation. Thus, the significant inhibition of histamine-induced contractions produced by ethanol extract of *Solanum xanthocarpum* flower on isolated goat tracheal chain preparation indicates that the *Solanum xanthocarpum* flower has antihistaminic (H1- receptor antagonist) action[8].

Solanim xanthocarpum and *Solanum trilobatum* are widely used in the siddha system to cure respiratory disease. Ethanolic extract of *S. xanthocarpum* used to study the anti-asthmatic activity by using the acetylcholine and histamine-induced constriction of guine pig respiratory track and paw oedemas induced by carrageenan, dextran, and histamine in rat They have a crucial role in killing parasites that have large size and thus are unable to phagocytose. They take part in allergic reactions associated with asthma and allergy along with basophils and mast cells.

VI. ***TYLOPHORA INDICA*** (Asclepiadoideae)

Tylophora is a perennial climbing plant and has been used in the Ayurvedic system of medicine. The leaves of the plant have been extensively used in the treatment of various inflammatory and allergic disorders like bronchial asthma, bronchitis, and whooping cough[9]. It has been used traditionally as a remedy for various anti-inflammatory activities against asthma, bronchitis, bronchial asthma, hay fever, and rheumatism. The major alkaloid tylophorine is conceivable to account for the therapeutic efficacies. Anti-inflammatory activity of phenanthroindolizidine alkaloid was examined in an in vitro system mimicking acute inflammation by studying the suppression of lipopolysaccharide (LPS)/interferon (IFN) induced nitric oxide production in RAW264.7 cells. Two of the phenanthroindolizidine alkaloids, tylophorine and ficuseptine-A, exhibited potent suppression of nitric oxide production and did not show significant cytotoxicity to the LPS/IFN stimulated RAW264.7 cells[10].

VII. ***BOSWELLIA SERRATA*** (Burseraceae)

Boswellia serrata is a plant that produces Indian frankincense. It is also known as Indian olibanum Salai guggul, and Sallaki in Sanskrit. The plant is native to much of India and the Punjab region that extends into Pakistan[11].

The mechanisms of action of antiinflammatory herbs and dietary supplements (DSs) have extensively been investigated. Some have a similar action to NSAIDs, that is, they inhibit

inflammatory pathways, whereas others mainly enhance the anti-inflammatory and antinociceptive effects of NSAIDs. The most widely explored supplements are those containing *Boswellia serrata* and *Curcuma longa*. *B. serrata* (Salai/Salai guggul) is a medium-sized tree of the Burseraceae family (genus *Boswellia*) growing in dry mountain areas in India, Northern Africa, and the Middle East, where its resin has been burnt as incense in religious and cultural ceremonies (frankincense) and used to treat a variety of inflammatory diseases since time immemorial (Khan & Abourashed, n.d.). It contains monoterpenes, diterpenes, triterpenes, tetracyclic triterpenic acid, and four major pentacyclic triterpenic acids β-boswellic acid, acetyl-β-boswellic acid, 11-keto-β- boswellic acid, and acetyl-11-keto-β-boswellic acid (AKBA) which participate in proinflammatory enzyme regulation. AKBA has the stronger anti-inflammatory action and inhibits 5-LO activity through a dual mechanism, where direct interaction with the enzyme is combined with regulation of the proteins that activate it[12]. 5-LO also generates inflammatory leukotrienes, which cause inflammation by promoting free radical damage, calcium dislocation, cell adhesion, and migration of inflammation-producing cells to the inflamed body area. AKBA reduces 5-LO activity and its proinflammatory and hyperalgesic effects. Singh and Atal have reported that it induced 25–46% inhibition of paw edema in rats and mice. Pure AKBA from *B. serrata* extract has demonstrated anti-inflammatory properties in human peripheral blood mononuclear cells and mouse macrophages via inhibition of tumor necrosis factor (TNF)-α, IL-1β, nitric oxide, and mitogen-activated protein kinase production[13]. The finding is interesting since this action would allow reducing the therapeutic doses of NSAIDs, hence their adverse effects. In a recent study of patients with knee arthritis, Vishal, Mishra, and Raychaudhuri showed that AKBA reduces pain and improves knee function. AKBA may thus provide an interesting alternative for patients with poor tolerance to NSAIDs. Also, whereas NSAIDs severely impair glycosaminoglycan (GAG) synthesis, accelerating joint damage in arthritis patients, AKBA significantly reduces their degradation[13].It is widely accepted that T cells play an important role in the injurious lung immune responses associated with asthma. CD4+. The cells can be divided into Th1 and Th2 groups functionally based on the various kinds of cytokine they produce. The different patterns of T cell differentiation generate the different inflammatory effectors, and those inflammatory effectors are correlated with the extent and type of damage observed in the airway. Under normal physiologic conditions, the ratio of Th1 to Th2 cells maintains a suitable level. Once the balance between Th1 and Th2 is broken, diseases will occur[14]. The two major Th-specific transcription factors, Tbet and GATA-3, regulating the expression of cytokine genes

are characteristics of Th1 or Th2, and play crucial roles in Th cell differentiation. Th2 cell differentiation is induced by Interleukin 4 (IL-4). Binding of IL-4 to its receptor leads to phosphorylation of signal transducer and activator of transcription protein 6 (STAT6), a Th2-cell transcription factor, through the Jak/STAT cascade. The phosphorylated STAT6 forms a homodimer and translocates into the nucleus where it binds to specific DNA sequences and activates transcription of cytokine responsive genes especially GATA3, which is the master regulator of Th2 cell differentiation. GATA3 activates the transcription of IL- 5 and IL-13 genes by directly binding to their promoters. This transcription factor is also involved in the remodeling of chromatin structure and the opening of IL-4 locus[15].

VIII.***CASSIA SOPHERA***(Fabaceae)

Cassia sophera is used traditionally for the treatment of asthma and bronchitis. Chloroform, ethyl acetate and ethanol fractions isolated from the ethanol extract of leaves of C. *Cassia sophera* have both peripheral and central analgesic properties. Its Peripheral analgesic activity was deduced from its inhibitory effect on chemical Induced nociceptive stimuli. The acetic acid-induced abdominal contractions Elucidate peripheral activity, while formalin test investigates both[16]. Acetic acid causes an Increase in prostaglandins such as PGE2 and PGF2, serotonin and histamine in the Peritoneal fluid which brings about characteristic writhing in mice. Drugs that primarily action the central nervous system inhibit both phases equally while peripherally acting drugs inhibit the last phase. It is used in local traditional medicine for asthma and bronchitis. Various Phytochemical analysis demonstrated the presence of flavonoids and anthraquinone glycosides. The antiasthmatic activity of different extracts of cassia has been proven. Histamine induced bronchoconstriction, and eosinophilia and other such tests have been performed. *C. sophera* significantly protected the bronchoconstriction in tested animals against histamine-induced bronchospasm. The parent extract, ethyl acetate, chloroform, and ethanol fractions reduced leukocyte count and eosinophil count .there was a significant decrease in oedema and anaphylaxis and can be concluded that *C. sophera* possesses significant antiasthmatic activity[17].

IX. ***DATURA STRAMONIUM*** *(Solanaceae)*

Datura is a genus of nine species of poisonous Vespertine flowering plants belonging to the family Solanaceae. They are commonly known as daturas, but also known as devil's trumpets. The alkaloids found in *D. stramonium*, are organic esters used clinically as

anticholinergic agents. *D. stramonium* in asthma treatment and possible effects on prenatal development were studied. Exposure of the foetus to *D. stramonium* when a mother uses it for asthma will cause a continuous release of acetylcholine, resulting in the desensitization of nicotinic receptors, this could ultimately result in permanent damage to the foetus[18].

X. ***ATROPA BELLADONNA*** (*Solanaceae*)

Atropa belladonna is a medicinal plant and main commercial source of tropane alkaloids including scopolamine and hyoscyamine, which are anticholinergic drugs widely used clinically. It has been found that belladonna alkaloids are competitive inhibitors of the muscarinic actions of acetylcholine, acting at receptors located in exocrine glands, smooth and cardiac muscle, and intramural neurons. The belladonna constituent scopolamine exerts greater effects on the CNS, eye, and secretory glands than the constituents atropine and hyoscyamine. Atropine exerts more activity on the heart, intestine, and bronchial muscle, and exhibits a more prolonged duration of action compared to scopolamine. Hyoscyamine exerts similar actions to atropine but has more potent central and peripheral nervous system effects[19].*Atropa belladonna* dilates respiratory tracts and eases the breathing process. It helps in asthma by reducing chest congestion and wheezing. *Atropa belladonna* contains alkaloids that reduce excess mucus production. It further reduces inflammation and suppresses the formation of inflammatory mediators that otherwise irritate the respiratory system. Besides this, *Atropa belladonna* decreases sputum and helps in clearing lung congestion. Furthermore, its antibacterial property helps to get rid of bacteria that get stuck in the mucus[20].

Atropa belladonna is beneficial in a cough that occurs due to laryngeal irritation. However, it may not alone beneficial in spasmodic cough. Other remedies also require curing this type of cough.

Nevertheless, it is beneficial in cough associated with congestion and throat irritation. It shortens the duration of whooping cough attacks and reduces the severity of the cough. It is more beneficial when irritation of nerves or tubular musculature is associated with cough.

CONCLUSION

Herbalism is the study of botany and the use of medicinal plants. Plants have been the basis for medical treatments through much of human history, and such traditional medicine is still

widely practiced today. Modern medicine makes use of many plant-derived compounds as the basis for evidence-based pharmaceutical drugs. Although herbalism may apply modern standards of effectiveness testing to herbs and medicines derived from natural sources, few high- quality clinical trials and standards for purity or dosage exist. The scope of herbal medicine is sometimes extended to include fungal and bee products, as well as minerals, shells, and certain animal parts.

Those using herbal medicines should be assured that the products they are buying are safe and contain what they are supposed to, whether this is a particular herb or a particular amount of a specific herbal component. Consumers should also be given science-based information on dosage, contraindications, and efficacy. To achieve this, global harmonization of legislation is needed to guide the responsible production and marketing of herbal medicines. If sufficient scientific evidence of benefit is available for an herb, then such legislation should allow for this to be used appropriately to promote the use of that herb so that these benefits can be realized for the promotion of public health and the treatment of disease.

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