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Review Article

Medicinal Plants with Therapeutic Potential in Bronchial Asthma: An Overview

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Abstract:
Bronchial asthma is a respiratory disease with complex etiology involving airway inflammation, airway hyper responsiveness, and airflow restriction and clinically manifesting as wheezing and respiratory distress. Medical management comprises of supportive therapy and aggressive pharmacotherapy with anti-inflammatory agents and bronchodilators given by both inhalation and systemic routes. Such treatment is commonly associated with safety concerns, loss of efficacy and cost issues over a long term – all of which influence treatment compliance. There is thus an unmet need to device effective alternative/complimentary forms of therapy for ensure better quality of life for asthma patients. Herbal drugs primarily derived from botanical sources. Can form a viable alternative for asthma by virtue of their multi-targeted approach to therapy. Many such medicinal plants have been documented in Indian traditional systems of medicine with well proven beneficial effects on different components of the asthma disease biology. Validation of these traditionally known effects by modern scientific methodology is one of the national initiatives for promoting interactions between traditional and modern medicine and developing and integrated approach for rational treatment of intractable disease states. The present review summarizes some of the commonly used medicinal plants for bronchial asthma and presents a comprehensive compilation of the existing research data.

Keywords: Bronchial asthma, medicinal plants, traditional medicine**,** integration of traditional and modern concepts, rational therapeutics.

Introduction

Respiratory disorders are one of the leading causes of mortality and morbidity affecting people of all ages and constitute a major global health problem. Anatomically, the parts of the respiratory tract involved include the alveoli, bronchi, bronchioles, pleura, pleural cavity, trachea and the nerves and muscles of breathing. There are three main types of respiratory disease: airway diseases, lung tissue diseases and lung circulation diseases.

Airway diseases affect the bronchi/bronchioles that carry oxygen and other gases into and out of the lungs. Such airway diseases usually result in narrowing or blocking of the passageways. Lung tissue diseases affect the structure of lung tissue and result in inflammation and scarring or of the lung tissue, which also impacts respiration. Lung circulation diseases occur when the pulmonary blood vessels are involved and may result in inflammation, elevated pressure, and embolism. Lung disorders can also be etiologically traumatic (lung injury), allergic/inflammatory (asthma, COPD), fibrotic (Idiopathic pulmonary fibrosis), infectious (bacterial/viral/fungal, pleural effusion) and neoplastic (lung cancer). More serious or life-threatening respiratory disorders include bacterial pneumonia, lung cancer and pulmonary embolism. Other disorders include bronchial asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea syndrome, pulmonary hypertension and tuberculosis. Some lung diseases may result in respiratory failure. Lung diseases may also result from primary cardiovascular pathophysiology and vice versa.

In addition, allergens, indoor air pollution, outdoor air pollution and tobacco smoking are common risk factors for respiratory disorders [1]. Bronchial asthma is a heterogeneous disorder characterized by chronic airway inflammation and bronchial hyper-responsiveness along with reversible airway obstruction. It is diagnosed by the history of

respiratory symptoms like wheezing, shortness of breath, cough, chest tightness that varies over intensity and in time, accompanied with inconsistent expiratory airflow obstructions. Variations in expiratory airflow obstructions are triggered by different stimuli, including allergen exposure, exercise, viral-infection (cold) and respiratory airflow irritants like changes in weather, smoke and vehicle exhaust fumes. The features mentioned above for asthma generally continue even when lung function is normal or symptoms are absent, but may be controlled with treatment. The overall worldwide prevalence of bronchial asthma is approximately 4.5 percent. About 334 million patients have been affected globally with asthma across all age groups. The disease prevalence of asthma has increased with time and an approximately 100 million more people globally are at a risk to develop asthma by the year 2025 (GINA 2018) [2]. Airway hyper-responsiveness is the main distinctive feature of bronchial asthma. Within atopic individuals, specific antigen re-exposure causes an instant early-phase response. Persistent inflammation in asthma may lead to structural changes in airway lumen and other components of the airway, known as airway remodeling. Changes in airway remodeling which consists of sub-epithelial fibrosis, airway wall thickening, and hyperplasia of myofibroblasts, goblet cell and smooth muscle [3]. This is followed by late phase response after 6-12 hours, consisting of mast cell degranulation mediated by IgE and production of inflammatory mediators like histamine is primarily linked with recruitment of eosinophils. Other inflammatory cells such as neutrophils, macrophages and T-cells are also infiltrated through late-phase reactions. Activation of mast cell, macrophages, eosinophil and neutrophil leads to release of pro-inflammatory cytokine TNF-α and other related cytokines, viz Th2 specific IL-4 and enhanced IgE reaginic antibody production. Inflammatory cells also produce reactive oxygen species (ROS) which lead to oxidative stress which further contribute to the pathophysiology of asthma [1,4,5].

Chronic asthma poses a huge challenge for developing interventions that exhibit a broad range of pharmacological actions to counter the complex pathophysiological changes seen in asthma. Conventional pharmacotherapy of asthma involves a wide array of drugs which affect different aspects disease biology. The current strategies of asthma pharmacotherapy are targeted towards (a) inhibiting airway inflammation with anti-inflammatory agents like inhaled and systemic corticosteroids eg. fluticasone, beclomethasone (inhalation), prednisolone (oral), methyl prednisolone, hydrocortisone, (inhaled/ intra venous) and (b) reversing bronchoconstriction with bronchodilator agents (β_2-agonists) eg. Salbutamol, salmeterol, and formoterol [6]. Corticosteroids (inhaled and systemic), inhaled bronchodilators (β_2-agonists, anticholinergic, and methylxanthines), leukotriene antagonists, mast cell stabilizers and anti-IgE antibodies (Omalizumab) are the commonly used drugs for asthma [7]. The standard therapy of asthma controls the symptoms in most patients, but chronic persistent asthma still poses a therapeutic challenge. In most asthmatic patients, relapse occurred after withdrawal of therapy. Inhaled corticosteroids are usually efficacious and safe but have a few unwanted/adverse effects. Long term use of inhaled/systemic corticocosteroids has safety and compliance concerns because of both systemic and local side effects such as oropharyngeal cadidiasis, voice hoarseness (Inhalation) and, osteoporosis, hyperglycemia, immune suppression causing increased susceptibility to infections, cataract in elderly patients, and behavioral changes [8]. Long term use of beta-2 agonists is also associated with effects like lowered bronchodilator response due to beta adrenoceptor receptor subsensitivity/down regulation. Airway remodelingin asthma is another area of concern as it may result in reduced or ineffective responses to anti-asthma agents. Taken together, all these issues result in increased morbidity and mortality in bronchial asthma patients. Thus, there is a constant search for viable alternatives/adjuncts for pharmacotherapy to improve the quality of therapy and life in this obstructive airway disease.

Indian traditional systems of medicine have well documented efficacy for the treatment of several chronic diseases including respiratory disorders. Medicinal plants and plant derived products have been the source of many important drugs in modern medicine. Such phytopharmaceuticals also play a key role as therapeutic agents in Indian traditional medicinal systems. In respiratory disorders, validation studies of various medicinal plants species-alone and in combination, have been shown to be effective and safe. As a result, focus on herbal drug research has been intensified globally and the immense potential of such herbal agents has been recognized [10,11]. A large archive of herbal preparations exists in traditional medicine including folklore medicine, for the treatment of asthma. The complementary therapeutic strategies have been regarded as being safer (and effective), and used as an adjunct therapy for various diseases [12]. Such natural products derived from botanical sources have been generally accepted in most of the countries and referred as Complementary and Alternative Medicine (CAM).The World Health Organization (WHO) also promotes and recommends herbal drugs and encourages the use of traditional herbal drugs in National Health Care Programmes because of their low cost, easy availability, efficacy and safety. Anti-inflammatory

agents and bronchodilators are central to the pharmacotherapy of bronchial asthma. Inhaled and systemic corticosteroids have been used as the main therapeutic agents along with beta adrenergic agonists. However, several issues are emerging regarding their efficacy on a long term basis. Further, both local and systemic adverse effects may result from prolonged use of such agents which may affect treatment compliance [13]. In view of these and the unfavorable pharmacoeconomic viability of such treatment modalities, there has always an unmet need for alternative safer and more viable therapeutic strategies for treating bronchial asthma.

In Ayurveda, bronchial asthma is referred to as Tamaka Swasa and advocates several modalities of it`s treatment. Among all the treatment modalities, polyherbal combinations are said to be well-accepted, safe and effective in asthma. The reason for the therapeutic efficacy of herbal combinations in asthma is due to the proposed holistic and multi-targeted approach and blockade of multiple complex and interdependent cellular and mediator networks/pathways which are involved in the inflammatory process of asthma. This is in contrast to conventional drug therapy, which is aimed at blocking one or other mediator/mechanisms alone, without much impact on the overall disease process [14].

Medicinal Plants in Bronchial Asthma

Adhatoda vasica

Adhatoda vasica belongs to the family Acanthaceae. It is an evergreen shrub growing throughout the states of Punjab, Bengal, Manipur and Kerala in the Indian subcontinent, at an altitude of approx. 135m. The plant is also seen distributed in Sri Lanka, Upper and Lower Myanmar, Southern China, Laos, and the Malay Peninsular and Indonesian Archipelago. The plant is commonly known as “Vasaka” in Sanskrit, “Arusha” in Hindi [15].Adhatoda vasica is a valuable plant and it has been proven for its medicinal properties against a broad array of diseases specially, for the respiratory ailments like dry cough, asthma, bronchitis, common cold, smoker’s cough etc. It has also been reported to be abortifacient, hepatoprotective, sedative, antiulcer, antispasmodic, anti-allergic, anti-inflammatory, anti-tubercular, and anti-helminthic [16].

Antioxidant properties of this plant and its active ingredients/components are suggested to be its main characteristic, responsible for the physiological effects [17]. Several studies have been carried out to investigate the antioxidant and anti-inflammatory activity and other therapeutic potentials of different extracts of Adhatoda vasica. Kumar et al., 2005 investigated the hematological changes in the blood of Swiss albino mice after the treating them with ethanolic extract of AV (800mg/kg body weight, 6-30 d post irradiation intervals [18]. Mulla et al..2006 have worked upon the antioxidant and anti-inflammatory activity of ethanolic extract of Adhatoda vasica against carrageenan and formalin-induced inflammation in albino rats. They showed that ethanolic extract of Adhatoda vasica possess antioxidant and anti-inflammatory activities and suggested that it may be due to the presence of flavonoids and other polyphenolic moieties in it, which supports the use of this plant in traditional medicine [19]. Srinivasrao et al., (2006) have worked upon the antioxidant and anti-inflammatory activity of vasicine against ovalbumin and aluminum hydroxide induced lung damage in rats. They demonstrated that vasicine treatment increased the activity of various anti-oxidants like superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase GPX), and reduced glutathione (GSH) (20). Gupta et al., (1977) had suggested that, the bronchodilatory activity of vasicine works through respiratory sensors and peripheral receptors [21]. Further, Dhuley (1999), reported that vasicine: 2, 4-diethoxy-6, 7, 8, 9, 10, 12-hexahydroazepino [2, 1-b] Synopsis 14 quinazolin-12-on exhibited marked bronchodilator activity on contracted trachea or constricted tracheobronchial tre [22]. Vasicine, an alkaloid, is one of the major components of the plant and is responsible for most of its antioxidant, anti-inflammatory, and bronchodilatory activities. The bronchodilatory and antitussive effects pure vasicine and its derivatives were also investigated, and one of those derivatives is bisolvon/ bromhexine (N-cyclo-N-methyl-(2-amino-3, 5-dibromo-benzyl) amine hydrochloride) has been reported to possess mucus liquefying/ expectorant activity [23,24]. Various other experimental evidences have also reported the antioxidant and anti-inflammatory properties of vasicine. It has been postulated by us that the plant, Adhatoda vasica, and the active molecule, vasicine, may be useful in the conditions where tobacco smoke induced initiation and/or aggravation of respiratory pathophysiology as well. However, no scientific evidence exists till date analyzing this plant for its protective potential in tobacco smoke induced toxicological manifestations in the human lung model system and the possible mechanisms [25].

Intravenous administration of this drug showed clearing of the airways by decreasing mucus secretion and opening of air passages. In vivo studies have shown its inhibitory action against antigen-induced mast cell degranulation and histamine release as well as bronchodilatory activity [26]. In vitro studies have shown Adhatoda vasica as an antioxidant through its effective induction of Glutathione-S-Transferase and DTdiaphorase in the lungs. Pre-exposure of Swiss albino mice to Adhatoda vasica followed by

cadmium chloride treatment showed decreased lipid peroxidation and xanthine oxidase levels. It also showed an increase in glutathione levels, thus proving its antioxidant potential [27]. The active compounds vasicine and vasicinone at a dose of 2.5-10 mg/kg caused vasoconstriction in histamine-induced anaesthesized guinea pigs. However, several other scientists have reported vasicine to be bronchodilatory in vitro and, bronchoconstrictive in vivo [28].

Glycyrrhiza glabra

Glycyrrhiza glabra Linn (Yashtimadhu in Hindi; Liquorice in English) (Fam. Leguminosae) is derived from the ancient Greek term glykos, meaning sweet, and rhiza, meaning root [29]. The plant has glycyrrhizin, glycyrrhizic acid, glycyrrhetinic acid, asparagine, sugars, resin and starch as main constituents. Liquorice has been known in pharmacy for thousands of years. In old Chinese pharmacy, it was considered to belong to the drug of first class and having rejuvenating properties on prolonged use. It was used to allay thirst, feverishness, pain, cough and distress of breathing. Glycyrrhiza plays an important part in Ayurveda and is one of the principle drugs of the 'Susruta'. In ancient Egypt, Greece and Rome, glycyrrhiza was also frequently used, and liquorice is reffered to by Theophrastus [30]. This plant continues to be used as a pharmacological agent as well as an ingredient in tobacco and confectionery throughout India. Studies over the past 50 years have yielded information which has prompted new interest in the pharmacological and physiological effects of this plant. The bronchorelaxant effect of Glycyrrhiza glabra was studied in a clinical trial (54 patients) in comparison with Boswellia carterii (Olibanum) and prednisolone (18 patients each group) for 21 days. Pulmonary function tests and serumelectrolytes viz. calcium, magnesium, potassium and selenium were done before and after the study. The results showed that the tested plants had significant elevation in the values of forced expiratory volume in first second (FEV1%) as (72.45±5.83 vs 61.33±6.04 and 81.10±11.07 vs 62.30±7.22) for olibanum and licorice respectively.

Also, elevation in the values of forced volume capacity (FVC) with marked reduction in asthmatic attacks as (2.63±0.82 vs 0.72±0.16, 3.60±0.02 vs 1.08±0.08, and 2.25±0.16 vs 1.05± 0.15) for olibanum, licorice and prednisolone respectively, with better symptomatic improvement in licorice group as compared to olibanum. Glycyrrhiza glabra significantly elevated Mg from 0.66±0.17 to 1.02±0.10, Se from 28.19±3.72 to 51.70±8.63, Ca from 1.90±0.06 2 to .30±0.08 and K from 3.60±0.03 to 4.10±0.12 [31]. Glycyrrhiza decreased irritations in the throat and produced expectorant effects. It was assumed that Glycyrrhiza was able to stimulate tracheal mucus secretions and produce demulcent and expectorant effects. The root of this plant has been used for cough, colds, asthma, and COPD [32]. Glycyrrhizin (the active ingredient) alleviated allergic asthma in an ovalbumin-induced experimental mouse model. In BAL fluid, the IFNγ level was increased and the IL-4 and IL-5 levels and eosinophil count were decreased. These results indicated that glycyrrhizin interfered with the production of IgE by decreasing the IgE-stimulating cytokines [33]. It also attenuated the carrageenan-induced lung inflammation and mucous production in mice [34].

In an OVA-induced murine asthma model, oral glycyrrhizin alleviated airway constriction and hyper-reactivity and pulmonary inflammation [35]. The liquorice powder and extract were found to be effective in treatment of sore throat, cough and bronchial catarrh. The specific mechanism of action is not known. Liquorice has been shown to work as efficiently as codeine in sore throat. It decreases irritation and produces expectorant effects. Carbenoxolone (a semi synthetic compound derived from Glycyrrhiza) stimulates gastric mucus secretion, and is used as an anti-ulcer agent. Likewise, liquorice extract may also be able to stimulate tracheal mucus secretions producing demulcent and expectorant effects [36]. Ethanolic extract of G. glabra was found to be responsible for inhibition of 35.62% SO2 gas induced cough in experimental animals (mice).

The extract of the powdered drug in water was found to be effective in the treatment of sore throat cough bronchial catarrh. It is anti-tussive and expectorant loosening tracheal mucus secretion, and the demulcent action is attributed to glycyrrhizin [37,38]. Isoliquiriti genin, a flavonoid isolated from the G. glabra roots, relaxed the tracheal smooth muscle of guinea pigs in vitro and in vivo [39]. The effects of glycyrrhetinic acid and liquiritigenin (a flavonoid of licorice root) have been tested on asthma both in vivo and in vitro. In vitro, glycyrrhetinic acid and liquiritigenin inhibit β-hexosaminidase release from RBL-2H3 cells induced by IgE/DNP, and from rat peritoneal mast cells challenged with C48/80. In vivo, they suppressed C48/80-induced passive cutaneous anaphylactic reactions in mice. In an OVA-induced murine asthma model, glycyrrhetinic acid, but not liquiritigenin, reduced the level of IgE in serum [40].

Flavonoids extracted from licorice root quenched LPS-induced pulmonary inflammation by inhibiting the recruitment of neutrophils, macrophages, and lymphocytes in BALF, and by suppressing the mRNA expression of TNF-α and IL-1β in LPS-challenged lung tissue in mice [41].

Hyssopus officinalis

The medicinal plant Hyssopus officinalis, commonly known as Hyssop (in English), Jufa (in Sanskrit), Zufah-yabis (in Hindi), Zufah (in Urdu) and belonging to family Lamiaceae, is a very important culinary, medicinal and perennial plant wildly cultivated in Asia, Europe and temperate regions of America The main constituents in H. officinalis are some polyphenolic compounds principally including flavonoids luteolin, diosmin, quercetin, apigenin and their glucosides along with some phenolic acids [42].Total flavonoids and phenolic contents found to be highest in H. officinalis L. ssp. Angustifolius leaves aqueous extracts were 1.3% (gallic acid equivalent) and 4.7% respectively [43].

Hyssopus officinalis has been shown to relieve coughing and asthma. Previous studies have shown that Hyssopus officinalis L. plays an anti-inflammatory role by regulating the secretion of IL-4, IL-17 and IFN-γ, as well as regulating the imbalance between Th1/Th2 cytokines. H. officinalis L. affects numerous cytokines in mice with induced asthma including IL-4, IL-6 and IL-17 and IFN-γ.The eosinophil ratio in bronchoalveolar lavage fluid and the levels of serum immunoglobulins IgG and IgE in the H. officinalis treatment group were decreased compared to ovalbumin and dexamethasone-treated group (chronic asthmatic) observed by enzyme-linked immunosorbent assay (ELISA). H. officinalis also affected the immune regulation [44].The expression of both TIMP-1 and MMP-9 decreased after being treated with standard dexamethasone and H. officinalis accompanied by the attenuations of pathological changes including smooth muscle proliferation, mucus secretion and collagen deposition - supporting its airway remodeling inhibition by correcting the imbalance of MMP-9/TIMP-1 ratio. H. officinalis could affect the levels of some cytokines (such as IL-17, IL-6, IL-4 and IFNγ) in asthmatic mice and could also influence the expression of some cytokines in the asthmatic mice [45].

Piper longum and Piper nigrum

Pippali (Piper longum Linn.) is one of the prime Rasayana (rejuvenator) drugs in Ayurveda and is widely used to treat various diseases especially for the treatment of respiratory disorders. The root of this plant is known as Pippali Mula in Ayurveda and its fruits (Spike) are mainly used for Rasayana purpose. Various biological activities like immunostimulatory, anti-ulcer, anti-amebic, anti-oxidant, hepatoprotective and anti-inflammatory activities were reported on the fruit of this plant [46]. Pippalı (Piper longum Linn.) fruit contains a number of constituents, including volatile oil, alkaloids, isobutylamides, lignans and esters. Piperine, which is the prime constituent of fruit, is reported to be having significant anti-inflammatory activity [47]. The fruit effectively reduced passive cutaneous anaphylaxis in rats and protected guinea pigs against antigen induced bronchospasm. A 30% protection of mast cell degranulation was observed in an in-vitro study [48]. Aller-7 a combination of seven medicinal plants including long pepper is used for allergic rhinitis, as antihistaminic and antispasmodic [49]. The fruits and roots of this plant have shown immunomodulatory potential and used in the treatment of childhood asthma [50]. Piperine is a major alkaloid isolated from the P. longum fruits and has been reported to inhibit the release of Th-2-mediated cytokines, eosinophil infiltration, and airway hyper-responsiveness in an ovalbumin-induced asthma model [51].Piper nigrum (Piperaceae) is commonly used as a spice and traditional medicine in many countries. P. nigrum has been reported to have anti-oxidant, anti-bacterial, anti-tumor, anti-mutagenic, anti-diabetic, and anti-inflammatory properties. The oral administration (200 mg/kg) of P. nigrum ethanol extracts (PNE)reduced the accumulation of inflammatory cells (eosinophils, neutrophils) in BAL fluid and mast cells in lung tissue; regulated the balance of the cytokines production of Th1, Th2, Th17 and T-reg cells. Specifically, it inhibited the expressions of GATA3, IL-4, IL-6, IL-1β, RORγt, IL-17A, TNF-α and increased the secretions of IL-10, INF-γ in BAL flud and lung homogenates. Moreover, PNE suppressed the levels of total IgE, anti-OVA IgE, anti-OVA IgG_1 and histamine release in serum. The histological examination showed that the fibrosis and infiltration of inflammatory cells were also ameliorated in PNE treated mice. On the other hand, PNE inhibited the allergic responses via inactivation of rat peritoneal mast cell degranulation. These results suggest that PNE has therapeutic potential for treating allergic asthma through inhibiting Th2/Th17 responses and mast cells activation [52].A study investigated the effect of piperine on airway hyperresponsiveness, pulmonary eosinophilic infiltration, various immune cell phenotypes, Th2 cytokine production, immunoglobulin E and histamine production in a murine model of asthma. Asthma was induced in Balb/c mice by ovalbumin sensitization and inhalation. Piperine (2.25 and 4.5 mg/kg) was orally administered 5 times/week for 8 weeks. Piperine-treated groups had suppressed eosinophil infiltration, allergic airway inflammation and airway hyperresponsiveness, and these occurred by suppression of the production of interleukin-4, interleukin-5, immunoglobulin E and histamine. Moreover, polymerase chain reaction products for thymus and activation regulated chemokine from lung cell RNA preparations were decreased in the

piperine-treated group compared with control groups, although transforming growth factor-beta products were increased in the piperine-treated group. It was inferred that the therapeutic mechanism by which piperine effectively treats asthma is based on a reduction of Th2 cytokines (interleukin-4, interleukin-5), eosinophil infiltration, and by marked reduction of thymus and activation regulated chemokine, eotaxin-2 and interleukin-13 mRNA expression (especially transcription of NFkB dependent genes) in lung tissue [53].

Boswellia serrata

Boswellia serrata (Salai/Salai guggul) (Family: Burseraceae; Genus: Boswellia) is a moderate to large sized branching tree that grows in dry mountainous regions of India, Northern Africa and the Middle East [54]. Boswellia serrata is one of the ancient and most valued herbs in Ayurveda. "Gajabhakshya", a Sanskrit name used for Boswellia, suggests that elephants enjoy this herb as a part of their diet. This gummy resin is also mentioned in traditional Ayurvedic and Unani texts as an effective remedy for diarrhoea, dysentery, ringworm, boils, fevers (antipyretic), skin and blood diseases, cardiovascular diseases, mouth sores, bad throat, bronchitis, asthma, cough, vaginal discharges, hair-loss, jaundice, hemorrhoids, syphilitic diseases, irregular menses and stimulation of liver. It is also diaphoretic, astringent, diuretic and acts both as internal and external stimulant. Modern medicine and pharmacology strongly point out to its use as an anti-arthritic, anti-inflammatory, anti-athero sclerotic, analgesic and hepatoprotective [55, 56]. In vitro studies and animal models show that boswellic acids were found to inhibit the synthesis of pro-inflammatory enzyme, 5-lipoxygenase (5-LO) including 5-hydroxyeicosatetraenoic acid (5-HETE) and leukotriene B4 (LTB-4), which cause bronchoconstriction, chemotaxis, and increased vascular permeability [57, 58]. Singh et al studied the anti-inflammatory activity of mixture of boswellic acids and observed 25-46% inhibition of paw oedema in rats and mice [59].B. serrata crude had inhibitory effect on phosphorylation of all the three mitogen activated protein kinases. The inhibitory effect MAPK suggests the regulatory role of crude on multiple targets when compared to pure. B. serrata demonstrated a significant inhibition of JNK and p38. JNK is one of the major kinases responsible for IL-2 production. It has been shown that boswellic acids inhibit the production of pro-inflammatory cytokine TNF- TNFα, IL-2, IL-6, IL-12 by suppressing the activation of NF-kB [60]. Clinical study suggests that B. serrata has potential benefit for asthma patients. Effects of Boswellic acid on allergen-induced airway inflammation and immune response in acute experimental asthma have been studied and shown to markedly reduced Th2 cytokines, OVA specific IgE, suppress airway inflammatory cells infiltration induced by allergens, resulting in decreased number of eosinophils and total inflammatory cells in BAL fluid. Lung histology also corroborated the boswellic acid effects on airway inflammation [61]. Extract of B. Serrata has been reported to inhibit hypersensivity reactions by regulating both cellular and humoural immune system. They decrease primary antibody synthesis, inhibit polymorphonuclear leukocyte proliferation and infiltration, enhance the phagocytotic function of macrophages and suppress the inflammation process, one of the critical features in asthma [62].

Curcuma longa

Curcuma longa (Turmeric, Haridra/haldi) is a rhizomatous herbaceous perennial plant belonging to the ginger family Zingiberaceae, and bears funnel-shaped yellow flowers which grow to a height of three to five feet. It is cultivated extensively in Asia mostly in India, China and other countries with a tropical climate. As many as 133 species of Curcuma have been identified worldwide. Most of them have common local names and are used for various medicinal formulations. The rhizome, from which the turmeric is derived, is tuberous, with a rough and segmented skin. The rhizomes mature beneath the foliage in the ground and are yellowish brown with a dull orange interior. The use of turmeric dates back nearly 4000 years to the Vedic culture in India, where it was used as a culinary spice and had some religious significance. According to Sanskrit medical treatises and Ayurvedic and Unani systems, turmeric has a long history of medicinal use in South Asia. Susruta's Ayurvedic Compendium, dating back to 250 BC, recommends an ointment containing turmeric to relieve the effects of poisoned food. C. longais also mentioned in Ayurvedic medicine for its anti-asthmatic and anti-dyspnea effects. Different pharmacological effects such as anti-asthmatic, antioxidant and anti-inflammatory effects for this plant have been reported [63,64]. Various studies have established anti-inflammatory effect both in vitro and in vivo by inhibiting iNOS production and scavenging the free radicals, inhibiting the activation of NF-kB and activating protein (AP-1), and suppressing the production of pro-inflammatory cytokines [65].Studies have also demonstrated that curcumin decreases the level of iNOS-induced by IFN-γ in lung tissue and expression of cytokines such as IL-2,IL-5 and GM-GSF by acting as a histone deacetylases (HDAC) activator and also inhibits histamine release from mast cells. It has been proved that curcumin can also restore HDAC activity, thereby restoring corticosteroid susceptibility [66].Various studies

have demonstrated the efficacy of curcumin in animal models of asthma, but there are very few human trials which explored the efficacy of oral curcumin in asthma. Kobayashi et al., showed that curcumin when added to Dermatophagoides farineae (Der-f)-stimulated lymphocyte cell cultures from allergic asthmatics inhibited Der-f-induced lymphocyte proliferation and production of IL-2, IL-4, IL-5 and GM-CSF thereby proving that curcumin blocks the allergen- triggered release of inflammatory chemicals in white blood cells taken from asthma patients. It also demonstrated that curcumin may have potential effects on controlling allergic diseases through inhibiting the production of cytokines, eosinophil function and IgE synthesis [67]. Ram et al (2003) studied the effect of curcumin on airway hyperresponsiveness in sensitized guinea pigs and demonstrated by a constant volume body plethysmograph that curcumin significantly inhibited ovalbumin-induced airway constriction and airway hyperreactivity in guinea pigs [68]. Kohli et al.(2005) showed that curcumin in a dose of 200 mg/kg helps to prevent allergic airway inflammation by inhibiting the actions of an inflammatory protein called NF-κB [69]. Moon et al.(2008) investigated the anti-inflammatory effect of curcumin in a different model of ovalbumin induced murine asthma and found that pre-treatment with curcumin caused low levels of ovalbumin induced nitric oxide, IL-4, IL-5, IFN-γ and IgE antibodies [70]. Aggarwal et al.(2009) showed that curcumin significantly inhibited the activity of NF-κB, thus inhibiting the airway inflammation and cell infiltration in asthma. It also proved that curcumin decreases the expression and release of eotaxin, MCP-1 and MCP-3 from IL1-stimulated human airway smooth muscle cells [71]. In another study, the protective effects of curcumin alone and in combination with piperine were evaluated in mouse model of allergic asthma. Balb/c mice were sensitized on days 0, 7, and 14 and challenged from days 16-30 on alternate days with ovalbumin (OVA). Mice were pre-treated with curcumin (10 and 20 mg/kg) and piperine (5 mg/kg) alone and in combination via the intraperitoneal route on days 16-30. Blood, bronchoalveolar lavage fluid (BALF), and lungs were collected after mice were sacrificed on day 31st. Mice immunized with OVA have shown significant increase in airway inflammation and oxidative stress as determined by oxidative stress markers. A significant suppression was observed with all the treatments, but intranasal curcumin treatment group has shown maximum suppression [72].

Albizia lebbeck

Albizia lebbeck (Sirish) plant belongs to leguminosae family. It is a large, erect, unarmed deciduous plant with compound leaves common all over India. Its Sanskrit name is Sirisa. Traditional Ayurveda texts describe its therapeutic use in eczema, leprosy, itching, cough, oedema, asthma, blood disorder, rhinitis and poisoning [73]. In Siddha system of medicine, the bark and the flowers of the plant are used to treat arthritis. Many Ayurvedic preparations contain Albizia lebbeck like Kada, Sirisatwakkvatha. The stem bark of this plant is used to treat diarrhea (Nadkarni, 1954), edema, poisoning, bronchitis and asthma [74]. It also possesses antiseptic, antibacterial, anti-allergic, anti-dysenteric and anti-dermatitis action [75].

Decoction of the leaves, flowers and barks have been found to be protective against bronchial asthma and other allergic disorders. Tripathi et al. (1979) studied the anti-asthmatic and anti-anaphylactic property of Albizia lebbeck and reported that the bark extract of A lebbeck protects the guinea pig against histamine and acetylcholine induced bronchospasm. Further, chronic treatment with bark decoction has been shown to provide protection in the sensitized guinea pigs against antigenic challenge. The levels of histamine were reduced and the plasma cortisol levels were raised in antigen challenged guinea pigs as well as in bronchial asthma patients [76]. The anti-inflammatory activities of Albizia lebbeck in acute and chronic animal model of inflammation using carageenan, dextran, cotton pellet and Freund's adjuvant induced rat models were also studied. The bark extract was obtained using petroleum ether, chloroform and ethanol and administered at concentration of 100, 200 and 400mg/kg.

The petroleum ether and ethanol extracts showed marked inhibition of paw edema induced by carrageenan, thus showing anti-inflammatory potency of the extract [77,78].There has also been a clinical study on 60 patients of bronchial asthma with the decoction of the plant in a dose of 25ml four times a day for a period of 3 weeks which showed varying degree of improvement in patients [79]. Furthermore, Albizialebbeck also showed antioxidant activity in experimental diabetic rats [80].In a recent study, the anti-inflammatory and immunomodulatory potentials of Albizialeb beck were evaluated in experimental model of bronchial asthma in rats. Wistar rats were immunised with ovalbumin (OVA) on day 0 and were challenged with 1% OVA aerosol for 20 minutes daily, from 15th to 22nd day to induce inflammatory model of bronchial asthma. Standardized aqueous extract of Albizia lebbeck (bark) was administered orally for 22 days at doses of 100, 200 and 400 mg/kg, in separate groups. Rats were anesthetized and blood and BAL fluid were collected and analyzed for markers of inflammation (inflammatory cell counts, TNF-α, IL-6) and immunomodulation (Ova

specific IgE, IL-4 and IFN-γ). The results showed that pre-treatment with Albizia lebbeck extract significantly attenuated the levels of eosinophils, neutrophils, OVA sp. IgE, TNF-α, IL-6, IL-4 whereas, elevated the levels of IFN-γ in both blood and BAL fluid- thus validating the anti-inflammatory and immunomodulatory effect of the extract. The study concluded that Albizia lebbeck has anti-inflammatory and immunomodulatory activity in the experimental model of asthma, as evident from the modulation of cellular and molecular markers of inflammation and immunity [81].

Solanum xanthocarpum

Solanum xanthocarpum (Kantakari) is an important medicinal herb in Ayurvedic medicinal system. Solanum xanthocarpum is commonly known as the Indian night shade or Yellow berried night shade (English) and Kantakari (Sanskrit). It is a bright green perennial herb which belongs to solanaceae family, found throughout India, mostly in dry places as a weed along roadsides and waste lands.

The botanical is used as anti-asthmatic, hypoglycaemic, anti-inflammatory, anti-tumor, anti-tussive, antipyretic, antispasmodic, antihistaminic and has cytotoxicity activity. Decoction of the plant is used in gonorrhea; paste of leaves is applied to relieve pains; seeds act as expectorant in cough and asthma; roots are expectorant and diuretic, useful in the treatment of catarrhal fever, coughs, asthma and chest pain [82].

It is widely used to treat respiratory disease in Ayurveda. It has various medicinal properties particularly in treatment of asthma, chronic cough and catarrhal fever. Vadenere et al. (2008) studied effects of 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 pathophysiology of asthma.

Further, they showed that ethanolic extract of Solanum xanthocarpum showed a significant antihistaminic activity in histamine induced contraction in goat tracheal chain preparation [83]. Thus, the significant inhibition of histamine induced contractions produced by ethanol extract of Solanum xanthocarpum flower on isolated goat tracheal chain preparation indicated that it had anti-histaminic (H1- receptor antagonist) action [84].

Solanum xanthocarpum is widely used by practitioners of the Siddha system of medicine in southern India to treat respiratory diseases. The powder of whole dried plant or a decoction is used for this purpose. Treatment with Solanum xanthocarpum improved the pulmonary functions to a significant level in patients suffering from mild to moderate asthma. Subjective relief from asthmatic symptoms was reported by the patients an hour after administration of Solanum xanthocarpum powder, and this effect lasted for about 6–8 hours. However, responses observed were apparently less when compared to that of the bronchodilator drug, salbutamol. A decrease in forced expiration volume (FEV1) and peak expiration flow rates (PEFR) are indicative of both large and small airway obstruction and muscle power [85]. The dose of Solanum xanthocarpum was well tolerated and no untoward effects were reported. It was suggested that relief from the symptoms of bronchial asthma produced by Solanum xanthocarpum may be due to: (a) a bronchodilator effect, (b) reduction in the bronchial mucosal edema, and/or (c) reduction in the secretions within the airway lumen.

In another recent study, the effects of standardized extracts of Solanum xanthocarpumon was assessed on airway inflammation and oxidative stress parameters in experimental model of asthma in rats. Wistar rats were immunized with ovalbumin (OVA) adsorbed on to aluminium hydroxide (i.p.) and were challenged with 1% OVA in saline aerosol from day 15 to 22. Standardized aqueous extracts of Solanum xanthocarpum (whole plant extract) were administered orally for 22 days in different treatment groups.

After 24h of last challenge, rats were anesthetized and blood and BAL fluid were collected, centrifuged and analysed for IgE levels, pro-inflammatory cytokines (TNF-α, IL-6), Th-2 type cytokine (IL-4) and IFN-γ, and oxidative stress parameters malondialdehyde (MDA) and reduced glutathione (GSH). The results showed that ovalbumin specific IgE levels were elevated in the immunized rats which were reduced by 37% and 20% respectively in blood and BAL fluid at the dose of 50 mg/kg of Solanum xanthocarpum extract as compared to control.

These results were comparable with the effects of the standard drug, prednisolone (10 mg/kg), which reduced IgE levels by 43% and 31% respectively in blood and BAL fluid, respectively. Similarly, TNF-α, IL-6 and IL-4 were attenuated maximum at dose 100 mg/kg as compared to control and IFN-γ was elevated maximum in both blood and BALF. The oxidative stress markers, i.e. MDA levels were also attenuated while GSH levels were elevated in rats treated with the plant extract at the dose of 100 mg/kg.

The results showed that aqueous extract of Solanum xanthocarpum has anti-inflammatory and immunomodulatory effects which is accompanied with reduction in oxidative stress. Thus, the results suggest that the beneficial effects of Solanum xanthocarpumin bronchial asthma could be due to

balancing influence on prooxidant-antioxidant status and reducing the airway inflammation [86].

Withania somnifera

Withania somnifera (Ashwagandha, Indian Ginseng, Dunal, Winter Cherry) belongs to the family solanaceae. It is a xerophytic plant, found in the drier parts of India, Sri Lanka, Afghanistan, Baluchistan and Sind and is distributed in the Mediterranean regions. It is found in high altitude ascending to 5,500 feet in the Himalayas. This shrub is common in Bombay and Western India, occasionally within Bengal [87, 88].In Unani system of medicine; roots of Withaniasomnifera commonly known as Asgand are used for the medicinal properties. However, leaves of the plant are also reported to be used medicinally. The fresh roots are collected during January to March and dried under shade for several days. The drug retains its therapeutic efficacy for about 2 years, and later, is prone to decomposition and loss of therapeutic potential. So, the fresh dried roots are preferred for medicinal uses. Two varieties of Asgand have been mentioned in classical Unani literatue: Asgand Nagori and Asgand Dakani. Asgand Nagori is preferred for its more potential medicinal properties [89,90].

In Ayurveda, Ashwagandha (Withania somnifera) (WS), a "Rasayana" drug, is recommended for balavardhan and mamsavardhan. The root and leaf extracts are extensively used for a variety of conditions as an adaptogen (anti-stress), immunomodulator, aphrodisiac, etc. The pharmacological activity of the roots is attributed to the presence of several alkaloids (glycowithanolides). The total extract (70% alcoholic) of the roots possesses the same properties as the total alkaloids, but is nearly half as potent [91]. Anti-inflammatory activity of a potent withanolide, Withaferin A, exhibits fairly potent anti-arthritic and anti-inflammatory activities. Anti-inflammatory activity has been attributed to biologically active steroids, of which Withaferin A is a major component. It is as effective as hydrocortisone sodium succinate dose for dose [92].It was found to suppress effectively arthritic syndrome without any toxic effect. Unlike hydrocortisone-treated animals which lost weight, the animals treated with Withaferin A showed gain in weight in arthritic syndrome. It is interesting that Withaferin A seems to be more potent than hydrocortisone in adjuvant-induced arthritis in rats, a close experimental approximation to human rheumatoid arthritis. In its oedema inhibiting activity, the compound gave a good doseresponse in the dose range of 12-25 mg/kg body weight of albino rats intraperitoneally and a single dose had a good duration of action, as it could effectively suppress the inflammation after 4 hours of its administration [93]. Ashwagandha or Asgand (Withania somnifera) has been shown to possess anti-inflammatory property in many animal models of inflammations like carrageenan-induced inflammation, cotton pellet granuloma and adjuvant-induced arthritis. Detailed studies were carried out to -1 globulin during inflammation-αinvestigate the release of serum by two models of inflammations viz. primary phase of adjuvant-induced arthritis and formaldehyde-induced arthritis. The experiments showed interesting results as most of the APR were influenced in a very short duration and also suppressed the degree of inflammation [94]. Root extract of WS is found to be effective against carrageenan induced air pouch granuloma on the dorsum of rats and it decreased the glycosaminoglycan content in the granuloma tissue more than hydrocortisone treatment.WS extract also shows potent analgesic and antipyretic effect by retarding amplification and propagation of the inflammatory response in monosodium urate crystal-induced experimental rat models, without causing any gastric damage compared to indomethacin, a non-steroidal anti-inflammatory drug [95].WS extract could reduce the ovalbumin-induced paw edema in mice, almost similar to that of standard drug disodium chromoglycate. It also showed protective effect in cyclophosphamide-induced myelosuppression by significant increase in white blood cell counts and platelet counts in mice. Treatment with WS extracts counteracted the Cyclophosphamide induced immunosuppression as evidenced by a significant increase in hemagglutinating antibody and hemolytic antibody responses towards sheep red blood cells [96].

All the above effects viz. anti-inflammatory, immunomodulatory and anti-oxidant effects could be speculated to its possible efficacy in bronchial asthma. In one isolated study, the murine asthmatic Balb/c mouse model was used to investigate the effect of W. somnifera L., the antioxidant selenium, W. somnifera and selenium in combination and hydrocortisone as positive control - on the number of white blood cells in blood smears and bronchial lavage smears as well as the platelet distribution of asthmatic Balb/c mice. The mice were sensitized, nebulized and treated over a period of 43 days and blood smears were made of each individual animal and bronchial lavage was performed by injecting 0.3ml of saline into the trachea of the mice, both on the day of termination. Light microscopy analysis of the bronchial lavage revealed a significant decrease in the number of eosinophils counted in the asthmatic and the different treatment groups. In the asthmatic group, numerous platelet clumps were found distributed between white blood cells. Platelets were also found in the other treatment groups but are not as prevalent as in the asthmatic group. Results from the blood smears showed the same trends, where cell counts in control and

hydrocortisone blood smears were decreased compared to that of the asthma group. It was concluded from the study that W. somnifera and W. somnifera + selenium significantly decreased the white blood cells in both bronchial lavage as well as blood smears, suggesting that W. somnifera indeed has an anti-inflammatory potential and it, in combination with an anti-oxidant like selenium, might successfully be used in the treatment of asthma [97].

In a recent study, the potential of *W somnifera* root extract was tested in an experimental model of allergic asthma. In OVA immunized rats, W somnifera extract at doses of 200 and 400 mg/kg orally, inhibited cellular and molecular markers of airway inflammation, viz. eosinophil counts, pro-inflammatory cytokines (IL-4, TNF-α), OVA-specific IgE, HDAC-2, and oxidative stress markers like MDA, NOx, in both blood and BAL fluid, – suggesting an anti-airway inflammatory and immunomodulatory role for the medicinal plant. Further, in experimental model of airway remodeling, the plant extract also attenuated the pro-fibrotic mediators (IL-13, TGF-β, hydroxyproline, periostin) as well as biomarkers of oxidative stress induced DNA damage (8-OHdG). These findings were supported by reversal of histopathological changes in rat lung tissue. [98, 99].

Hedychium spicatum

H. Spicatum is a small rhizomatous perennial herb belongs to family Zingiberaceae. It grows to around 1-2m in South-East Asian countries, Bhutan, Nepal, Japan, Thailand, Pakistan, China and subtropical Himalayan region in India [100]. It is also known as Shati in Indian medicinal system (Ayurveda), and commonly known as "Spiked Ginger lily". The rhizomes have a bitter taste with aromatic odor, and the extract has been reported to contain low polar volatile oils, coumarins, flavonoids, glycosides and fatty acids, which has been proven for treatments of inflammation and asthma. Antimicrobial activity of essential oil against bacteria and fungi has been reported in several studies. Essential oil content in rhizome about 4% and its phytochemical screening has shown the presence of high amounts of terpenoids (monoterpenoids, sesquiterpenoids and diterpenoids) which are known to reducebronchial asthma and pulmonary eosinophilia [101].

Furanoid diterpene compound 'Hedychinone' was reported to be the main bioactive constituent accountable for its anti-inflammatory activity. The pharmacological activity of rhizomes of H. spicatum has been evaluated in a study conducted by Srimal et al.(1984), and indicated that they possess anti-inflammatory and analgesic activity against carrageenan-induced hind paw oedema in rat and mice. The extracts were administered orally at a dose of 200 mg/kg and 100 mg/kg to rats and mice, respectively. The percentage of inhibition of oedema volume varied and based on extraction solvents. Hexane soluble extract showed inhibition activity of 42.16% in mice (200 mg/ kg) and 27.2% in rats (100 mg/kg) compared to 37% of indomethacin in mice and 27.2% of phenylbutazone in rats [102]. Another study included the evaluation of aqueous and ethanolic extracts of the dried rhizome of H. spicatum for its anti-inflammatory and analgesic activities in rat. Both the extracts showed an anti-inflammatory effect against carrageenan-induced paw edema. A single dose of aqueous and ethanolic extracts (200 mg/kg) and indomethacin (10 mg/kg) was administrated orally 60 min before carrageenan administration. The volume of rat hind paw up to the ankle joint was measured by plethysmography in a successive interval of 1 h, 2 h and 3 h.

The results revealed a significant decrease in paw volume against carrageenan-induced inflammation from 1 h onwards to 3 h of the study period (% decrease in inflammation due to aqueous extract was 11.00– 28.10%; ethanolic extract 8.79–25.62% and indomethacin 16.49–41.32%, respectively [103]. Anti-inflammatory and central nervous system depressant activity of ethanolic extract of powdered rhizomes of H. spicatumhas been evaluated in a study conducted by Dhar et al [104]. In another experiment, the ethanolic extract of rhizome suspended in Tween- 80 and orally administrated in mice and rats. The oedema volume significantly reduced by alcoholic extract (30 mg/kg) in carrageenan induced hindpawoedema. The results showed maximum percentage of oedema volume inhibition (64.2%) with alcoholic extract of H. spicatum, while it reduced up to 49.1% by acetyl salicylic acid in a dose of 300 mg/kg [105].

In a clinical study, paroxysmal attacks of dysopnea and cough was completely relieved in 36 % of the patients after 4 weeks of oral administration 10 g of powdered rhizome of H. spicatuminin divided doses to 25 patients. Eosinophil count reduced by 55.6 %, mean respiration rate reduced by 25 %, and the lung vital capacity was increased by 20 % [106].Efficacy of H. spicatum rhizome extract against tropical pulmonary eosinophilia has been evaluated in a clinical study conducted on children suffering from the same disease. The results revealed that H. spicatum reduced the blood eosinophil count in a dose of 70 mg/kg of body weight and significant improvement in signs and symptoms within one to three weeks period; radiology and lymphadenopathy findings were normalafter a prolonged period [107]. Another clinical study included 23 male and 7 female patients from 21-40 years age group to evaluate the

efficacy and safety of Shati (Hedychium spicatium), Shunthi (Zingiber officinale) and Sugandhavala (Pavonia odorata) in tropical pulmonary eosinophilia. A positive result for tropical eosinophilia with improvement in respiration rate has been obtained after administration of compound powder of herbs. No patients under this therapy showed any untoward effect of the drugs (18). Anti-histaminic activity of the dried rhizome of H.spicatum in guinea pigs (GP) has been evaluated by Ghildiyal S et al., the extracts were administered orally, once daily for 7 days in three dose levels (100, 200 and 400 mg/kg) against histamine induced broncospasm. The results showed dose dependent bronchospasm protection by increase the pre-convulsive dyspnoea time (PCD) from 39.2 to 75.1% compared with Chlorpheniramine 71.3% [108]. In vitro antioxidant activity of H. spicatum has also been reported by other studies. For the management of asthmatic syndrome, there is a dire need of standardized and scientifically evaluated herbal based products with possible immunomodulatory, antiinflammatory, anti-oxidative effects – all relevant to asthma pathopgysiology. With enhanced bronchodilator activity [109]. A most recent study assessed the effects of standardized extracts of Hedychium spicatum on airway inflammation and immunomodulatory parameters in experimental model of bronchial asthma in rats. Wistar rats were immunized with ovalbumin (OVA) adsorbed on to aluminium hydroxide (i.p.) and challenged with aerosolized ovalbumin from day 15 to 22. Standardized extracts of Hedychium spicatum were administered orally for 22 days in different treatment groups. After 24h of last challenge, rats were anesthetized and blood and bronchoalveolar lavage fluid (BALF) were collected, centrifuged and analyzed for proinflammatory cytokines TNF-α, NF-κB, Th2 type cytokines IL-4 and cell count. The results showed that eosinophil cells levels were elevated in the immunized rats which were reduced in the treatment group Hedychium spicatum extract as compared to control. These results were comparable with the effects of the standard drug prednisolone. The results showed that extract of Hedychium spicatum has anti-inflammatory and immunomodulatory effects. Thus, the results suggest that the beneficial effects of Hedychium spicatum in bronchial asthma could be due to balancing influence on prooxidant-antioxidant status and reducing the airway inflammation. [110]

Table 1: Medicinal plants with therapeutic potential in bronchial asthma

Botanical name	Family	Chemical constituents	Pharmacological Uses
Adhatoda vasica	Acanthaceae	Vasicine, bromhexine	Asthma, bronchitis, anti-inflammatory, anti-tubercular
Glycyrrhiza glabra	Leguminosae	Glycyrrhizin, glycyrrhizic acid, glycyrrhetinic acid	Pain, cough
Hyssopus officinalis	Lamiaceae	Luteolin, diosmin, quercetin, apigenin	Cough, asthma, antihistaminic
Boswellia serrata	Burseraceae	Boswellic acids, 5-lipoxygenase (5-LO) including 5-hydroxyeicosatetraenoic acid	Cardiovascular diseases, mouth sores, bad throat, bronchitis, asthma
Curcuma longa	Zingiberaceae	Curcumin	Anti-asthmatic, antioxidant and anti-inflammatory effects
Albizia lebbeck	Leguminosae	Alkaloids, flavonoids, tannins, saponins	Cough, oedema, asthma, blood disorder, rhinitis
Solanum xanthocarpum	Solanaceae	Alkaloids, sterols, saponins, flavonoids and their glycosides and also carbohydrates, fatty acids	Antiasthmatic, hypoglycaemic, anti-inflammatory, anti-tumor, anti-tussive
Withania somnifera	Solanaceae	Glycowithanolides (Withaferin A; withanolide A; withanoside IV)	Immunomodulator, Anti-inflammatory activity; bronchial asthma, anti-oxidant, anti-stress
Hedychium spicatum	Zingiberaceae	Coumarins, flavonoids, glycosides and fatty acids, Hedychinone	Inflammation and asthma

Conclusion: Medicinal plants have served as an important source for many effective drugs in modern medicine. However, many other well documented uses in traditional medicine needs validation for use as alternatives and/or adjuncts in modern medicine. Bronchial asthma is a respiratory disorder with complex etiology and a multi-targeted approach to therapy could be a significant

advancement in the effective and rational treatment of this pathophysiology. In view of the fact that current modern medicines have their limitations, an alternative/complimentary approach to treatment is desirable. Several medicinal plant derived herbal agents have been used in classical Indian traditional medicine for asthma and recent research has attempted to validate some of these consistently observed effects. Advanced research using cellular and molecular markers/techniques is likely to pave way for the identification of important botanicals for the effective and safe treatment of bronchial asthma and related pathophysiology. Integration of traditional and modern systems of medicine for rational drug development in chronic intractable disorders is a matter of great contemporary national relevance and more validation studies with medicinal plants of historic importance in traditional medicine like Ayurveda is the need for the hour.

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