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Role of Herbs in the Management of Asthma

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Abstract:
Herbs have been the highly esteemed source of medicine throughout human history. They are widely used today indicating that herbs are a growing part of modern, high-tech medicine. About 25-30 percent of today's prescription drugs contain chemical moieties derived from plants. The Indian system of medicine i.e Ayurveda alongwith classic texts like Bheshajya Ratnavali has a long-standing tradition that offers a unique insight into comprehensive approach to asthma management through proper care of the respiratory tract. Ayurvedic formulations used in the management of asthma, therefore, judiciously combine herbs to support the physiology of respiration, these herbs apart from exerting bronchial action also possess concomitant properties like anti-oxidant to support the digestive, cardiac, nerve functions and expectorant as well as just plain soothing herbs. Scientifically explored exhaustive reports have been published in Indian and International journals. Some of these herbs and their active chemical constituents which have a role in the management of asthma are compiled here and discussed in this review.
KEYWORDS: Asthma, Herbs.
ABBREVIATIONS: IP3- Inositol 1, 4, 5 – trisphosphate, APCs- Antigen-Presenting Cells, PAF- platelet-activating factor, MEBH- Methanolic extract of *Benincasa hispida,* FEV- Forced Expiration volume,

INTRODUCTION

Asthma is a disease of the human respiratory system in which the airways constrict and become narrow, often in response to a "trigger" such as exposure to an allergen, cold air, exercise, or emotional stress (1). Asthma affects 7% of the total population (2-3) and approx 300 million worldwide (4). During attacks (exacerbations), the smooth muscle cells in the bronchi constrict, and the airways become inflammed and swollen. Breathing becomes difficult. Asthma causes 4,000 deaths a year in the U.S. Attacks can be prevented by avoiding triggering factors and by drug treatment (5).

Historical background:

The modern school of thought regarding asthma as a disease is so powerful that it is difficult to imagine asthma, as it was once conceptualized. During the seventeenth century, Once English physicians Thomas Willis and Sir John Floyer began arguing that asthma was different from other breathing disorders and is the same from person to person. They mentioned that asthma, as a specific form of disordered breathing, must be treated differently from other forms of breathlessness cases. By the late nineteenth century, physicians believed that asthma was a disease which had a specific set of causes, clinical consequences, and requirements for treatment, despite the diversity of individual experiences (6). (Table 1)

Because of the spectrum of severity within asthma, some people with asthma only rarely experience symptoms, usually in response to triggers, where as other more severe cases may have marked airflow obstruction at all times.

Asthma exists in two states: the steady-state of chronic asthma, and the acute state of an acute asthma exacerbation. The symptoms are different depending on what state the patient is in. Common symptoms of asthma in a steady-state include: nighttime coughing, shortness of breath with exertion but no dyspnea at rest, a chronic 'throat-clearing' type cough, and complaints of a tight feeling in the chest. Severity often correlates to an increase in intensity of symptoms. Symptoms can worsen gradually and rather insidiously, up to the point of an acute exacerbation of asthma. It is a common misconception that wheezing is common in patients with asthma—some never wheeze, and their disease may be confused with another Chronic obstructive pulmonary disease such as emphysema or chronic bronchitis (5).

An acute exacerbation of asthma is commonly referred to as an ***asthma attack***. The cardinal symptoms of an attack are shortness of breath (dyspnea), wheezing and chest tightness (8). Although the former is often regarded as the ***sine qua non*** of asthma (9). Some patients present primarily with coughing, and in the late stages of an attack, air motion may be so impaired that no wheezing may be heard (10). When present the cough may sometimes produce clear sputum. The onset may be sudden, with a sense of constriction in the chest, breathing becomes difficult, and wheezing occurs (primarily upon expiration, but can be in both respiratory phases). (Table 2)

Asthma is classified according to the frequency of symptoms, FEV1 and peak expiratory flow rate (7).

Table 1: Classification of asthma

Severity	Symptom frequency	Symptoms at night	Peak expiratory flow rate or FEV1 of predicted	Variability of peak expiratory flow rate or FEV1
Intermittent	< once a week	≤ twice per month	≥ 80% predicted	< 20%
Mild persistent	> once per week but < once per day	> twice per month	≥ 80% predicted	20–30%
Moderate persistent	Daily	> once per week	60–80% predicted	> 30%
Severe	Daily	Frequent	< 60% predicted	> 30%

Table 2 : Severity of asthma attack (10)

Sign/Symptom	Mild	Moderate	Severe	Imminent respiratory arrest
Alertness	May show agitation	Agitated	Agitated	Confused/Drowsy
Breathlessness	On walking	On talking	Even at rest	
Talks in	Sentences	Phrases	Words	
Wheeze	Moderate	Loud	Loud	Absent
Accessory muscle	Usually, not used	Used	Used	
Respiratory rate (/min)	Increased	Increased	Often >30	
Pulse rate (/min)	100	100-120	>120	<60 (Bradycardia)
PaO2	Normal	>60	<60 ,possible cyanosis	
PaCO2	<45	<45	>45	

Though symptoms may be very severe during an acute exacerbation, between attacks a patient may show few or even no signs of the disease (11).

Main causative factors:

Asthma is caused by environmental and genetic factor (11) which can influence how severe asthma is and how well it responds to medication (12). Some environmental and genetic factors have been confirmed by further research, while others have not been.

Environmental

Many environmental risk factors have been associated with asthma development and morbidity in children, but a few stands out as well-replicated or that has a meta-analysis of several studies to support their direct association.

Environmental tobacco smoke, especially maternal cigarette smoking, is associated with high risk of asthma prevalence and asthma morbidity, wheeze, and respiratory infections (13). Poor air quality, from traffic pollution or high ozone levels, has been repeatedly associated with increased asthma morbidity and has a suggested association with asthma development that needs further research (14). Recent studies show a relationship between exposure to air pollutants (e.g. from automobile exhaust) and childhood asthma. This research finds that the occurrence of the disease and excervation of childhood asthma are affected by outdoor pollutants (15).

Caesarean sections have been associated with asthma when compared with vaginal birth; a meta-analysis found a 20% increase in asthma prevalence in children delivered by Caesarean section compared to those who were not. It was proposed that this is due to modified bacterial exposure during Caesarean section compared with vaginal birth, which modifies the immune system (as described by the hygiene hypothesis)biological stress has long been suspected of being an asthma trigger, but only in recent decades has convincing scientific evidence substantiated this hypothesis. Rather than stress directly causing the asthma symptoms, it is thought that stress modulates the immune system to increase the magnitude of the airway inflammatory response to allergens and irritants (13,17).

Viral respiratory infections at an early age, along with siblings and day care exposure, may be protective against asthma, although there have been controversial results, and this protection may depend on genetic context (13,18-21). Antibiotic use early in life has been linked to development of asthma in several examples; it is thought that antibiotics make one susceptible to development of asthma because they modify gut flora, and thus the immune system (as described by the hygiene hypothesis) (19). The hygiene hypothesis is a hypothesis about the cause of asthma and other allergic disease, and is supported by epidemiologic data for asthma. For example, asthma prevalence has been increasing in developed countries along with increased use of antibiotics, c-sections, and cleaning products (16). Use of these things may negatively affect exposure to beneficial bacteria and other immune system modulators that are important during development, and thus may cause increased risk for asthma and allergy.

Recently scientists connected the rise in prevalence of asthma, to the rise in use of paracetamol, suggesting the possibility that paracetamol can cause asthma (20). It has been suggested that viral infections such as HSV, VSV and CSV are correlated to asthma episodes (13,18,21).

Genetics:

Over 100 genes have been associated with asthma in at least one genetic association study. However, such studies must be repeated to ensure the findings are not due to chance. Through the end of 2005, 25 genes had been associated with asthma in six or more separate populations (22).

• GSTM1	• LTA	• STAT6	• IL4	• HLA-DQB1
• IL10	• GRPA	• NOS1	• IL13	• TNF
• CTLA-4	• NOD1	• CCL5	• CD14	• FCER1B
• SPINK5	• CC16	• TBXA2R	• ADRB2 (β-2 adrenergic receptor)	• IL4R
• LTC4S	• GSTP1	• TGFB1	• HLA-DRB1	• ADAM33

Many of these genes are related to the immune system or to modulating inflammation. However, even among this list of highly replicated genes associated with asthma, the results have not been consistent among all of the populations that have been tested.This indicates that these genes are not associated with asthma under every condition, and that researchers need to do further investigation to figure out the complex interactions that cause asthma. One theory is that asthma is a collection of several diseases, and that genes might have a role in only subsets of asthma. For example, one group of genetic differences (single nucleotide polymorphisms in 17q21) was associated with asthma that develops in childhood (23).

Pathophysiology of asthma:

Asthma is an airway disease that can be classified physiologically as a variable and partially reversible obstruction to air flow, and pathologically with overdeveloped mucus glands, airway thickening due to scarring and inflammation, and bronchoconstriction, the narrowing of the airways in the lungs due to the tightening of surrounding smooth muscle. Bronchial inflammation also causes narrowing due to edema and swelling caused by an immune response to allergens.

Bronchoconstriction

During an asthma episode, inflammed airways react to environmental triggers such as smoke, dust, or pollen. The airways narrow and produce excess mucus, making it difficult to breathe. In essence, asthma is the result of an immune response in the bronchial airways (24). The airways of asthma patients are "hypersensitive" to certain triggers, also known as *stimuli* (see below). (It is usually classified as type I hypersensitivity) (25). in response to exposure to these triggers, the bronchi (large airways) contract into spasm (an "asthma attack"). Inflammation soon follows, leading to a further narrowing of the airways and excessive mucus production, which leads to coughing and other breathing difficulties. Bronchospasm may resolve spontaneously in 1–2 hours, or in about 50% of subjects, may become part of a 'late' response, where this initial insult is followed 3–12 hours later with further bronchoconstriction and inflammation (8). The normal caliber of the bronchus is maintained by a balanced functioning of these systems, which both operate reflexively. The parasympathetic reflex loop consists of afferent nerve endings which originate under the inner lining of the bronchus. Whenever these afferent nerve endings are stimulated (for example, by dust, cold air or fumes) impulses travel to the brain-stem vagal center, then down the vagal efferent pathway to again reach the bronchial small airways. Acetylcholine is released from the efferent nerve endings. This acetylcholine results in the excessive formation of inositol 1, 4, 5 - trisphosphate (IP3) in bronchial smooth muscle cells which leads to muscle shortening and this initiates bronchoconstriction.

Bronchial inflammation

The mechanisms behind allergic asthma - i.e., asthma resulting from an immune response to inhaled allergens - are the best understood of the causal factors. In both people with asthma and people who are free of the disease, inhaled allergens that find their way to the inner airways are ingested by a type of cell known as antigen-presenting cells, or APCs. APCs then "present" pieces of the allergen to other immune system cells. In most people, these other immune cells (T_H0 cells) "check" and usually ignore the allergen molecules. In asthma patients, however, these cells transform into a different type of cell (T_H2), for reasons that are not well understood.

The resultant T_H2 cells activate an important arm of the immune system, known as the humoral immune system. The humoral immune system produces antibodies against the inhaled allergen. Later, when a patient inhales the same allergen, these antibodies "recognize" it and activate a humoral response. Inflammation results: chemicals are produced that cause the wall of the airway to thicken, cells which produce scarring to proliferate and contribute to further 'airway remodeling', causes mucus producing cells to grow larger and produce more and thicker mucus, and the cell-mediated arm of the immune system is activated. Inflamed airways are more hyper-reactive, and will be more prone to bronchospasm.

The "hygiene hypothesis" postulates that an imbalance in the regulation of these T_H cell types in early life leads to a long-term domination of the cells involved in allergic responses over those involved in fighting infection. The suggestion is that for a child being exposed to microbes early in life, taking fewer antibiotics, living in a large family, and growing up in the country stimulate the T_H1 response and reduce the odds of developing asthma (26).

Stimuli

- Allergens from nature, typically inhaled, which include waste from common household pests, the house dust mite and cockroach, as well as grass pollen, mold spores, and pet epithelial cells (27).
- Indoor air pollution from volatile organic compounds, including perfumes and perfumed products. Examples include soap, dishwashing liquid, laundry detergent, fabric softener, paper tissues, paper towels, toilet paper, shampoo, hairspray, hair gel, cosmetics, facial cream, sun cream, deodorant, cologne, shaving cream, aftershave lotion, air freshener and candles, and products such as oil-based paint (27).
- Medications, including aspirin, (28), β-adrenergic antagonists (beta blockers) (29-30) Food allergies

such as milk, peanuts, and eggs. However, asthma is rarely the only symptom, and not all people with food or other allergies have asthma (31).

- Use of fossil fuel related allergenic air pollution, such as ozone, smog, summer smog, nitrogen dioxide, and sulfur dioxide, which is thought to be one of the major reasons for the high prevalence of asthma in urban areas (8).
- Various industrial compounds and other chemicals, notably sulfites; chlorinated swimming pools generate chloramines—monochloramine (NH_2Cl), dichloramine ($NHCl_2$) and trichloramine (NCl_3)—in the air around them, which are known to induce asthma (32).
- Early childhood infections, especially viral upper respiratory tract infections. Children who suffer from frequent respiratory infections prior to the age of six are at higher risk of developing asthma (5), particularly if they have a parent with the condition. However, persons of any age can have asthma triggered by colds and other respiratory infections even though their normal stimuli might be from another category (e.g. pollen) and absent at the time of infection. In many cases, significant asthma may not even occur until the respiratory infection is in its waning stage, and the person is seemingly improving (8). In children, the most common triggers are viral illnesses such as those that cause the common cold (35). Exercise or intense use of respiratory system. The effects of which differ somewhat from those of the other triggers, since they are brief. They are thought to be primarily in response to the exposure of the airway epithelium to cold, dry air.
- Hormonal changes in adolescent girls and adult women associated with their menstrual cycle can lead to a worsening of asthma. Some women also experience a worsening of their asthma during pregnancy whereas others find no significant changes, and in other women their asthma improves during their pregnancy (8).
- Psychological stress. There is growing evidence that psychological stress is a trigger. It can modulate the immune system, causing an increased inflammatory response to allergens and pollutants (17). Cold weather can make it harder for patients to breathe (35). Whether high altitude helps or worsens asthma is debatable and may vary from person to person (36).

Pathogenesis:

The fundamental problem in asthma appears to be immunological: young children in the early stages of asthma show signs of excessive inflammation in their airways. Epidemiological findings give clues as to the pathogenesis: the incidence of asthma seems to be increasing worldwide, and asthma is now very much more common in affluent countries.

In 1968 Andor Szentivanyi first described *The Beta Adrenergic Theory of Asthma*; in which blockage of the Beta-2 receptors of pulmonary smooth muscle cells, causes asthma (37). Szentivanyi's Beta Adrenergic Theory is a citation classic (38) using the Science Citation Index and has been cited more times than any other article in the history of the Journal of Allergy and Clinical Immunology.

In 1995 Szentivanyi and colleagues demonstrated that IgE blocks beta-2 receptors (39). Since overproduction of IgE is central to all atopic diseases, this was a watershed moment in the world of allergy (40).

Significance of medicinal plants & traditional medicines in management of asthma:

Medicinal plants, since time immemorial, have been used in virtually all cultures as a source of medicine. It has been estimated that about 80-85% of population both in developed and developing countries rely on traditional medicine for their primarily health care needs and it is assumed that a major part of traditional therapy involves the use of plant extracts or their active principles (41,42,43). Due to lack of organized health care systems in developing countries, people with chronic diseases like asthma are among the worst suffers in their communities today. Hence, majority of the populations still have limited access or no access, especially those in remote areas, to modern medicines. Instead they use traditional medicines for a range of disease complications (44-45).

The active principles of many plant species are isolated for direct use as drugs, lead compounds or pharmacological agents. Different species of medicinal plants are used in the treatment of asthma.

There are many natural herbs and herbal supplements that can be used for asthma treatment. Natural Asthma treatment incorporates vitamins, minerals and herbs to relieve symptoms and prevent further attacks (45).

Important medicinal plants having anti-asthmatic potential:

Acorus calamus: *(*Family-Araceae : Common name-Sweet flag). It is highly beneficial in the treatment of asthma; it removes catarrhal matter and phlegm from the bronchial tubes. About 65 centigrams of the herb is taken every 2 or 3 hours in this condition (46).

Asystasia gangetica: (Family-Acanthaceae: Common name-Foxglove).

Asystasia gangetica is a traditional medicine which is used to treat a wide variety of diseases in Nigeria and other parts of world, commonly known as creeping foxglove. The leaf of *Asystasia gangetica* T. Adams is also used in many parts of Nigeria for the management of asthma. Therefore a study was performed to evalutate the antiasthmatic effect of the plant. Result indicated that hexane, ethylacetate, and methanol extracts of the leaves of *Asystasia gangetica*, obtained by successive sohxlet extraction inhibited the contraction evoked by spasmogens and the IC (50) values were calculated. The extracts relaxed histamine-precontracted tracheal strips in the following degree of potency-ethylacetate extract>hexane extract=methanol extract. This study shows that the leaves of *Asystasia gangentica* have antiasthamatic potency (47).

Adhatoda vasica: **(**Family-Acanthaceae : Common name-Adusa).

The traditional healers are using this herb for the treatment of chronic Asthma. Adusa is known as Vasa or Vasak in Sanskrit and is a reputed drug for Asthma mentioned in Ayurveda (48,49). *Adhatoda vasica* is considered in the east to be the best possible treatment for all chest diseases and used in India as an expectorant, antitussive and in other respiratory disease. It is also used widely to relieve asthma. *Adhatoda vasica* has been traditionally used in the management of allergic disorders and bronchial asthma. Research performed over the last three decades revealed that the alkaloids present in the leaves, vasicine and vasicinone, possess powerful respiratory stimulant activity (48). Its essential oil exhibited antitussive (cats), expectorant (rats and rabbit), and antiasthmatic (guinea pig) activity in *in-vivo* experiments (50).

Aegle marmelos: **(**Family-Rutaceae: Common name-Golden apple/ Bael fruit).

Its leaf extract is being used in Indian system of medicine as an antidiabetic gent and traditional text of India prescribe it in the management of asthma. Therefore the effect of the alcoholic extract of the leaves of *Aegle marmelos* Corr. on guinea pig isolated ileum and tracheal chain was investigated using the isolated organ bath method. 1mg/ml and 2mg/ml doses of the alcoholic extract of this plant produced a positive relaxant effect in isolated guinea pig ileum and tracheal chain, respectively. In addition, they antagonized the contractions, which are produced by histamine. Because the alcoholic extracts elicited the antagonistic effect against histamine and also relaxed the histamine-induced contractions, it can be concluded that relaxations induced by *A. marmelos* in both guinea pig ileum and tracheal chain were due to the depression of H_1-receptors. This study shows that *Aegle marmelos* can be used effective in the treatment of asthmatic disorders (51).

Alstonia scholaris: (Family-Apocynaceae: Common name-Sitwan chaal/ milky pine).

The ethanol extract of *Alstonia scholaris* leaves, induced pronounced bronchodilator activity in anaesthetized rats with the probable involvement of prostaglandins. However, *in-vitro* preparations of guinea-pig trachea did not confirm this property, indicating that bronchodilation is not due to the direct tracheal smooth muscle relaxation (52).

Andrographis paniculata: (Family-Acanthaceae: Common name- Creat, Kalmegh, Indian Echinacea).

Persistent activation of nuclear factor (NF) - kappa B has been associated with the development of asthma. Andrographolide, the principal active component of the medicinal plant *Andrograhphis paniculata* has been shown to inhibit NF-Kappa B activity. Findings implicate a potential therapeutic value of Andrographolide in the treatment of asthma and it may act by inhibiting the NF-kappa B pathway at the level of inhibitory kappa B kinase-beta activation (53).

Astercantha longifolia: **(**Family-Acanthaceae: Common name-Kulikhara, Kokilaksah).

The methanolic extracts of *Astercantha longifolia* Inhibits the biosynthesis of leukotriene B_4 in bovine polymorphonuclear leukocytes and exhibited potent inhibitory action with IC_{50} values of 20 (54).

Allium cepa: *(*Family-Lilliaceae: Common name-Pyaaz,Onion*).*

Dorsch W et.al, had studied the effect of onion oil on platelet-activating factor-induced bronchial obstruction by onion oils. In this study lyophilized onion extract and ether extracts of onions were separated by chromatographic methods into several subfractions and tested for their effects on asthmatic reactions of guinea pigs to allergen, histamine, acetylcholine and platelet-activating factor (PAF) inhalation as well as on thromboxane biosynthesis of human platelets and lung fibroblasts. Onion oils are counteracting the bronchial obstruction due to PAF inhalation. Thus onion oil can be effectively used in the treatment of asthma (55).

Acacia catechu: (Family-Mimosaceae: Common name-Black catechu/Khair).

The extracts of gum, flowering tops, leaves, young shoots, bark and fruits are used in asthma, cough, and bronchitis (56).

Albizia lebbeck: (Family-Leguminosae: Common name-Pit Shirish shirisha)

Albizia originates from India. The bark is used to treat asthma (57). Traditional Medicinal Use is in Asthma, antihistamine, allergies, and bronchitis. Scientific Evidence allergic-induced bronchospasm, mast cell degranulation, antihistamine (58).

Atropa belladonna*:* (Family-Solanaceae : Common name-Devils Cherries*).*

Synonyms -Belladonna. It is a powerful antispasmodic in intestinal colic and spasmodic asthma. Occasionally the leaves are employed as an ingredient of cigarettes for relieving asthma (59).

Acalypha indica: (Family-Euphorbiaceae: Common name-Kuppi).

According to Siddha Materia Medica, the leaf powder when given in the dose of 950 mg to 1300 mgs, cures respiratory diseases. Expressed juice of the leaves is useful in chronic bronchitis, asthma and consumption (60).

Boswellia serrata: **(** Family-Bruseraceae : Common name-Indian olibanum tree).

Boswellia is an Ayurvedic plant that contains anti-inflammatory triterpenoids called boswellic acids. Boswellic acid and its derivatives have anti-carcinogenic, anti-tumor, and blood lipid lowering activities. Dried extracts of the resin of the *Boswellia serrata* tree have been used since antiquity in India to treat inflammatory conditions. It inhibits proinflammatory 5-lipoxygenase chemicals and blocks leukotriene synthesis and thus boswellia may helpful in medical conditions involved in inflammation including asthma (46). From a clinical study involving 40 patients, it was concluded that gum resin of *Boswellia serrata* was quit beneficial in the management of asthma (61).

Benincasa hispida: (Family-Cucurbitaceae: Common name-Ash Gourd).

Methanolic extract of *Benincasa hispida* (MEBH) showed excellent protection in guinea pigs against the histamine induced bronchospasm even at a very low dose, 50mg/kg, p.o However at a higher dose of 400 mg/kg, MEBH did not offer

any significant protection against acetylecholine challenge. Therefore it can be deduced that the MEBH is unlikely to have muscarinic action. Result suggested that the plant has a protective effect against bronchospasm induced by histamine (62).

Blumea lacera: *(*Family-Compositeae: Common name-Kukurmutta / kukronda).

In case of acute Asthmatic attack the patients are advised to inhale the fumes of dried Blumea leaves. For regular use, healers recommend to prepare herbal cigarrette using this herb in combination of other herbs. In many parts of India, it is known as Janglimuli (49).

Cuminum cyminum: (Family-Umbelliferae : Common name-Jeera).

The relaxant effect of *Cuminum cyminum* is well established. It acts as a powerful Bronchodilator. It makes breathing easy and free of blocks (48).

Cinnamomum cassia **: (**Family**-**Laureaceae : Common name-.Chinese cinnamon / Dalchini).

Enhances expectoration of fluids in lungs. It has powerful anti edemic properties - prevents stagnation of fluids (mucous) in lungs (48).

Clerodendrum serratum: (Family-Verbenaceae : Commonname**-** Bharnagi).

Clerodndrum serratum is called as Bharnagi in Indian system of traditional medicine and the juice of bharangi root is given in cough and asthmatic conditions with some other drugs like ginger etc. It is given with ghee and honey in bronchial asthma and also gives with hot water when one suffers with high cough and asthma (63).

Cissus quandrangularis: **(**Family-Vitaceae.: Common name-Hajora**/** Asthisanhari).

The leaves and stem are frequently eaten with curry in southern India The entire plant is considered to be an alterative, anthelmintic aphrodisiac, antiasthmatic Quadrangularins A, Band C, resveratrol, piceatannol, pallidol and parthenocissin are present in the stem.Quadrangularins A, Band C, resveratrol, piceatannol, pallidol and parthenocissin are present in the stem (64).

Curcuma longa: (Family-Zingiberaceae : Common name-Turmeric/Haldi).

Curcuma longa has been known to Indians since centuries. It has been purported to have anti-inflammatory actions (65-66). Anti-asthmatic property of *Curcuma longa* has been tested in experimental animal model of airway hyperresponsiveness and has been documented to be effective in improving the impaired airways features (67) .A study from Journal of Alternative and Complementary Medicine confirms that curcumin is safe in several human trials and inhibits a number of pro-inflammatory mediators that play an important role in asthma (68).

Camellia sinensis **:** (Family-Theaceae : Common name**-** Tea).

The anti-allergic effect of tea-leaf saponin (TLS), which was a mixture of saponins separated from the leaves of Camellia sinensis var. sinensis, in guinea pigs and rats. TLS (20-100 mg/kg) dose-dependently inhibited experimentally-induced asthma, and ID50 was 61.7 mg/kg. TLS (20-100 mg/kg) dose-dependently inhibited a 48 h homologous PCA (passive cutaneous anaphylaxis) reaction, and the inhibitory effect was similar to that of tranilast. TLS (1-100 microg/ml) also inhibited the release of antigen-induced leukotriene (LT) C4 from sensitized guinea pig lung samples in a dose-dependent fashion, but did not prevent histamine release. TLS (0.01-0.5 microg/ml) inhibited histamine release from rat peritoneal mast cells induced by compound 48/80. At higher concentrations, TLS elicited histamine release. These findings suggest that TLS may be a useful protective agent against clinical allergy, and that the inhibitory effects of TLS on mediator release are in some way related to its inhibitory effect on experimentally-induced asthma and PCA reaction (69).

Calotropis procera: (Family-Asclepiadaceae: Common name-Madaar/ Dead Sea Apple/Arka)

In a traditional treatment of asthma patients arka flowers have been shown to have therapeutic effect. It is differentiated by other species by the color of its flower i.e. *Calotropis gigantea* (70).

Cannabis sativa: (Family-Cannabaceae: Common name-Bhang*)*

Tetrahydrocannabinol (THC), the chief pure component of cannabis is a bronchodilator when administered orally or as an aerosol and the effect is of long duration.(71)

Callicarpa Macrophylla: (Family-Verbenaceae: Common name-Beauty Berry*)*

Flowers and fruits are useful in rheumatoid arthritis, asthma (72).

Datura metel: (Family-Solanaceae: Common name- Thorn Apple).

The whole plant, but especially the leaves and seed, is, antiasthmatic, antispasmodic, antitussive, and bronchodilator. In China, the plant is used in the treatment of asthma (73). In Vietnam, the dried flowers and leaves are cut into small chips and used in antiasthmatic cigarettes (74). Total alkaloid content of the leaves is 0.426%, which is mainly atropine. The seeds contain 0.426% alkaloids, which is mainly hyoscyamine. The roots contain 0.35% hyoscyamine (75).

Ephedra sinica: *(*Family-Ephedraceae: Common name-Ma Huang*)*

. This is the most widely known Chinese herb used to treat asthma,.Ephedra plants contain about 2 to 3% naturally-occurring ephedra alkaloids, mostly ephedrine and pseudoephendrin Both alkaloids stimulate the alpha and beta-adrenergic receptors, and in general act similarly to norepinepherine (adrenaline). This in turn will act to dilate the bronchial tubes (for asthma, hay fever etc) as well as increase CNS and cardiac activity. The only safe recommended use of ephedra is for short-term bronchodilation (76).

Ganoderma lucidum: (Family-Ganodermataceae. : Common name-Reishi***)***

During 1970s and 1980s, Reishi's anti-allergy action became the subject of ongoing research in both China and Japan. Studies showed that Reishi extract significantly inhibited all four types of allergic reactions, including positive effects against asthma and contact dermatitis. Researchers at the University of Texas Health Science Center proved the positive

effect of drug on bronchitis, rheumatism, and improving competence of the immune system without any significant side-effects (77-78).

Glycyrrhiza glabra: (Family-Fabaceae: Common name-Mulethi, Liquorice)

Induces the adrenal cortex to make more natural cortisone, thus having a systemic anti-inflammatory effect on the lungs and most other organs (48).

Grindelia camporum: (Family-Asteracea: Common name-Great valley gum plant).

This is an expectorant herb with bronchospasmolytic activity. It is traditionally recommended for the treatment of spasmodic respiratory conditions such as asthma and bronchitis. The British Herbal Pharmacopoeia 1983 lists the specific indication as bronchial asthma with tachycardia. Californian Native Americans used grindelia not only for skin infections but also for bronchial conditions where grindelia eventually gained the attention of the Catholic missionaries. The dried leaf and flowering tops of grindelia were official in the United States Pharmacopoeia 1882– 1926, and have been in the National Formulary, 1926–1960 (45).

Hedychium spicatum: (Family- Zingiberaceae: Common name-Kapur Kachari).

The drug is valued for treatment of bronchial asthma in Ayurveda (79).In a clinical study powdered rhizome of the plant was administered to 25 patients with bronchial asthma for a period of 4 weeks and the result was considered satisfactory (80).

Inula racemosa: (Family- Asteraceae: Common name-Pushkarmoola).

Devadaru compound was shown to be beneficial in *Tamak Swasa* (Bronchial asthma). Clinical findings revealed higher percentage of relief in cardinal and general symptoms with decrement in the pulse rate and in the respiration rate. A significant linear increase in PEFR value was observed before and after treatment and an increase in FEV_1, values measured in Group I subjects. There was relief of all symptoms in a significant number of patients. Occurrence of relief was observed only among patients who suffer less than 10 years duration with *Tamak Swasa* and among those the frequency of attacks of *Tamak Swasa* was at fortnightly or monthly intervals. Antispasmodic activity of Devadaru Compound (DC) on acetylcholine (Ach) induced contractions using rat ileum preparation was studied. The results demonstrated that DC inhibits Ach induced contractions significantly and bears a dose-response relationship. This suggests that DC has got anti-spasmodic activity and corroborates the clinical findings. The clinical findings and experimental studies show that DC is of significant use in the treatment of *Tamak Swasa* Bronchial Asthma) and superior to the standard and placebo therapy (81).

Lobelia inflate: (Family- Campanulaceae: Common name-Indian Tobacco)

Indian tobacco has been used for many decades in homeopathic medicine and is still considered as an important medicinal plant. It has been used internally in various preparations to treat spasmodic asthma, bronchitis and whooping cough (82-83).

Lafoensia pacari: (Family-Lythraceae: Common name-Didal).

The ethanolic extract of *Lafoensia pacari* inhibits eosinophilic inflammation induced by *Toxocara canis* infection, and that ellagic acid is the secondary metabolite responsible for the anti-eosinophilic activity seen in a model of β-glucan peritonitis. A study was done to investigate the preventive and curative effects of *L. pacari* extract and ellagic acid on allergic lung inflammation using a murine model of ovalbumin-induced asthma. The study proved that *L. pacari* and ellagic acid are effective eosinophilic inflammation suppressors, suggesting a potential for treating allergies (84).

Morus alba: (Family-Moraceae: Common name-mulberry fruit).

The root bark is antiasthmatic, antitussive, diuretic, expectorant, hypotensive and sedative. It is used internally in the treatment of asthma, coughs, bronchitis, oedema, hypertension and diabetes (85).

Moringa oleifera: (*Family*-Moringaceae: Common name-Sehjan, Drumstick Tree).

The present study was carried out to investigate the efficacy and safety of seed kernels of *Moringa oleifera* in the treatment of bronchial asthma. Twenty patients of either sex with mild-to-moderate asthma were given finely powdered dried seed kernel

s in dose of 3 g for 3 weeks. The clinical efficacy with respect to symptoms and respiratory functions were assessed using a spirometer prior to and at the end of the treatment. Hematological parameters were not changed markedly by treatment with *M. oleifera*. Significant improvement was observed in symptom score and severity of asthmatic attacks. Treatment with the drug for 3 weeks produced significant improvement in forced vital capacity, forced expiratory volume in one second, and peak expiratory flow rate values by 32.97 [+ or -] 6.03%, 30.05 [+ or -] 8.12%, and 32.09 [+ or -] 11.75%, respectively, in asthmatic subjects. Improvement was also observed in % predicted values. None of the patients showed any adverse effects with *M. oleifera*. The results of the present study suggest the usefulness of *M. oleifera* seed kernel in patients of bronchial asthma (86).

Nigella sativa: (Family-Ranunculaceae: Common name-Kalajira).

Petroleum ether fraction of *N. sativa* seed extract has been shown to possess spasmolytic and bronchodilatory activities in in vitro (isolated rabbit jejunum and guinea pig tracheal preparation) experiments.Activity is possibly mediated through calcium channel blockade (87).

Nardostachys jatamansi: (Family-Valerianaceae: Common name-Jatamansi)

The alcoholic extract of rhizomes of Jatamansi exhibited bronchodialatory effects in experimental animal models. The extract also showed antispasmodic effect in experimental models on the isolated smooth muscles (colon, intestine, uterus) (88).

Oscimum sanctum: (Family-Labiateae : Common name-Tulsi).

The anti-asthmatic activity of a 50% aqueous ethanol extract of dried and fresh leaves, and the volatile and fixed oils of *Ocimum sanctum* was evaluated against histamine and-acetylcholineinduced pre-convulsive dyspnea (PCD) in guinea pigs. The 50% ethanol extract of fresh leaves, volatile oil extracted from fresh leaves and fixed oil from the seeds significantly protected the guinea pigs against histamine- and acetylcholine-induced PCD. However, the 50% ethanol extract of dried leaves did not protect the guinea pigs against histamine-induced PCD (88-89-90).

Picrorhiza kurroa: (Family- Scrophulareaceae: Common name-Kutki)

It is a potent antiasthmatic herb in Indian traditional medicine (79-91). The major constituents in picrorhiza are the glycosides picroside I, kutkoside, androsin, and apocynin. They have been shown in animal studies to be antiallergic, to inhibit platelet-activating factor (an important pro-inflammatory molecule) (92). Two preliminary trials suggest that picrorhiza may improve breathing in asthma patients and reduce the severity of asthma (93-94).

Plantago major: (Family-Plantaginaceae: Common name-Plantain*)*.

Plantain depresses the secretion of mucus, particularly in the respiratory system. In vitro research suggest that the antiallergic effect is due to the effect of *Plantago major* on inhibiting mast cell degranulation (95) .Its mucilage has a soothing effect protecting the mucus lining from irritation and helps prevent spasm in asthma.The tannins are astringent, usefull to reduce swelling and inflammation (96).

Piper longum: (Family-Piperaceae: Common name- Pippali*)*.

It is highly valued in Ayurveda for treating several clinical manifestations mostly relating to asthma and cough (79). In an open clinical study carried out on 20 paediatric patients of asthma *Piper longum* fruit powder was given with milk, in a gradually increasing dose for a period of 5 weeks. This treatment significantly decreased the frequency and severity of asthmatic attacks in 85% of the patients (88).

Pimpinella anisum: *(*Family-Umbelliferaceae: Common name-Anise, Anason, Anis, Anasur, Anisu).

It is a flowering plant, native of Egypt, Greece, Crete and Asia Minor studied the relaxant effect of *Pimpinella anisum* on isolated guinea pig tracheal chains and its possible mechanism(s). The bronchodilatory effects of aqueous and ethanol extracts and essential oil were examined on precontracted isolated tracheal chains of the guinea pig by 10 μM methacholine in two different conditions including: non-incubated tissues (group 1) and incubated tissues with 1 μM propranolol and 1 μM chlorpheniramine (group 2). Aqueous and ethanol extracts, essential oil and theophylline (1 mM) showed significant relaxant effects compared to those of controls. Although relaxant effect of essential oil was lower than theophylline, there was no significant difference between the effect of aqueous and ethanol extracts and that of theophylline. There was also no significant difference between the relaxant effects obtained in group 1 and 2 experiments These results indicated bronchodilatory effects of essential oil, aqueous, and ethanol extracts from *P. anisum* (97).The volatile oil, mixed with spirits of wine forms the liqueur Anisette, which has a beneficial action on the bronchial tubes, and for bronchitis and spasmodic asthma (102).

***Sida cordifolia*:** (Family- Malvaceae: Common name- Flannel weed.)

In traditional Chinese medicine, ephedrine has been used in the treatment of asthma and bronchitis for centuries. Ephedrine is used primarily as a chronic medication for mild or only acute cases, especially in children. In sever asthma the response to ephedrine is usually poor. Compared with epinephrine, ephedrine is less reliable, is slower in action and longer in duration and probably more often produces undesired side effects. The average dose is 25-50mg orally, repeated ¾ times a day (98).

Solanum melongena: (Family-Solanaceae: Common name-Eggplant / Brinjal).

The methanol extract of fresh leaves of *Solanum melongena* L. was evaluated for its capacity to alter the tone of isolated, pre-contracted guinea pig tracheal chains, as well as for its possible mechanism(s) of action. Using serial dilutions between 0.0025 and 2.5 mg/ml, the extract was found to cause a dose-dependent increase in the force of muscle contraction. The EC_{50} value was 0.46 ± 0.01 mg/ml. The concomitant use of acetylcholine 10^{-5} M did not significantly affect the force of contraction induced by the extract. Histamine 10^{-5} M added at about 40% to, and salbutamol 10^{-6} M antagonized by about 30% its constrictive effect. Chlorpheniramine 10^{-6} M, propanolol 10^{-5} M, and nifedipine 10^{-6} M did not significantly influence the extract-induced force of contraction, but atropine 3×10^{-7} M reduced it by approximately 60%. These data suggest that the *Solanum melongena* extract exerted a bronchospasmogenic rather than a bronchospasmolytic effect, probably through muscarinic receptor (99).

Saussuria lappa*: (Family*-Asteraceae: Common name-Costus, Kut Root).

Pharmacological studies have shown that the costus root has significant smooth muscle relaxant effect on isolated guenia pig ileum. So in bronchial asthma this drug relaxes bronchi and decreases bronchial muscle inflammation (100). Alcohol extract, essential oil and crude alkaloidal fraction were demonsrated to antagonise bronchospastic action of histamine and acetylcholine on the isolated bronchopulmonary specimen of guinea pig. From these and other experiments, it was concluded that the bronchodialatory action of these materials occure directly on the bronchial smooth muscle. In a clinical usage alcoholic extract of the roots at a dose level of 4-6 gm has been reported to relieve the patient of their bronchial asthma and prevented relapse (101).

Scutellaria baicalensis: *(*Family- Labiatae: Common name-Baikal skullcap)

The root of this plant has been used in traditional Chinese medicine (TCM) for a variety of conditions including asthma (102). Chinese skullcap contains flavone derivatives including baicalin, wogonin and baicalein which inhibit histamine release from mast cells in vitro. Baicalin showed antiasthmatic activity

(antihistaminic and anticholinergic activity) in isolated tracheal muscle from asthmatic guinea pigs. Reducing hypesensitivity and inflammation in airways is vital to managing asthma (46). Baicalein, a flavonoid, is anti-allergic but only slightly soluble in water. The soluble derivatives of baicalein, disodium baicalein-6-phosphate (BPS) and sodium baicalein-6-sulfate (BSS) were synthesized and examined regarding their effects on hypersensitivity reactions. These derivatives inhibited type I and II reactions as classified by Coombs and Gell. The Arthus reaction belonging to type III reaction, however, was hardly affected with either BPS or BSS. The experimental asthma caused by passive systemic anaphylaxis in guinea pigs was prevented with application of BPS. Thus even by the oral route, BPS appears to be clinically applicable to extensive allergy related diseases (103).

Tamarindus indica: **(**Family- Leguminosae: Common name- Tamarind, tamarind)

The plant has powerful anti inflammatory properties. It instantly relieves inflammation in lungs and respiratory tract. It builds strong immunity to allergy. A decoction of bark of the tree is used in cases of gingivitis and asthma and eye inflammations (48).

Terminalia belerica: (Family-Combretaceae : Common name-Vibhitaki***)***

The dried fruit contains about 20% of both condensed and hydrolysable tannins. Other constituents include lipids, β-sitosterol, saponins, gallic and ellagic acids alongwith their derivatives, glycosidesand various carbohydrates (104). *Terminalia belerica* has proven anti asthmatic, anti-spasmodic, expectorant and anti-tussive (anti cough) effects. It is commonly used to treat coughs and sore throat (48). An open clinical study in 93 patients suffering from respiratory conditions found that *vibhitaki* (*Terminalia bellerica*) had anti-asthmatic, anti-spasmodic, expectorant activity (105).

Tragia involucrate: (Family**-** Euphorbiaceae : Common name- Bichuti.).

Tragia has powerful wound healing properties particularly in the respiratory tract. It heals the inflammation and polyps in the respiratory tract. The relaxant effect *of Cuminum cyminum* is well established. It acts as a powerful Bronchodilator (48).

Tussilago farfara*:* (Family- Asteraceae : Common name-Clotsfoot)

It is a native to Europe and Asia. Due to its expectorant and cough-suppressing properties, coltsfoot has been used to treat a variety of respiratory conditions, including asthma, emphysema, and smoker's cough (106). In a Chinese trial 75% of patients suffering from bronchial asthma showed some improvement after treatment with this plant, though the anti-asthmatic effect was short-lived (107).

Tinospora cordifolia: *(*Family-Menispermaceae: Common name-Guduchi*)*

the medicinally valuable part is the stem .Dry stems, with bark intact, constitute the drug of commerce. The stem extract significantly reduced bronchospasms (allergic) induced by 5.0% histamine aerosol in guenia pigs and capillary permeability in mice (108).

Ulmus rubra*: (*Family-Ulmaceae : Common name-Slippery elm).

Thins down the thick sticky mucus that clogs the airways (109).

Withania somnifera: (Family- Solanaceae: Common name-Indian Ginseng)

Withania somnifera is an anti stress herb having powerful anti inflammatory properties. It significantly reduces inflammation and blockages in respiratory tract. Taken over a period it builds immunity to allergic triggers (48).

Xanthoxylum nepalensis*: (*Family- Berberidaceae: Common name-Prickly Ash, Toothache Tree).

Xanthoxylum nepalensis is used in traditional herb remedies to treat inflammatory diseases such as asthma, bronchitis, rheumatism, and skin disorders presumed to be mediated by leukotrienes. The methanolic extracts of The leaves of *Zanthoxylum nepalensis* were tested for their activity to inhibit the biosynthesis of leukotriene B_4 in bovine polymorphonuclear leukocytes. The leaves of *Zanthoxylum nepalensis* were shown to be the most potent inhibitor with an IC_{50} value of 11 μg/ml (110).

Zingiber officinale: (Family- Zingiberaceae: Common name-Ginger)

It is a powerful natural expectorant used widely in Chinese as well as Indian formulations for coughs, colds, and chronic bronchitis. The dried rhizome of ginger contains approximately 1–4% volatile oils. It is considered to be a powerful natural anti allergy agent specially acting on respiratory system (48).

CONCLUSION

Among many disease or disorders, asthma is a serious disorder effecting large population of the world. Although there is a significant increase in the prevalence of number of patients suffering from asthma in every age group during the last decade, the largest increase of 73 per cent was reported among children and young adults under the age group of 18 years. India has documented an estimated approx 15-20 million asthmatic patients. Some of the Medically advanced countries like United States of America have developed and maintained a national database of their citizens along with the natural allergy (Asthma) causing plants detail, this detail includes the pollen releasing time, along with the main geographical distribution to assist its citizens in selection of a living as well as working place that may be free of trees responsible for causing asthma to particular individual. This reflects the seriousness of any country towards the healthcare needs of their citizens. The authors perceive the similar development, or atleast initiation of such type of database in our country also, Herbs are highly esteemed for millennia as a rich source of therapeutic agents for prevention and treatment of asthma and its ailments. Although the contribution of modern synthetic medicine for elevating the human sufferings cannot be under-estimated, equally true is the fact that most of them leave unwanted harmful side/toxic effects on the human system disturbing the basic physiology. During the last three decades or so there has been serious realization of these problems associated with synthetic drugs and as a result the

world has started exploring the herbs as agents of therapy which, apart from being comparatively economical and easily available, are relatively free from the hazardous side effects, toxicity and development of resistance towards causative organisms, here it does not mean that plants are hundred percent safe but in-depth review of literature and scientific work is still required in the field of medicinal plants regarding assessment of heavy metals and presence of aflatoxins (WHO Guidelines) etc to call them safe Indian medicinal plants.

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