

Indian Herbal Medicine- A Natural Cure to Asthma

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ABSTRACT

Asthma is one of the most common chronic respiratory disorders in the world. The adoption of western lifestyles and hasty urbanization has led to the increased prevalence which WHO estimates about 300 million people suffer from asthma and 2, 55,000 people died of asthma in 2011. Current therapeutic regimens used in pharmacotherapy of Asthma are not up to the mark to prevent the progression of various stages of asthma. Plants have always provided a basis for cure of variety of diseases and disorders with advantages like less cost, strength, effectiveness, better tolerance, more safety and less side-effect. Various herbal formulations have been developed that act as anti-asthmatics. The herbal alternatives have proved to be anti-inflammatory, bronchodilators, mast cell stabilizers, anti-allergic, anti-anaphylactic, etc that covers all components involved in the progression asthma.

Keywords: Chronic, Prevalence, Therapeutic regimens, Less Side-Effect, Herbal Formulations

INTRODUCTION

Being universal, role of plants have always stood a golden mark to exemplify the outstanding phenomenon of symbiosis. The existence of life in the universe is not endurable without the plants. The plants being in tremendous amount are associated with certain unique and a few common active principles known as secondary plant metabolites. These metabolites are referred to as organic compounds that are not directly involved in the normal growth, development or reproduction of organism. Unlike primary metabolites, absence of secondary metabolites doesn't cause immediate death, but is involved with the long-term impairment of the organism's survivability or aesthetics and sometimes represents no significant change at all.

According to World Health Organization (WHO), the herbal medicines have been defined as the finished, labeled medicinal products that contain active ingredients, aerial or underground parts of the plant or other plant material or combinations. For the assessment of safety, efficacy and quality of herbal medicines, specific set of guidelines has been set by World Health Organization (WHO). As per the estimation of WHO, around 80% of the world's population presently use herbal medicine for primary health care (WHO technical report series 1996).

The use of herbal medicines is as old as human civilization. Herbal medicine today is a major component in ayurvedic, homeopathic, naturopathic and other medicine systems. Its 80% use itself defines its harmless nature since the origin is entirely natural. The overlong use of herbal medicine has provided a basis to develop the formulations that are acceptable and consumable by living entities. With the advance and rapid growth in pharmaceutical market, one needs the methods that meet the urgent demand of people for medicinally useful herbal products. The increasing consumption of herbal medicines have proved that how

exceptional and elegant are plants for human lives. Each and every single part of the plant is being used over millennia like seed, leaf, stem, bark, roots, flowers, and twigs, etc, as antimicrobial, anti-asthmatic, anti-diabetic, analgesic, sedative, anti-inflammatory, antispasmodic, anti-anxiety, anti-fertility, and so on. The graceful and affable advantages of herbal medicines like eco-friendly nature, less cost, great strength, more safety, ready availability, better tolerance explains all itself. Disadvantages of herbal medicines includes not able to treat most emergency cases, accidents, risk with self dosing, and difficulty in standardizations (Atmakuri 2010).^[1] Seasonal variation of bioactive constituent in a plant hampers efficacy of the system.

The term "asthma" comes from the Greek meaning, "to breathe hard". According to the National Institute of Health (NIH 1997)^[2], asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. This chronic inflammation is associated with hyper responsiveness that leads to persistent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are associated with airflow obstruction within the lungs that is often reversible either spontaneously or with the treatment. According to WHO estimates, 300 million people suffer from asthma and 2, 55, 000 people died of asthma in 2005. It is estimated that there may be an additional 100 million persons with asthma by 2025. The rate of asthma increases as communities adopt western lifestyles and become urbanized. The regularity varies from region to region depending upon the clarity used for the diagnosis of asthma. The diagnosed asthma in adults is generally reported as 2.7 to 4.0% in most European countries, 12% in England and 7.1% in the U.S. in Australia, the prevalence is rather high (9.5 to 17.9%). Tristan da Cunha

Table 1: Herbal bronchodilators:

Sr.No.	Plant	Part used/ extract/ fraction	Major chemical constituent (s)	Reference
1.	<i>Artemisia caerulescens</i>	Aerial parts/Butanol Leaves/Ethanol	Quercitin, isorhamnetin	[10]
2.	<i>Alstonia scholaris</i>	Fruits/Methanol	Ditamine, Echitamine and Echitenines	[11]
3.	<i>Benincasa hispida</i>	Leaves/Ethanol	Triterpenes, Glycosides, Sterols Tectorigenin	[12]
4.	<i>Belamcanda chinensis</i>	Roots	Forskolin (Diterpenoid)	[13]
5.	<i>Coleus forskohli</i>	Leaves and root	Warifteine, - bisbenzylisoquinoline	[14]
6.	<i>Cissampelos sympodialis</i>	bark/Aqueous Stem Bark/Aqueous	alkaloid Phenolic glycosides	[15], [16]
7.	<i>Clerodendron serratum</i>	Fruits/Aqueous, Pet-ether, Benzene,	Glycoside, Steroids, Alkaloid,	[17], [18]
8.	<i>Elaeocarpus sphericus</i>	Acetone and ethanol Aerial/Alcohol extract/Ethyl-acetate Leaves	Flavanoids	[19]
9.	<i>Galphimia glauca</i>		Tetragalloylquinic acid, Quercitin	[20]
10.	<i>Ginkgo biloba</i>		Ginkgolides	[21]

Table 2: Herbal Mast Cell Stabilizers

Sr.No.	Plant	Part used/ extract/ fraction	Major chemical constituent (s)	Reference
	<i>Albizzia lebbek</i>	Stem bark/Aqueous Stem/Aqueous extract	Saponins	[22]
	<i>Aquillaria agallocha</i>	Leaves/Juice	Triterpenoids	[23]
	<i>Azadirachta indica</i>	Leaves/Ethanol	Nimbin, Nimbinine, Nimbandiol, Quercitin	[24]
	<i>Bacopa monniera</i>	Leaves/Ethanol	Bacosides, Alkaloids, Glycosides Anthraquinones, Flavanoids	[25]
	<i>Cassia alata</i>	Seeds Seeds/Glycosidal fraction	Gentiobiosides Anthraquinones, Betulinic acid	[26]
	<i>Cassia torosa</i>	Peels	Flavanoids	[27]
	<i>Cassia obtusifolia</i>	Wood oil Latex	Himacholol - amyryn, - amyryn	[28]
	<i>Citrus unshiu</i>		calotropin	[29]
	<i>Cedrus deodara</i>		(Triterpenoid)	[30]
	<i>Calotropis procera</i>	Rhizome	Tumerones, Curcuminoids	[31]
	<i>Curcuma longa</i>	Methanol extract Fruits/Ethanol Roots/Alcohol	— Saponins Inulolide- a new Sesquiterpene lactone	[32]
	<i>Drymaria cordata</i>		Flavanoidal glycosides	[33]
	<i>Gleditsia sinensis</i>	Leaves	Honokiol, Magnolol	[34]
	<i>Inula racemosa</i>	Bark/Aqueous Leaves/Aqueous	Myrcenol, Nerol, Eugenol Casticin, isoorientin, Chrysophenol D, Luteolin	[35] [36]
	<i>Mentha piperita</i>			[37]
	<i>Magnolia officinalis</i>	Leaves/Ethanol		[38]
	<i>Ocimum sanctum</i>			[39]
	<i>Vitex negundo</i>			[39]

is an unique example where more than half the population (56%) is reported to suffer from asthma. The current estimation in India for the disease is estimated to be about 15 million (A.N Aggarwal et al., 2006)^[31]. With all such outcomes that would harm the human system for obvious reasons, the subject of herbal and Ayurvedic drugs have regained its importance. The use of herbs is not new for the therapy of any disease but has been increased to such an extent that it has become the trustful part of the treatment.

There are tremendous examples of the herbs that have proved to be useful in the treatment of respiratory diseases especially in asthma.

Pharmacotherapy of asthma: A few years back when asthma emerged as an inflammatory disorder rather than primarily a bronchospastic disorder, the basic pharmacotherapy was switched from control of symptoms to control of underlying airway inflammation (Barns 1989)^[4]. According to guidelines of The National Asthma

Table 3: Herbal Anti-Allergics

Sr.No.	Plant	Part used/extract/fraction	Major chemical constituent(s)	Reference
	<i>Asiasarum sieboldi</i>	Roots/Methanol	Methyleugenol, gamma-asarone, Elemicin, Asarinin Saponins	[40]
	<i>Albizia lebbeck</i>	Stem bark/Aqueous	Alisol - monoacetate, Alismaketones-23- acetate and C 23- acetate	[41]
	<i>Alisma orientale</i>	Rhizomes/Aqueous, Methanol	Flavonoids	[42]
			Flavonoids, Pseudoguaninide, sesquiterpene lactones	
		Leaves	Osthol	
	<i>Camellia sinensis</i>	Aerial parts	Triterpenoid saponin	[43]
	<i>Centipeda minima</i>		Tetragalloylquinic acid, Quercitin	[44]
			Glycosides	[44]
			Solasodine	
			Ellagic acid, Tannins, Chebulagic acid	
	<i>Cnidium monnieri</i>	Fruits/Ethanol		[45]
	<i>Desmodium adscendens</i>	Aqueous		[46]
	<i>Galphimia glauca</i>	Aerial/Alcohol extract/ Ethyl-acetate		[47]
		Leaves		
	<i>Hydrangea macrophylla</i>	Roots/Alkaloidal fraction		[48]
	<i>Solanum xanthocarpum</i>	Fruits/Aqueous		[49]
	<i>Terminalia chebula</i>			[50]

Education and Prevention Program (NAEPP) for the diagnosis and management of asthma, the treatment should be based upon some goals like:

1. How to maintain normal pulmonary function.
2. How to maintain normal activity levels.
3. Prevent chronic as well as symptoms that would render therapy ineffective.
4. Prevent recurrent exacerbations.
5. Avoid adverse effects from medications.
6. Avoid any contraindications involved.

The pharmacotherapy of any disease depends upon the severity of the disease. The rate at which the disease has been developing ensures the management steps to be taken. If the asthma is in its initial stages, the management can be done on that level with mild doses, but when it becomes severe the preventive therapy needs to be used. The category of allopathic drugs used in asthma includes:

1. Bronchodilators:
 - A. -adrenergic agonists: e.g. Adrenaline, Ephedrine, Albuterol, Terbutaline, Salmeterol, Isoprenaline.
 - B. Methylxanthines: e.g. Theophylline, Aminophylline, Diprophylline, Proxophylline.
 - C. Anticholinergics: e.g. Atropine methonitrate, Ipratropium bromide, Tiotropium bromide.
- 2 Mast cell stabilizers: e.g. Cromolyn Sodium, Nedocromil Sodium.
- 3.Corticosteroids: e.g. Hydrocortisone, Prednisolone, Dexamethasone, Budesonide, Fluticasone propionate, Beclomethasone.

Bronchodilators: Bronchodilators reverse the airway obstruction in asthma patients. There is direct effect on airway smooth muscle. Nowadays only three types of

bronchodilators are in clinical use: -adrenergic agonists, methylxanthines, and anti-cholinergics.

-adrenergic agonists: Adrenergic drugs cause bronchodilation through receptor stimulation which increases cAMP formation in bronchial muscle cell resulting in relaxation. Adrenergic drugs are the mainstay of treatment of reversible airway obstruction but should be cautiously used in hypertensive, heart patients, etc. They are the fastest acting bronchodilators when inhaled. Adrenaline, + 1 + 2 agonist causes prompt but short lasting bronchodilation. The action is masked by dominant 2 mediated relaxation. In addition, adrenergic agonists increase mucus secretion from sub mucosal glands and ion transport across airway epithelium (Pavia et al 1980)^[5]

Methylxanthines: Since 1930, Theophylline and its compounds have been used to treat asthma. They act by various mechanisms including, Inhibition of phosphodiesterase, thereby increasing cAMP levels

Inhibition of calcium ion influx into smooth muscle
Prostaglandin antagonism

Stimulation of endogenous catecholamines
Adenosine receptor antagonism

Inhibition of release of mediators from mast cells and leukocytes.

Theophylline inhibits release of mediators from mast cells, increases mucociliary clearance and prevents the development of micro vascular leakiness as would an anti-inflammatory drug (Persson and Draco 1988)^[6]. It also inhibits some actions of T-lymphocytes, which may be relevant to control chronic inflammation of the airway.

Table 4: Herbal Anti-Inflammatory

Sr.No.	Plant	Part used/extract/fraction	Major constituent(s)	chemical	Reference
	<i>Aloe vera Tourn.ex Linn</i>	Leaves/Aqueous, Chloroform and ethanol	Anthraquinones, saponins and carbohydrate	sterols, and glycoside,	[51]
	<i>Asystasia gangetica</i>	Leaves/Methanol, acetate	Isoflavone dalhorinin		[52]
	<i>Bryonia laciniosa</i>	Leaves/Chloroform extract Oil	Flavanoids		[53]
	<i>Cinnamomun Zeylanicum</i>	Rhizomes	Eugenol, Cinnamic aldehyde and Tumerones, Curcuminoids	- terpeniol	-
	<i>Curcuma longa</i>	Heartwood	Flavanoids, Tannins Glycoside, Steroids,		[32]
	<i>Dalbergia odorifera</i>	Fruits/Aqueous, Benzene, Acetone and ethanol	Pet-ether, Alkaloid, Flavanoids		[54]
	<i>Elaeocarpus sphaericus</i>	Leaves/ethanol extract	Flavanoids		[19]
		Leaves/Aqueous	Myrcenol, Eugenol, Nerol,		
	<i>Nelsonia canescens</i>	Root/Aqueous extract	Ruscogenin and ophiopogonin D		[55]
	<i>Ocimum sanctum</i>	Leaves/Aqueous	Flavanoids, anthraquinones	Tannins,	[56]
	<i>Ophiopogon japonicas</i>	Leaves/Alkaloidal	Tylophorine		[57]
	<i>Pavetta crassipes</i>				[58]
	<i>Tylophora asthmatica</i>				[59]

Table 5: Herbsl Antispasmodic

Sr.No.	Plant	Part used/extract/fraction	Major constituent(s)	chemical	Reference
	<i>Asiasarum sieboldi</i>	Roots/Methanol	Methyleugenol, asarone, Elemicin, Aegelin,	gamma-Asarinin, Aegelemine,	[40]
	<i>Aegle marmelos</i>	Leaves/Ethanol	Aegeline		[60]
	<i>Asystasia gangetica</i>	Leaves/Methanol/Ethyl acetate	Isoflavone dalhorinin	glycoside,	[52]
	<i>Belamcanda chinensis</i>	Leaves/Ethanol	Tectorigenin		
	<i>Cissampelos glaberrina</i>	Leaves, Root bark/Aqueous	Warifteine, - bisbenzylisoquinoline		[13]
		Fruits/Ethanol	alkaloid		[15]
	<i>Cnidium monnieri</i>	Bark	Osthol		
	<i>Drymis winteri</i>	Aerial parts/Ethanol	Terpene		[61]
	<i>Ferula ovina</i>		Carvacrol, alpha- pinene, geranyl isovalerate and geranyl propionate		[62]
		Roots/Ethanol	Resins		[63]
	<i>Ferula sinica</i>	Alkaloidal fraction	Sesquiterpene lactone, Terpenoids		[64]
	<i>Saussurea leppa</i>	Aerial parts/Ethanol	-		[65]
		Ethanol	Flavanones		
	<i>Striga orobanchioids</i>				[66]
	<i>Thymus vulgaris</i>				[67]

The other derivatives of Theophylline are less effective like Acepihylline, Proxophylline (Weinberger 1984) [7].

Anticholinergics: These are the drugs which block the actions of acetylcholine on cholinergic effectors and in the CNS exerted through muscarinic receptors. They inhibit

reflex cholinergic bronchoconstriction and do not significantly block the direct effects of inflammatory mediators such as histamine and leukotrienes on bronchial smooth muscle and vessels. Anticholinergics usually are less effective as compared to adrenergic agonists. *Datura* plants rich in tropane alkaloids contain the muscarinic antagonist and were smoked for relief of asthma centuries ago. *Adhoda vasica* leaves when smoked do give relief to much patients due to presence of vasicine.

Now a days, Atropine and Ipratropium bromide are the most commonly available Anticholinergics. Atropine reduces mucociliary clearance in normal subjects and in patients with asthma and chronic bronchitis. Ipratropium bromide has been shown to decrease the effectiveness of voluntary cough on clearing mucus from the airways, which may affect its role in the treatment of patients who have excessive mucus production. Tiotropium bromide on the other hand shows approximately 10 fold more potency than Ipratropium and protects against cholinergic bronchoconstriction for more than 24 hours.

Mast cell stabilizers:

Cromolyn Sodium: This synthetic chromone derivative is an Egyptian herbal remedy. Release of mediators of asthma like histamine, LTs, PAF, interleukins etc. from mast cells as well as other inflammatory cells is prevented by this category of mast cell stabilizers. Cromolyn has variable inhibitory actions on other inflammatory cells including macrophages and eosinophils that may participate in allergic inflammation. It is used for prophylactic treatment and consequently needs to be taken

regularly. It is the first choice anti-inflammatory drug for children because it has few adverse effects (Bernstein 1985)^[8]. Nedocromil Sodium is the newer drug used for prophylaxis.

Corticosteroids: Corticosteroids inhibit the release of arachidonic acid metabolites and PAF from lungs and macrophages by enhancing the production of proteins called "lipocortin". Thus, they inhibit the formation of prostaglandins and leukotrienes. They potentially inhibit the accumulation of neutrophils, inhibit secretion of human pulmonary macrophages and leukotrienes, inhibit formation of interleukins (ILs) such as IL-1, IL-2, IL-3, and IL-5, inhibit degranulation and adherence of eosinophils; reduce number of circulating T-lymphocytes and formation of an IgE binding suppressive factor. They also inhibit release of ACTH and secretion of cortisol by a negative feedback effect on the pituitary gland. Several adverse effects are associated with them like hypertension, peptic ulceration, cataract, weight gain, fluid retention, and osteoporosis etc (Dajani et al 1981)^[9].

Newer targets in asthma therapy: The basic pharmacotherapy that we just discussed above for the asthma has certain limitations. With the help of current therapy we can achieve results but the severity of the disease would still remain up to certain level. First, there is no evidence that prevention is possible in susceptible patients and the cure for asthma is not known till now. Thus, patients are still at a high risk of symptoms and mortality remains a great threat. Secondly, adverse effects are there with the medications.

Table 6:Herbal Immunomodulators

Sr.No.	Plant	Part used/extract/fraction	Major chemical constituent(s)	Reference
	<i>Picrorhiza scrophulariiflora</i>	Rhizomes/Pet. Ether, Diethyl ether and methanol	Apocynin, androsin and picroside II	[68]
	<i>Trichilia glabra</i>	Leaf/Aqueous	Polysaccharides	[69]
	<i>Cedrela tubiflora</i>	Leaf/Aqueous	Gallic acid, polysaccharides	[70]
	<i>Ipomoea carnea</i>	Leaf /Aqueous	Nortropane alkaloids, calystegines 2	[71]
	<i>Withania somnifera</i>	Coded extracts	Phenolic compounds,	[72]
	<i>Clausena excauata</i>	Wood/Aqueous	furanocoumarins, flavanoids and carbazole alkaloid	[73]
	<i>Magnifera indica</i>	Bark/Alcohol, ether	Magniferin	
	<i>Cleome viscosa</i>	Aerial parts/Aqueous, ethanolic	Alkaloids, saponins	[74]
	<i>Plantago ovate</i>	Seeds/Aqueous	Polysaccharides glycosides	[75]
	<i>Typhae angustifolia</i>	Pollen/Ethanol	Phenolic compounds, flavones	[76]
	<i>Angelica sinensis</i>	Roots/Aqueous and ethanolic	Polysaccharides	[77]
	<i>Boerhaavia diffusa</i>	Roots/Ethanol	Alkaloids	[78]
	<i>Tephrosia purpurea</i>	Aerial parts/Ethanol	Flavanoids	[79]
				[80]

Cytokine inhibitors: Two humanized anti-IL-5 monoclonal antibodies, Sch-55700 and SB-240563 reduced blood eosinophil count for several weeks and prevented eosinophils recruitment into airways after allergen challenge in asthmatic patients. IL-5 inhibitor inhibited IL-5 mediated survival of eosinophils. IL-4 receptor antibodies inhibited allergen induced airway hyperresponsiveness.

Adhesion molecule antagonists: Eosinophils are thought to be necessary to interact with intra cellular adhesion molecule-1 (ICAM-1) for the recruitment of eosinophils into airways. Antibodies to ICAM-1 blocked both eosinophils recruitment and increase in airway reactivity. TXA2 inhibitors

Serabenast, Domitroban, and Ozagrel are the examples under this category. Ozagrel reduced cough sensitivity to capsaicin due to acetaldehyde.

Chemokine inhibitors: Eotaxin, a chemo-attractant secreted by inflamed lung tissue attracts eosinophils. The investigations are being going on to prove whether eosinophils are the major contributors to the pulmonary damage seen in asthma.

Why herbals?

There are many reasons to choose herbal medicine, but herbalism remains largely misunderstood by many consumers. Herbalism isn't about rejecting science, self-experimentation, or expecting nebulous "plant spirits" to cure terminal illnesses. It's about embracing the rock-solid union that occurs when ancient wisdom and modern science meet. Herbal medicine is a safe, sustainable, spiritually balanced, evidence-based alternative to the alienating form of medicine that pervades the modern era. This isn't to say that all herbs are, by default, completely safe. There is danger in automatically equating "natural" with "harmless". Some of the most toxic pharmaceutical drugs are derived from herbal extracts. To cite a few examples: foxglove (*digitalis*) is the source of a digitoxin (trade name Crystodigin), which is used to treat heart conditions This compound has an alarmingly narrow therapeutic index and can be either powerfully effective or deadly, *Datura stramonium* is a highly effective treatment for asthma symptoms when smoked, because it contains atropine, which act as an antispasmodic in the lungs. However, *Datura* is also an extremely powerful hallucinogen and overdoses of the tropane alkaloids present in it can result in hospitalization or death.

Classification of Herbal anti-asthmatics on the basis of mechanism of action: On the basis of mechanism of action, herbal anti asthmatics can be classified as follows under tables 1, 2, 3, 4, 5, and 6.

CONCLUSION

Herbal approaches have regained their popularity, with their efficacy and safety aspects being supported by controlled clinical studies. The herbal approaches have offered effective mast cell stabilizers like sodium cromolyn and sodium cromoglycate developed from khellin and anti-leukotriene products like—boswellic acids. Herbal approaches have given us the ample aspect to explore flora for the betterment and eradication of

various diseases. Ongoing research worldwide has provided valuable herbal alternatives and these herbs, have shown interesting results in various target specific biological activities such as bronchodilation, mast cell stabilization, anti-anaphylactic, anti-inflammatory, anti-spasmodic, anti-allergic, immunomodulatory and inhibition of mediators viz., leukotrienes, lipoxygenase, cyclooxygenase, platelet activating, phosphodiesterase and cytokine, in the treatment of asthma. Some herbal alternatives employed in these traditions are proven to provide symptomatic relief and assist in the inhibition of disease development as well. In nutshell, attempt should be made to develop such polyherbal formulations which not only act at particular sites of the pathophysiological cascade of asthma but also give us the vast scope for the treatment of asthma and subsequent clinical studies on them.

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