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Review

Pharmacological classification of herbal anti-asthmatics

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SUMMARY

Bronchial asthma is a major public health problem worldwide and the morbidity and mortality of asthma have increased in last few decades. There is high prevalence of usage of alternative traditional system of medicines for the treatment of asthma. Large numbers of medicinal plant preparations have been reported to possess anti-asthmatic effects. Plant cells are now considered to be the chemical factories synthesizing a large variety of chemical compounds. Further, Ayurvedic system of medicine has an elaborate description of asthma from the earliest times describing it as '*Shwasa*' meaning disease pertaining to breathing. This review classifies the anti-asthmatics herbs based on the possible mechanism of action reported. Thus, these plants can be used to obtain a polyherbal formulation which contains various herbs acting at particular sites of the pathophysiological cascade of asthma for prophylaxis as well as for the treatment of asthma.

Key words: Anti-asthmatics herbs; Asthma

INTRODUCTION

Primary respiratory diseases are responsible for a major burden of morbidity and ultimately deaths and lungs are often affected in multi-system diseases. Bronchial asthma is a major public health problem worldwide and the morbidity and mortality of asthma have increased in last few decades. The past decade has witnessed phenomenal increases in the incidences of asthma, asthma-related deaths and hospitalization. An estimated 12 million persons in United States have asthma. India has an estimated 40 million asthmatics (WHO Fact Sheet, 2000). The activation of cells bearing allergen-specific IgE initiates the *early phase reaction*. It is characterized primarily by the rapid activation of airway mast cells and macrophages. The activated cells rapidly release pro-inflammatory mediators such as histamine, eicosanoids and reactive oxygen species that induce contraction of airway smooth muscle, mucus secretion and vasodilatation. Inflammatory mediators induce microvascular leakage with exudation of plasma in the airways. Together these effects contribute to airflow obstruction. The second, *late-phase response*, i.e. the delayed response, occurs 6 to 9 h after allergen provocation and involves the recruitment and activation of eosinophils, $CD4^+$ T cells, basophils, neutrophils and macrophages. The activated T-lymphocytes also direct the release of inflammatory mediators from eosinophils, mast cells and lymphocytes. In addition, the subclass 2 helper T-lymphocytes

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subset of activated T-lymphocytes produces interleukin (IL)-4, IL-5 and IL-13. IL-4 in conjunction with IL-13 signals the switch from IgM to IgE antibodies. IL-5 activates the recruitment and activation of eosinophils. This phase is in essence a progressing inflammatory reaction. Regardless of the triggers of asthma, the repeated cycles of inflammation in the lungs with injury to the pulmonary tissues followed by repair may produce long-term structural changes ("remodeling") of the airways (Fireman, 2003).

Current pharmacotherapy of asthma comprises the use of bronchodilators (selective β_2 agonists, xanthines and anti-cholinergics), anti-inflammatory agents (mast cell stabilizers and corticosteroids), leukotriene antagonists and lipoxygenase inhibitors. Increase in bronchial hyperresponsiveness (Schayck *et al.*, 1990), diminish the duration of bronchoprotective effects is seen with β_2 agonists. Xanthines have narrow therapeutic index. Anti-cholinergics like ipatropium incompletely protects against bronchoconstriction induced by histamine, cold air, allergen, exercise, prostaglandins, bradykinin, serotonin and other mediators. Mast cell stabilizers are not indicated for the relief of acute symptoms of asthma as they don't have bronchodilator effects. Long term complications are seen with corticosteroids. Further, none of these agents is able to act at all the stages of asthma and thus do not give complete cure of the disease. As a result, there is high prevalence of usage of alternative traditional system of medicines for the treatment of asthma. Ayurveda offers a unique insight into comprehensive approach to asthma management through proper care of the respiratory tract. Large numbers of medicinal plant preparations have been reported to possess anti-asthmatic effects. Plant cells are now considered to be the chemical factories synthesizing a large variety of chemical compounds. The wide range of structures of the plant constituents, which appear to be the active anti-asthmatic principles, suggests different sites of action within the body. This article is intended to classify anti-asthmatic herbs based on the possible mechanism of action reported.

INDIAN AYURVEDIC CONCEPT OF ASTHMA

Ayurveda is one of the major traditional medicinal systems from India. The ancient Ayurvedic system of medicine has an elaborate description of this disease from the earliest times. *Shwasa* word in normal terminology means respiration. In the present context, *Shwasa* means disease pertaining to breathing. According to Ayurveda, different types of *Shwasa* (asthma) are *Kshudra Shwasa, Maha Shwasa, Urdhva Shwasa, Chhinna Shwasa, Tamak Shwasa.*

Kshudra Shwasa

Because of vititation of *vayu* (air) in the alimentary tract, minor dyspnoea is caused. This condition does not give much pain; it does not interfere in the course of food and breathing. It does not disturb the sensory organs. This condition is mainly because of excessive intake of ruksha eatable and excessive exercise. It is, however, not much harmful to the body as compared to the other types of *Shwasa*. In allopathic system of medicine, such types of conditions are grouped under the exertional dyspnoea. Both the systems of medicine consider this condition to be easily curable.

Maha Shwasa

This condition is caused because of disturbance in respiratory movement of *Vayu*. The patient feels great obstruction in respiration, breaths without break with a very loud and long stertore making a sound like intoxicated bull. The patient looses all senses of understanding and knowledge, having restless look in eyes, distorted voice, going into semi-comatose condition now and then. In such a condition, the patient is not able to pass urine and faces both. In this condition, usually the voluntary control disappears and the wheezing sounds are audible from a distance. The allopathic system of medicine indicates such conditions in Biot's breathing which is generally found in heart, kidney and brain disorders as a complication. Ayurveda describes it as a dyspnoea major where the patient generally succumbs to it.

Urdhva Shwasa

Under this condition the expiratory phase is prolonged and the inspiratory process is just insignificant. Mouth and the respiratory tract get obstructed with *Kaph.* The patient's eyes are turned upwards and are restless. The patient is almost obvious to his surroundings. Affected with severe pain, the patient enters into stupor. Having provoked expiratory process and obstruction in inspiration, the patient suffers from delusions and senselessness. Such condition is described by Ayurvedic physicians as harmful for the life. Such conditions are described by the allopathic system of medicine under stertorous breathing and falling of inspiration. Such a condition can be found in pneumonia, abscesses of the lungs, gangrene or acute inflammation in the lungs and also in different types of epilepsy.

Chhinna Shwasa

Under this condition, the whole of the breathing system is depressed. The patient has to breathe with full force and with great difficulty. The patient breaths with interruption. The patient suffers from constipation, excessive sweating, repeated fainting, burning and retention of urine, having eyes full of tears and entering unconsciousness every now and then having dry mouth. The patient normally breaks down with such a difficult breath ultimately losing his life. The allopathic system of medicine groups such condition under interrupted respiratory dyspnoea (Cheyne-stoke's respiration).

Tamaka Shwasa

Acharya classified *Tamak Shwasa* in two conditions viz. *Pratamaka Shwasa* and *Santamak Shwasa*. Febrile dyspnoea appears in a patient with fever and fainting in *Pratamaka Shwasa*. It is excited by misperistalsis, inhalation of dust, indigestion, old age or debilitated condition or the suppression of natural urges. *Santamak Shwasa* or cardiac asthma is greatly aggravated during night and alleviated by cold medicines and in which the patient feels as if he is submerged in a sea of darkness.

ANTI-ASTHMATIC HERBS

Many Ayurvedic plants have been described to be useful in the treatment of various bronchial disorders including bronchial asthma. The use of medicinal plants and natural products increased dramatically in the last two decades in all over the world. More than 400 medicinal plant species have been used ethnopharmacologically and traditionally to treat the symptoms of asthmatic and allergic disorders worldwide.

CLASSIFICATION OF ANTI-ASTHMATIC HERBS BASED ON MECHANISM OF ACTION

Some herbal alternatives employed in asthma are proven to provide symptomatic relief and assist in the inhibition of disease development as well. These herbs therefore have multifaceted roles to play in the management of asthma suggesting different sites of action within the body. Based on the possible mechanism of action reported, plant anti-asthmatics may be classified as follow.

Bronchodilators

Adhatoda vasica, Albizzia lebbeck, Artemisia caerulescens, Belamcanda chinensis, Benincasa hispida, Cissampelos sympodialis, Clerodendron serratum, Coleus forskohlii, Elaeocarpus spharicus, Galphimia glauca, Gardenia latifolia, Ginko biloba, Ocimum sanctum, Passiflora incarnate, Pavetta crassipes, Picrorrhiza kurroa, Sarcostemma brevistigma, Tephrosia purpurea, Tylophora indica, Vitex negundo (Table 1).

Mast cell stabilizers

Achyranthes aspera, Albizzia lebbeck, Allium cepa, Aquillaria agallocha, Azadirachta indica, Bacopa monniera, Bidens parviflora, Calotropis procera, Cassia

Table 1. Bronchodilators

Name of plant	Part used/Extract/Fraction	Major chemical constituent (s)	References
Adhatoda vasica	Leaves, roots	Alkaloids	Paliwa *et al*, 2000
Albizzia lebbeck	Stem bark/Aqueous	Saponins	Tripathi and Das, 1977
Artemisia caerulescens	Aerial parts/Butanolic	Quercetin, isorhamnetin	Moran *et al.*, 1989
Belamcanda chinensis	Leaves/Ethanolic	Tectorigenin	Singh *and* Agrawal, 1990
Benincasa hispida	Fruits/Methanolic	Triterpenes, glycosides, sterols	Kumar and Ramu, 2002
Cissampelos sympodialis	Leaves and root bark/ Aqueous	Warifteine, α-bisbenzyliso-quinoline alkaloid	Thomas *et al.*, 1995; Thomas *et al.*, 1997; Cortes *et al.*, 1995
Clerodendron serratum	Stem bark/Aqueous	Phenolic glycoside	Gupta, 1968; Gupta and Tripathi, 1973
Coleus forskohlii	Roots	Forskolin (diterpenoid)	Marone *et al.*, 1987
Elaeocarpus spharicus	Fruits/aqueous, pet-ether, benzene, acetone and ethanol	Glycoside, steroids, alkaloid, flavanoids	Singh *et al.*, 2000
Galphimia glauca	Aerial/alcoholic extract/ ethyl-acetate	Tetragalloylquinic acid, quercetin	Campos *et al.*, 2001
Gardenia latifolia	Bark	Saponins	Gupta, 1974
Ginko biloba	Leaves	Ginkgolides	Puglisi *et al.*, 1988
Ocimum sanctum	Leaves/Ethanolic	Myrcenol, nerol, eugenol	Singh and Agrawal, 1991
Passiflora incarnata	Leaves/Methanolic		Dhawan *et al.*,, 2003
Pavetta crassipes	Leaves/Aqueous	Flavanoids, tannins, anthraquinones	Amos *et al.*, 1998
Picrorrhiza kurroa	Roots	Androsin	Stuppner *et al.*, 1991, 1993
Sarcostemma brevistigma	Twigs/Alkaloidal fraction	Bregenin	Saraf and Patwardhan, 1988b
Tephrosia purpurea	Aerial parts/Ethanolic extract	Flavanoids, tephrosin	Gokhale *et al.*, 2000
Tylophora indica	Leaves/Alkaloidal fraction	Tylophorine	Nayampalli and Sheth, 1979
Vitex negundo	Leaves/Ethanolic	Casticin, isoorientin, chrysophenol D, luteolin	Nair and Saraf, 1995

alata, Cassia obtusifolia, Cassia torosa, Cedrus deodara, Citrus unshiu, Clerodendron serratum, Cnidium monnieri, Coleus forskohlii, Crinum glaucum, Elaeocarpus sphaericus, Gleditsia sinensis, Impatiens textori, Inula racemosa, Magnolia officinalis, Mentha piperita, Ocimum sanctum, Picrorrhiza kurroa, Siegesbeckia glabrescence, Solanum xanthocarpum, Striga orobanchioids, Tephrosia purpurea, Terminalia chebula, Tinospora cordifolia, Tylophora asthmatica, Vitex negundo (Table 2).

Anti-allergic agents

Adhatoda vasica, Albizzia lebbeck, Alisma orientale, Aquillaria agallocha, Asiasarum sieboldi, Camellia sinensis, Centipeda minima, Citrus unshiu, Cnidium monnieri, Crinum glaucum, Curcuma longa, Dalbergia odorifera, Desmodium adscendins, Galphimia glauca, Ginko biloba, Gleditsia sinensis, Hydrangea macrophylla, Inula racemosa, Magnolia officinalis, Sarcostemma brevistigma, Siegesbeckia glabrescence, Solanum xanthocarpum, Terminalia chebula, Vitex negundo (Table 3).

Anti-inflammatory agents

Asystasia gangetica, Calotropis procera, Curcuma longa, Dalbergia odorifera, Elaecarpus spharicus, Eucalyptus globules, Ocimum sanctum, Pavetta crassipes, Tylophora asthmatica (Table 4).

Table 2. Mast cell stabilizers

Name of plant	Part used/Extract/Fraction	Major chemical constituent (s)	References
Achyranthes aspera	Aerial parts/Aqeous	Oleanolic acid	Agrawal *et al.*, 2003
Albizzia lebbeck	Stem bark/Aqueous	Saponins	Tripathi *et al.*, 1979
Allium cepa	Bulbs/Juice	α and β unsaturated thiosulphinates	Johri *et al.*, 1985
Aquillaria agallocha	Stem/Aqueous extract	Triterpenoids	Kim *et al.*, 1997
Azadirachta indica	Leaves/Juice	Nimbin, nimbinine, nimbandiol, quercetin	Acharya *et al.*, 2003
Bacopa monniera	Leaves/Ethanolic	Bacosides, alkaloids, glycosides	Samiulla *et al.*, 2001
Bidens parviflora	Aerial parts	Glycosides	Wang *et al.*, 2001
Calotropis procera	Latex	α-amyrin, β-amyrin calotropin (triterpenoid)	Kumar and Basu, 1994
Cassia alata	Leaves/Ethanolic	Anthraquinones, flavanoids	Palanichamy *et al.*, 1991
Cassia obtusifolia	Seeds/Glycosidal fraction	Anthraquinones, betulinic acid	Kitanaka *et al.*, 1998
Cassia torosa	Seeds	Gentiobiosides	Kanno *et al.*, 1999
Cedrus deodara	Wood oil	Himacholol	Shinde *et al.*, 1999
Citrus unshiu	Peels	Flavanoids	Kim *et al.*, 1999
Clerodendron serratum	Bark/Aqueous	Phenolic glycoside	Gupta, 1968
Cnidium monnieri	Fruits/Ethanolic	Osthol	Chen *et al.*, 1988
Coleus forskohlii	Roots	Forskolin (diterpenoid)	Marone *et al.*, 1987
Crinum glaucum	Leaves/Aqueous	Alkaloids, lycorine, crinamine	Okpo and Adeyemi, 2002
Curcuma longa	Rhizome	Tumerones, curcuminoids	Ammon and Wahl, 1991
Elaeocarpus spharicus	Fruits/Aqueous, pet-ether, benzene, acetone and ethanol	Glycoside, steroids, alkaloid, flavanoids	Singh *et al.*, 2000
Gleditsia sinensis	Fruits/Ethanolic	Saponins	Dai *et al.*, 2002
Impatiens textori	Flowers/Ethanolic	Apigenin, luteolin, chrysoeriol	Ishiguro *et al.*, 2000
Inula racemosa	Roots/Alcoholic	Inulolide-a new sesquiterpene, lactone	Srivastava *et al.*, 1999
Magnolia officinalis	Bark/Aqueous	Honokiol, magnolol	Shin *et al.*, 2001b
Mentha piperita	Leaves	Flavanoidal glycosides	Inoue *et al.*, 2002
Ocimum sanctum	Leaves/Aqueous	Myrcenol, nerol, eugenol	Sen, 1993
Picrorrhiza kurroa	Roots	Androsin	Stuppner *et al.*, 1991
Siegesbeckia glabrescence	Aerial parts/Aqueous		Kang *et al.*, 1997
Solanum xanthocarpum	Roots/Alkaloidal fraction	Solasodine	Chitravanshi *et al.*, 1990
Striga orobanchioids	Aerial parts/ Ethanolic		Harish *et al.*, 2001
Tephrosia purpurea	Aerial parts/Ethanolic extract	Flavanoids, tephrosin	Gokhale *et al.*, 2000
Terminalia chebula	Fruits/Aqueous	Ellagic acid, tannins, chebulagic acid	Shin *et al.*, 2001a
Tinospora cordifolia	Stem/Aqueous	Tinosporin	Nayampalli *et al.*, 1986
Tylophora asthmatica	Leaves/Alkaloidal	Tylophorine	Geetha *et al.*, 1981
Vitex negundo	Leaves/Ethanolic	Casticin, isoorientin, chrysophenol D, luteolin	Nair *et al.*, 1994

Anti-spasmodics

Aegle marmelos, Asiasarum sieboldi, Asystasia gangetica, Bacopa monniera, Belamcanda chinensis, Cissampelos glaberrina, Clerodendron serratum, Cnidium monnieri,

Table 3. Anti-allergics

Name of plant	Part used/Extract/Fraction	Major chemical constituent (s)	References
Adhatoda vasica	Leaves/Methanolic	Vasicinol, vasicine	Muller *et al.*, 1993
Albizzia lebbeck	Stem bark/Aqueous	Saponins	Baruah *et al.*, 1997
Alisma orientale	Rhizomes/Aqueous, methanolic	Alisol B monoacetate, alismaketones-B 23-acetate and -C 23-acetate	Kubo *et al.*, 1997
Aquillaria agallocha	Stem/Aqueous extract	Triterpenoids	Kim *et al.*, 1997
Asiasarum sieboldi	Roots/Methanolic	Methyleugenol, γ-asarone, elemicin, asarinin	Hashimoto *et al.*, 1994
Camellia sinensis	Leaves	flavanoids	Suzuki *et al.*, 2000
Centipeda minima	Aerial parts	flavanoids, pseudoguainolide, sesquiterpene lactones	Wu *et al.*, 1985
Citrus unshiu	Peels	flavanoids	Kim *et al.*, 1999
Cnidium monnieri	Fruits/Ethanolic	osthol	Matsuda *et al.*, 2002
Crinum glaucum	Leaves/Aqueous	Alkaloids, lycorine, crinamine	Okpo *and* Adeyemi, 2002
Dalbergia odorifera	Heart Wood	Flavanoids, tannins	Chan *et al.*, 1998
Desmodium adscendins	Aqueous	Triterpenoid saponin	Addy, 1989
Galphimia glauca	Aerial/Alcoholic extract /Ethyl-acetate	Tetragalloylquinic acid, quercetin	Neszmelyi *et al.*, 1993
Ginko biloba	Leaves	Ginkgolides	Touvay *et al.*, 1985
Gleditsia sinensis	Fruits/Ethanolic	Saponins	Dai *et al.*, 2002
Hydrangea macrophylla	Leaves	Glycosides	Matsuda *et al.*, 1999
Inula racemosa	Roots/Alcoholic	Inulolide-a new Sesquiterpene lactone	Srivastava *et al.*, 1999
Magnolia officinalis	Bark/Aqueous	Honokiol, magnolol	Shin *et al.*, 2001b
Sarcostemma brevistigma	Twigs/Alkaloidal fraction	Bregenin	Saraf and Patwardhan, 1988a
Siegesbeckia glabrescence	Aerial parts/Aqueous		Kang *et al.*, 1997
Solanum xanthocarpum	Roots/Alkaloidal fraction	Solasodine	Chitravanshi *et al.*, 1990
Terminalia chebula	Fruits/Aqueous	Ellagic acid, Tannins chebulagic acid	Shin *et al.*, 2001a
Vitex negundo	Leaves/Ethanolic	Casticin, isoorientin chrysophenol D, luteolin	Nair and Saraf, 1995

Coleus forskohlii, Crinum glaucum, Drymis winteri, Ferula ovina, Ferula sinica, Pavetta crassipes, Saussurea leppa, Striga orobanchioids, Thymus vulgaris, Tylophora asthmatica (Table 5).

Lipoxygenase inhibitors
Allium cepa, Boswellia serrata, Coleus forskohlii, Lonicera japonica (Table 6).

Platelt activating factor (PAF) inhibitors
Allium cepa, Galphimia glauca, Impatiens textori, Picrorrhiza kurroa (Table 6).

Cyclooxygenase inhibitor
Allium cepa (Table 6).

SOME COMMONLY USED ANTI-ASTHMATIC HERBS

Adhatoda vasica

The medicinal properties of *Adhatoda vasica* Nees (natural order: Acanthaceae), called *Vasa* or *Vasaka* has been recommended by Ayurvedic physicians for the management of various types of respiratory disorders. The leaves of the plant were found to

Table 4. Anti-inflammatory agents

Name of plant	Part used/Extract/Fraction	Major chemical constituent (s)	References
Asystasia gangetica	Leaves/Methanolic, ethyl acetate	Isoflavone glycoside, dalhorinin	Akah *et al.*, 2003
Calotropis procera	Latex	α-amyrin, β-amyrin calotropin (triterpenoid)	Kumar and Basu, 1994
Curcuma longa	Rhizomes	Tumerones, curcuminoids	Ammon and Wahl, 1991
Dalbergia odorifera	Heart Wood	Flavanoids, tannins	Chan *et al.*, 1998
Elaeocarpus spharicus	Fruits/Aqueous, pet-ether, benzene, acetone and ethanol	Glycoside, steroids, alkaloid, flavanoids	Singh *et al.*, 2000
Ocimum sanctum	Leaves/Aqueous	Myrcenol, nerol, eugenol	Singh and Agrawal, 1991
Pavetta crassipes	Leaves/Aqueous	Flavanoids, tannins, anthraquinones	Amos *et al.*, 1998
Tylophora asthmatica	Leaves/Alkaloidal	Tylophorine	Manez, 1990

Table 5. Anti-spasmodic agents

Name of plant	Part used/Extract/Fraction	Major chemical constituent (s)	References
Aegle marmelos	Leaves/Ethanolic	Aegelin, aegelemine, aegeline	Arul *et al.*, 2004
Asiasarum sieboldi	Roots/Methanolic	Methyleugenol, γ-asarone, elemicin, asarinin	Hashimoto *et al.*, 1994
Asystasia gangetica	Leaves/Methanolic, ehyl acetate	Isoflavone glycoside, dalhorinin	Akah *et al.*, 2003
Bacopa monniera	Leaves/Ethanolic	Bacosides, alkaloids, glycosides	Dar and Channa, 1997; Channa *et al.*, 2003
Belamcanda chinensis	Leaves/Ethanolic	Tectorigenin	Singh and Agrawal, 1990
Cissampelos glaberrina	Leaves, root bark/ Aqueous	Warifteine, α-bisbenzylisoquinoline alkaloid	Thomas *et al.*, 1995; Cortes *et al.*, 1995
Clerodendron serratum	Stem bark/Aqueous	Phenolic glycoside	Gupta, 1968
Cnidium monnieri	Fruits/Ethanolic	Osthol	Chen *et al.*, 1988
Coleus forskohlii	Roots	Forskolin (diterpenoid)	Marone *et al.*, 1987
Crinum glaucum	Leaves/Aqueous	Alkaloids, lycorine, crinamine	Okpo and Adeyemi, 2002
Drymis winteri	Bark	Terpene	El-Sayah *et al.*, 1998
Ferula ovina	Aerial parts/Ethanolic	Carvacrol, α-pinene, geranyl isovalerate and geranyl propionate	Khalil *et al.*, 1990
Ferula sinica	Roots/Ethanolic		Aqel *et al.*, 1991a
Pavetta crassipes	Leaves/Aqueous	Flavanoids, tannins, anthraquinones	Amos *et al.*, 1998
Saussurea leppa	Alkaloidal fraction	Sesquiterpene lactone, terpenoids	Dutta *et al.*, 1968
Striga orobanchioids	Aerial parts/Ethanolic		Harish *et al.*, 2001
Thymus vulgaris	Ethanolic	Flavanones	Meister *et al.*, 1999
Tylophora asthmatica	Leaves/Alkaloidal	Tylophorine	Haranath *et al.*, 1975; Udapa *et al.*, 1991

contain an essential oil and the quinazoline alkaloids vasicine, vasicinone and deoxyvasicine, which found to possess respiratory stimulant activity (Amin and Mehta, 1959). Of the two alkaloids, vasicinone was found to be more potent than vasicine, with potential anti-asthmatic activity comparable to that of disodium cromoglycate (Atal and Kapur, 1982). Subacute toxicity of the alcoholic extract of leaves revealed that LD_{50} of the extract by i.p. route was 581 mg/kg. The acute toxicity studies showed that extract was

Table 6. Miscellaneous agents

Name of plant	Part used/Extract/Fraction	Major chemical constituent (s)	References
Lipoxygenase inhibitors			
Allium cepa	Bulbs/Juice	α and β unsaturated thiosulphinates	Bayer *et al.*, 1989
Boswellia serrata	Gum resin/Ethanolic extract	Bosewellic acid	Ammon *et al.*, 1991
Coleus forskohlii	Roots	Forskolin (diterpenoid)	Marone *et al.*, 1987
Platelet Activating Factor (PAF) inhibitors			
Allium cepa	Bulbs/Juice	α and β unsaturated thiosulphinates	Dorsch *et al.*, 1987
Galphimia glauca	Aerial/Alcoholic extract/ Ethyl-acetate	Tetragalloylquinic acid, quercetin	Neszmelyi *et al.*, 1993
Impatiens textori	Flowers/Ethanolic	Apigenin, luteolin, chrysoeriol	Ueda *et al.*, 2003
Picrorrhiza kurroa	Roots	Androsin	Stuppner *et al.*, 1991
Cyclooxygenase inhibitor			
Allium cepa	Bulbs/Juice	α and β unsaturated thiosulphinates	Bayer *et al.*, 1989

not lethal up to the dose of 100 mg/kg, i.p. and up to 4 g/kg (Rao and Krishnaiah, 1981). The LD_{50} of alcoholic extract of the aerial parts of the plant is reported to be more than 1,000 mg/kg, i.p. in mice (Bhakuni *et al.*, 1990).

Albizzia lebbeck

Albizzia lebbeck has been used by Ayurvedic physicians for centuries in the management of asthma. The effect of decoction of the bark and flower were studied for its anti-asthmatic and anti-anaphylactic activity. The decoction protected the guinea pig against histamine and acetylcholine-induced bronchospasm (Tripathi and Das, 1977). The decoction of the bark of *Albizzia lebbeck* was also studied on degranulation rate of sensitized peritoneal mast cells of albino rats when challenged with antigen (horse serum) and triple vaccine was used as adjuvant. Disodium cromoglycate (DCG) and prednisolone were used for comparison. Studies revealed the significant cromoglycate like action on the mast cells, which has been attributed to the heat-sable and water-soluble saponins present in the plant (Tripathi *et al.*, 1979). Crude extract of seeds and a pure saponin fraction of Albizzzia have also been studied on the mast cells in the mesentery and peritoneal fluid of rats subject to anaphylaxis (Johri *et al.*, 1985). The Maximum Tolerated Dose (MTD) of 50% ethanolic extracts of the root, the pods and stem bark was 25, 50 and 100 mg/kg i.p. in mice (Dhar *et al.*, 1968).

Ammi visnaga

Ammi visnaga, conventional anti-asthmatic compounds, such as sodium cromolyn and sodium cromoglycate, were developed from analogs of the naturally occurring furanochromone khellin (visammin), found in this Asian plant. Other furanochromones, such as visnagin, khellol and khellinol have also been identified in the extracts of *Ammi visnaga*. Khellin has been found to be an effective smooth muscle relaxant with an oral LD_{50} of 80 mg/kg in rats. Controlled clinical studies have verified the anti-allergic action of sodium cromolyn, which is currently used in the treatment of allergic rhinitis, asthma and allergic gastrointestinal reactions (Johri *et al.*, 1985). The LD_{50} of aqueous extract of Ammi visnaga of intraperitoneal (i.p.) and oral administration was 3.6 and 10.1 g/kg, respectively (Juoad *et al.*, 2002).

Boswellia serrata

The gum resin of *Boswellia serrata*, known in Indian Ayurvedic system of medicine as Salai guggal, contains boswellic acid. It specifically inhibits leukotriene biosynthesis by inhibiting the activity of the enzymes, which leads to their formation. It also proved to be the most potent inhibitors of the classical component pathway of the inflammatory response. Boswellic acids also decrease the activity of human leukocyte elastase (HLE), which may be involved in the pathogenesis of emphysema. Boswellic acids are therefore effective in the prevention and or control of inflammatory processes, which are typically characterized by increased leukotriene formation (Safayhi *et al.,* 1997). Boswellia specifically blocks the synthesis of pro-inflammatory 5-lipoxygenase products, including leukotrieneB_4 (Ammon *et al.,* 1991), which cause bronchoconstriction, chemotaxis, and increased vascular permeability. Therefore Boswellic acid might be used for their anti-allergic/anti-asthmatic activity (Ammon *et al.,* 1991). LD_{50} of alcoholic extract of gum resin was more than 2 g/kg, p.o. and i.p. in mice (Atal *et al.,* 1981; Singh and Atal, 1986). The Maximum Tolerated Dose (MTD) values of the root, fruit and stem extracts were 50, 500 and 250 mg/kg i.p. respectively in mice (Dhar *et al.,* 1968).

Clerodendron serratum

Clerodendron serratum is widely used to alleviate the symptoms of respiratory conditions, including asthma. The root bark yields a phenolic glycoside (Vasavada *et al.,* 1967) and about 10% D-mannitol (Kirtikar and Basu, 1993). A sterol glycoside mixture was isolated. Hydrolysis of the crude sapogenin mixture of the bark yielded three major triterpenoid constituents-oleonolic acid, queretoroic acid and serratagenic acid. Gamma-sitosterol has also been isolated (Gupta and Gupta, 1967). It blocked the histamine-induced contractions of tracheal preparations from guinea pig without affecting the response to acetylcholine (Vasavada *et al.,* 1967). It is reported that the continuous daily administration of the plant extract to sensitized guinea pig, gradually developed protection against anaphylaxis. The saponin also disrupted rat peritoneal mast cells and blocked the effect of horse serum antigen. Saponins from the root caused disruption of cells of rat mesentery in a dose related manner (up to a dose of 40 μg), and the maximum disruption effect was exerted in 30 min (Gupta *et al.,* 1971).

Curcuma longa

Curcuma longa, by virtue of its antioxidant properties is an effective anti-asthmatic agent. It has been employed by Ayurvedic practitioners since ancient times in the treatment of respiratory disorders. The active ingredients, the curcuminoids, are potent inhibitors of inflammatory prostaglandins. The overall anti-inflammatory action of curcuminoids is also related to their well-known antioxidant properties. For example, curcumin inhibited lipid peroxidation, a phenomenon associated with antioxidant as well as anti-inflammatory activities. Toxicity studies of *Curcuma longa* revealed that acute doses of 0.5, 1.0, and 3 g/kg body weight and the chronic doses of 100 mg/kg/day of ethanolic extract were found to be non-toxic (Quereshi *et al.,* 1998).

Ephedra sinica (Ma Huang)

Ephedra sinica, a native plant species of China is the original source of the alkaloid ephedrine. Ephedrine stimulates the sympathetic nervous system, and thereby helps in the management of allergic conditions. The compound also helps to relieve the bronchial spasm that underlies conditions such as asthma and emphysema through this effect. As ephedrine use is now restricted in several countries, alternatives such as *Citrus aurantium* (containing synephrine) are now being explored in the management of respiratory conditions. Other ancillary alternative phytonutrients useful in asthma include licorice which has been used as an expectorant. Phytonutrients are often included in anti-asthmatic formulations, with antioxidants such as N-acetylcysteine which prevent mucus build-up and inhibit free radical mediated disease processes. Oral LD_{50} of d-pseudoephedrine and 1-ephedrine was 1,550 (1,360 - 1,767) mg/kg and 1,400 (1,102 - 1,778) mg/kg, respectively. LD_{50} of d-pseudoephedrine and 1-ephedrine given intraperitoneally was 245 (229 - 262) mg/kg and 300 (259 - 348) mg/kg, respectively (Akiba *et al.*, 1979).

Picrorhiza kurroa

Picrorhiza kurroa Royle is a perennial herb that grows in the Himalayas in Asia, at altitudes of 9,000 - 15,000 feet above sea level. It belongs to the Natural Order *Scrophulariaceae*. The underground parts of this plant have been used in the traditional Indian systems of medicine since ancient times to treat liver troubles and bronchial problems (Kirtikar and Basu, 1993). Several biologically active principles, particularly glycosides have been identified in extracts obtained from *Picrorhiza kurroa*. Of these a mixture of the iridoid glycosides picroside I and kutkoside has been found to be an efficient liver protectant. "Androsin", a phenolic glycoside isolated from *Picrorhiza kurroa*, has been attributed with anti-asthmatic properties (Dorsch *et al.*, 1991).

The authors suggest that androsin may act by depressing the activity of PAF which plays a major role in the pathogenesis of bronchial asthma. PAF has been shown to provoke long-lasting inflammatory responses in the lungs. This leads to bronchial hypereactivity and subsequent bronchial obstruction (Dorsch *et al.*, 1991). Another study suggests that *Picrorhiza kurroa* extracts possess anti-allergic activity, probably mediated through mast cell stabilizing activity (Mahajani and Kulkarni, 1977).

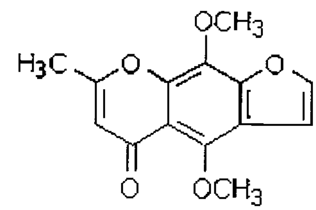

Fig. 1. Chemical structure of khellin.

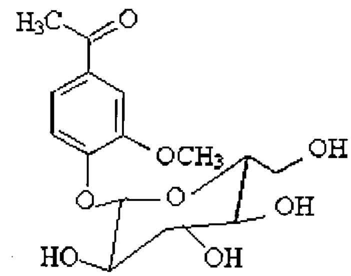

Fig. 2. Chemical structure of androsin.

Tylophora asthmatica (syn. *Tylophora indica*)

The medicinal properties of the plant *Tylophora asthmatica* have been known since ancient times. Powder from the dried leaves, root powder, and decoction of the leaves or infusion of the root bark have been used traditionally in the treatment of respiratory affactions such as chronic bronchitis and asthma (Nadkarni, 1976). Preparations containing dried, powdered plant material are available for the treatment of bronchial asthma and tropical eosinophilia. The anti-asthmatic activity of the plant is attributed to the presence of phenanhroindolizidine alkaloids, which has been isolated from the aerial parts of the plant (Ali and Bhutani, 1989). A water extract of the plant showed anti-anaphylactic effect, leucopenia and inhibition of Schulz-Dale's reaction in experimental animals. The extract also showed brief nonspecific anti-spasmodic action in isolated tissues of g. pig ileum, rabbit duodenum, frog's rectus and rat stomach. The mode of action of the plant may be cell-mediated immunity (Haranath and Shyamalakumari, 1975). The plant extracts were found to produce significant anti-inflammatory effects in rats (Manez 1990). Immunosuppressive and anti-inflammatory effects of *Tylophora asthmatica* are due to increased secretion of corticosteroids by adrenal cortex (Udupa, 1991). *Tylophora asthmatica* also produced significant improvement in lung functions, when the effect of the plant was studied on the patients of bronchial asthma (Gore, 1980). Preliminary studies on animals have found *tylophora* extracts to be toxic only in extremely high doses; these extracts were apparently safe in the far smaller doses needed to produce a therapeutic effect (Dikshith *et al.*, 1990).

CONCLUSIONS

Herbal approaches have regained their popularity, with their efficacy and safety aspects being supported by controlled clinical studies. The herbal approach have offered effective mast cell stabilizers like sodium cromolyn and sodium cromoglycate developed from khellin and anti-leukotriene product - boswellic acids. Ongoing research worldwide has provided valuable clues regarding the precise mechanism of action of these herbal alternatives and these herbs, therefore, have multi-faceted roles to play in the management 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. Thus, these plants can be used to obtain a polyherbal formulation which contains various herbs acting at particular sites of the pathophysiological cascade of asthma for prophylaxis as well as for the treatment of asthma. Further, different formulations can be prepared which can be used in different types of respiratory disorders including different types of asthma.

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