



THERAPEUTIC MANAGEMENT OF PEDIATRIC ALLERGIC DISORDERS BY INDIAN MEDICINAL PLANTS WITH MAST CELL STABILIZING POTENTIAL: A REVIEW

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ABSTRACT

Every fifth child develops an allergic disorder sometime during childhood and these conditions gravely trouble the health status and quality of life of children. Conventional agents are being used to control allergic disorders. However, these are not entirely affordable and effective. Numerous medicinal plants have been used successfully for the prevention and management of pediatric allergic disorders in Indian traditional systems of medicine, Ayurveda. Medicinal plants with mast-cell stabilizing activity are being more desired, owing to lesser side-effects and low cost. This review focuses on the various plants with mast cell stabilizing activity that has been reported to be effective in various allergic disorders. These include *Abrus precatorius* (Gunja), *Albizia lebeck* (Shirish), *Allium cepa* (Palandu), *Aristolochia bracteolata* (Ishwari moola), *Bacopa monnieri* (Brahmi), *Boswellia serrata* Roxb. (Shallaki), *Cedrus deodara* (Roxb.) Loud (Devadaru), *Elaeocarpus sphaericus* (Rudraksha), *Ficus religiosa* (Ashwatha), *Inula racemosa* (Pushkarmoola), *Sphaeranthus indicus* (Mundi) and *Vitex Negundo* (Nirgundi). All of them have shown a certain degree of mast cell stabilizing activity as evidenced by various research studies.

Key words: Allergic disorders, Mast cell stabilizers, Ayurveda

INTRODUCTION

Allergic disorders among pediatric population are one of the major health problems of most modern societies. Although allergic diseases are well-known for almost two hundred years, their prevalence has increased dramatically over the last decades. One in every five children develops an allergic disorder some time during childhood. Some conditions are short lived causing mild disturbance while others may be life threatening.¹ Mast cells play a crucial role in allergic disease and inflammation. These cells are tissue-dwelling hematopoietic effector cells that are endowed with a range of potent inflammatory effector molecules. Mast cells constitutively reside in a perivascular distribution in connective tissues and are especially abundant in tissues that form interfaces with the external environment i.e. skin, conjunctiva, intestinal and airway mucosa, suggesting a strategic placement so as to function in a first line of host defense. These cells are released straight into the blood, and they differentiate upon reaching the tissue. They express receptors IgE, and binding of the antibody to its receptor followed by a second exposure to the specific antigen results in massive degranulation of mast cells. The mediators released by mast cells include histamine, prostaglandin D₂, leukotriene C₄, heparine, serine proteases and a plethora of cytokines²

Mast cell stabilizers are indicated in the management of various pediatric allergic disorders including bronchial asthma, allergic conjunctivitis etc.³ These agents inhibit the release of mediators on the surface of mast cells. The best known substance is disodium cromoglycate which is used in different galenic formulation for the conjunctive, the nasal mucosa, the bronchial tract, and the gastrointestinal tract. Cromoglycates can only be used topically on the mucosal surface. They do not penetrate the epidermis and are not

absorbed from the gut. Neither systemic treatment nor topical skin treatment is possible with them.

The primary objective of this review paper is to screen indigenous medicinal plants with significant mast cell stabilizing activity, which can be used in future for developing therapeutics for the prevention and management of various pediatric allergic disorders effectively. PUBMED, MEDLINE databases were searched for studies published with key words 'mast cell stabilizers, Indian medicinal plants, Ayurveda etc. In-vitro analysis, as well as experimental trials was included in the review. Only research articles in English language were considered. Other languages were approved when there was an English abstract containing data essential for extraction.

Medicinal Plants with Mast Cell Stabilizing

Systematic search revealed that Indian medicinal plants like *Abrus precatorius* (Gunja), *Albizia lebeck* (Shirish), *Allium cepa* (Palandu), *Aristolochia bracteolata* (Ishwari moola), *Bacopa monnieri* (Brahmi), *Boswellia serrata* Roxb. (Shallaki), *Cedrus deodara* (Roxb.) Loud (Devadaru), *Elaeocarpus sphaericus* (Rudraksha), *Ficus religiosa* (Ashwatha), *Inula racemosa* (Pushkarmoola), *Sphaeranthus indicus* (Mundi) and *Vitex Negundo* (Nirgundi) possess mast cell stabilizing activity. The important studies are summarized below:-

Abrus precatorius

Taur et al (2011) investigated effects of ethanol extract of *Abrus precatorius* leaves on egg albumin induced mast cell degranulation in mice and passive cutaneous anaphylaxis in rats. It was observed that extract (100-150 mg/kg, i.p.) significantly protect egg albumin induced degranulation of mast cell.⁴

Albizia lebbek

In an in-vitro study, methanolic extract of leaf and methanolic and water extracts of bark was found to possess mast cell stabilizing effects comparable to that of Disodium cromoglycate.⁵ Venkatesh et al (2010) evaluated mast cell stabilization activity of standardized extract of *Albizia lebbek* with reference to catechin as a phytomarker. It was observed that *Albizia lebbek* at different concentrations has got potent mast cell stabilizing property. The IC (50) value of *Albizia lebbek* was found to be 85 microg/ml.⁶ In a similar experimental study involving rat as model, crude extracts of seeds and a pure saponin fraction of *Albizia lebbek* was found to possess mast cell membrane stabilizing effect.⁷

Allium cepa

Quercetin, a bioflavonoid obtained from *Allium cepa* was found to possess mast cell membrane stabilizing activity.⁸ Similar property of quercetin has been also reported by Shaik et al (2006). They observed that Quercetin act as an inhibitor of mast cell secretion causes a decrease in the release of tryptase, MCP-1 and IL-6 and the down-regulation of histidine decarboxylase (HDC) mRNA from few mast cell lines which shows its future potential in management of allergy and inflammation.⁹

Aristolochia bracteolata

In a recently conducted experimental study, anti-allergic activity of *Aristolochia bracteolata* Lank was investigated. It was found that the chloroform extract of *Aristolochia bracteolata* had potent and significant Mast cell membrane stabilization activity in compound 48/80 induced mast cell activation.¹⁰

Bacopa monnieri

Successive petroleum ether, chloroform, methanol and water extracts of *Bacopa monnieri* were tested (in vitro) for mast cell stabilising effect. The methanolic fraction demonstrated potent mast cell stabilizing activity comparable to disodium cromoglycate.¹¹

Boswellia serrata Roxb.

In an investigation, extract of gum resin of *B. serrata* containing 60% acetyl 11-keto beta boswellic acid along with other constituents such as 11-keto beta-boswellic acid, acetyl beta-boswellic acid and beta-boswellic acid was evaluated for mast cell stabilizing activity using compound 48/80 induced degranulation of mast cell method. A significant inhibition in the compound 48/80 induced degranulation of mast cells in dose-dependent manner (20, 40 and 80 mg/kg, po) was observed thus showing mast cell stabilizing activity.¹²

Cedrus deodara (Roxb.) Loud

In an investigation conducted by Shinde et al (1999), it was observed that, the volatile oil of *Cedrus deodara* significantly inhibited compound 48/80 induced degranulation of isolated rat peritoneal mast cells at concentrations ranging from 25-200 micrograms/ml.¹³

Elaeocarpus sphaericus

In an experimental study conducted by Singh et al (2000), it was observed that petroleum ether, benzene, chloroform, acetone and ethanol extracts of *Elaeocarpus sphaericus* fruits were found to have mast-cell stabilizing activity.¹⁴

Ficus religiosa

Kapoor et al (2011) reported that aqueous extract of *F. religiosa* leaves potentiate the number of intact cells in the mast cell stabilizing model. Mast cell stabilizing activity of aqueous extract of *F. religiosa* leaves was compared with ketotifen at 10 g/mL.¹⁵

Inula racemosa

Alcoholic extract of root of *Inula racemosa*, was evaluated for its mast cell degranulation activity in albino rats. It was observed that protection against compound 48/80 induced mast cell degranulation by alcoholic extract of *Inula racemosa* (single dose) was similar to that of disodium cromoglycate. The seven days drug treatment schedule showed greater protection than disodium cromoglycate intraperitoneally.¹⁶

Solanum nigrum

In a recent experimental study, Petroleum ether, ethanol and aqueous extracts of *S. nigrum* berries (50, 100 and 200mg/kg, i.p.) were assessed for mast cell stabilizing activity in mice. It was observed that Petroleum ether extract had mast cell stabilizing potential better than other extracts.¹⁷

Sphaeranthus indicus

Recently, the effects of *Sphaeranthus indicus* on mast cell stabilizing activity were investigated. Ethanol extract of *Sphaeranthus indicus* at the doses of 150 mg/kg and 300 mg/kg and ethyl acetate extract at the dose of 100 mg/kg, 150 mg/kg and 300 mg/kg showed slightly better protection of mast cell degranulation (77-86%) than the standard drug ketotifen (75%) in the sheep serum model. These extracts also showed better mast cell stabilizing activity (77-88%) than the standard drug (69%) when peritoneal mast cells are treated with compound 48/80.¹⁸

Vitex Negundo

Patel et al (2011) reported that Ethyl acetate fraction of leaves of *V. negundo* possess mast cell stabilizing activity. In their study, Mast cell degranulation was studied on isolated mesentery of rat by exposure to compound 48/80. Dexamethasone (5 mg/kg) was used as a reference standard. Ethyl acetate fraction of leaves of *V. negundo* (500 µg/ml) showed significant protection of rat mesenteric mast cells from disruption caused by compound 48/80.¹⁹

CONCLUSION

In recent times there has been a renewed interest in medicinal plants with mast cell stabilizing potential. All the medicinal plants discussed in this review have shown significant potential mast cell stabilizing activity. The efficacy of some medicinal plants like *Shirish (Albizia lebbek)*, *Inula racemosa (Pushkar moola)* is quite significant and possesses negligible adverse reactions as compared to synthetic mast cell stabilizing agents. Isolation and identification of more active constituents from these natural products will play crucial role in developing plant based mast cell stabilizing agent in near future which is efficacious, safe and affordable to the community.

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