

Mast cell degranulation: A target for bioactive natural products

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Abstract

Mast cells are well known for their involvement in allergic, anaphylactic reactions and variety of inflammatory diseases. Many plants show anti-allergic activity by inhibiting histamine release from mast cells. Degranulation of mast cells can be prevented by various mechanisms. As histamine is one of the important mediators for asthma, plant extracts that could prevent degranulation of mast cells may be effective in the treatment of asthma. Extract that can stabilize mast cells can inhibit mast cell-derived allergic inflammation by inhibiting release of phorbol 12-myristate 13-acetate (PMA), TNF- α , IL-6, IL-8 and related mediators of inflammation. Therefore, natural products that could prevent degranulation of mast cells can be effective in the treatment inflammatory diseases, such as asthma, atopic dermatitis, and allergic inflammation.

Keywords: Mast cell, allergic inflammation, inflammatory diseases, asthma, plant extracts.

Introduction

Mast cells are cells found throughout the body as part of our immune system. Mast cells appear to induce a rapid inflammatory response to outside invaders, such as germs and viruses. Mast cells play a large role in allergic responses, as they release the chemical known as histamine. For the majority of this time their function was linked almost exclusively to allergy and allergic disease with few other roles in health and disease. Mast cells play critical roles in both innate and adaptive immunity, including immune tolerance. MCs can aid in maintaining a healthy physiology by secreting mediators that promote wound healing and homeostasis as well as interacting with neurons. Major developments have been made in understanding MC function in defense against pathogens, in recognition of pathogens as well as direct effector functions.

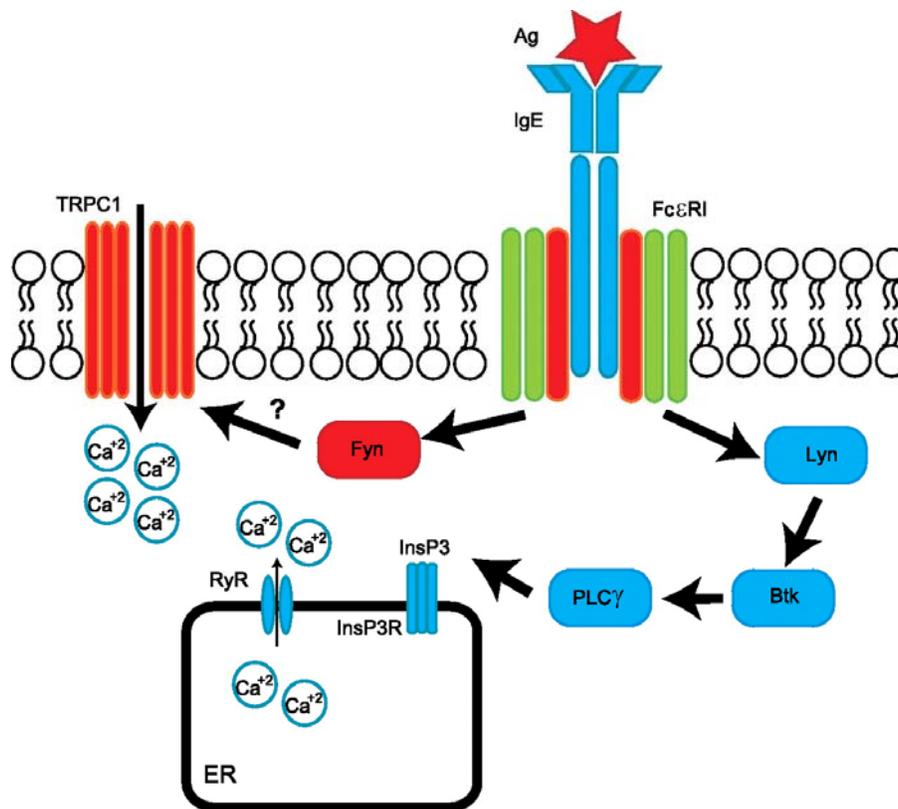


Figure 1. Schematic representation of calcium response during FcεRI-mediated mast cell activation.

Mechanisms of mast cell degranulation

Mast cells play a central role in adaptive and innate immune responses. IgE antigen stimulation of the high-affinity IgE receptor (FcεRI) results in rapid secretion of various granule-stored mediators responsible for allergies and other inflammatory diseases. This degranulation process depends on an increase in intracellular Ca^{+2} concentrations. Calcium needed for degranulation comes from intracellular stores and from Ca^{+2} influx from the extracellular medium through plasma membrane channels. The release of Ca^{+2} is mediated by the PLCγ signaling pathway (Galli et al., 2005) (Figure 1).

IgE-antigen complexes bind the high-affinity FcεRI receptors, activating the Lyn-Btk-PLCγ cascade. Inositol triphosphate (InsP3) is synthesized, binds the InsP3R, and causes the release of Ca^{+2} from the ER through ryanodine receptors (RyR), followed by SOCE mediated by STIM-ORAI channels.

Release of Histamine from mast cells

Mast cells release histamine during inflammatory or allergic reactions. When exposed to allergens, humans produce IgE antibodies that are directed against the allergen. Mast cells have receptors that can bind to the Fc region of IgE antibodies. Binding of monomeric IgE to the Fc receptor does not cause mast cell activation and degranulation; initial exposure to an allergen causes large numbers of IgE antibodies to attach to mast cells surfaces without

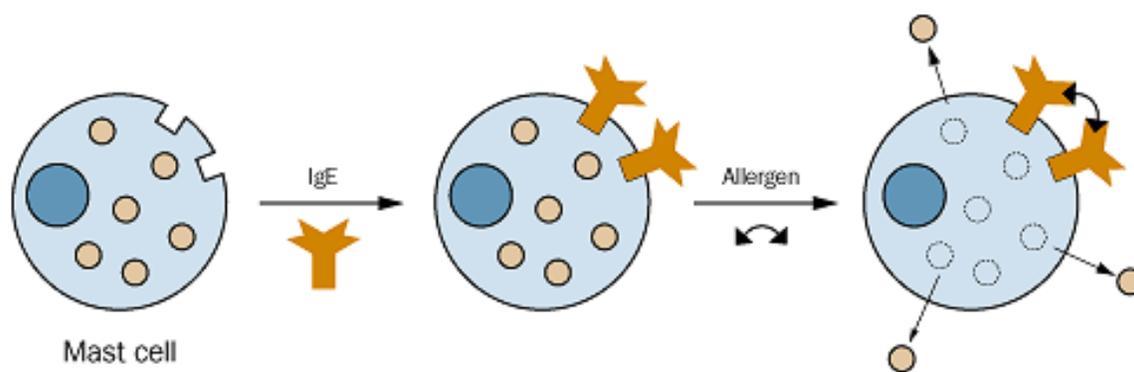


Figure 2. Degranulation of a Mast Cell.

activating them (Metcalf et al., 1997). Upon second exposure to an allergen, the IgE molecules bound to the mast cell surface can bind to allergen. The allergen causes crosslinking of the IgE molecules on the cell surface, which clusters the Fc receptors. This clustering stimulates a signal transduction that causes the mast cell to ‘degranulate’, or dump their granules into the tissues (Sompayrac, 1999). Important step in mast cell activation appears to be the crosslinking of IgE molecules, which causes the clustering of Fc receptors. This step also appears necessary because the bridging of receptors forms hydrophilic channels that allow calcium levels to increase intracellularly, which triggers mediator release. It has also been established that IgE acts as an anchor for antigen and helps to amplify the transduction signal generated by the bridging due to antigen-binding (Froese, 1980) (Figure 2).

Mast cells detain histamine in intracellular granules. Binding of IgE to cell surface receptors on a mast cell primes the cell to respond to allergen. Introduction of allergen and its subsequent binding to IgE induces crosslinking of IgE and clustering of Fc receptors. Clustering initiates a signal transduction event that stimulates the mast cell to degranulate, or release the contents of its granules. Mediators, such as histamine, which is represented by the tan circle, are released from granules and can bind to specific receptors to carry out their actions.

Bioassays for measurement of mast cell degranulation

Exocytosis Stimulation Protocol

Maintain MC-9 cells at the density of 5×10^6 cells/ml. Treat the cells with dimethyl sulfoxide (DMSO) or ionophore at 37°C. dimethyl sulfoxide (DMSO) or ionophore for different times at 37°C. Collect the cells for enzymatic analysis and then process for flow cytometry. Stimulate RBL-2H3 cells by washing the cells once in MT and then adding MT (1 ml/ 10^6 cells) containing the stimulus. Incubate the cells at 37°C for 30 min, and the supernatant was harvested for further analysis. Stain the plate-bound cells with annexin-V and then remove from the flask using No-Zyme containing 3 mM CaCl₂ for further processing for flow cytometry. For stimulation of RBL-2H3 cells with antigen crosslinking, the cells are incubated for 2 h at 37°C with IgE anti-DNP in complete media at different concentrations. Take up the cells processed for stimulation and staining in MT on ice and filter through a 100-µm filter prior to cytometry. Analyze it with a suitable cytometer (Demo et al., 1999).

Table 1. Various plants useful for mast cell stabilization along with their active extract or isolated compounds and mechanism of action.

Plant	Action / Mechanism	Reference
<i>Lecythis pisonis</i> Camb. (Lecythidaceae)	The compound 48/80-elicited degranulation of rat peritoneal mast cells was markedly reduced in animals pretreated with ethanol extract of leaves	Silva et al., 2012
<i>Myrica nagi</i> Hook. (Myricaceae)	Ethyl acetate and aqueous extracts of bark showed better protection of mast cell degranulation in egg albumin induced degranulation of mast cells in rats. Phytochemical screening revealed the presence of flavonoids and steroids.	Patel et al., 2011
<i>Matricaria recutita</i> L.	The methanol extract showed significant dose dependent anti-pruritis property by inhibiting the mast cell degranulation this suggest its anti-allergic activity by inhibition of histamine release from mast cells.	Chandrashekhar et al., 2011
<i>Elsholtzia ciliata</i> (Thunb.) Hyland (Labiatae)	Water extract inhibits mast cell-mediated allergic inflammatory reactions by suppressing histamine release.	Kim et al., 2011
<i>Glycyrrhiza glabra</i> with <i>Solanum xanthocarpum</i> and <i>Adhatoda vasica</i>	Pretreatment of mast cell with Liquorice Extract, <i>S. xanthocarpum</i> Extract and <i>A. vasica</i> Extract showed significant protection against Compound 48/80 and egg albumin induced degranulation.	Manek et al., 2011
<i>Barleria prionitis</i>	The hydroalcoholic extract significantly inhibited the compound 48/80 induced mast cells degranulation in a dose dependent manner.	Maji et al., 2011
Marmin or (7-(6',7'-dihydroxygeranyl-oxy) coumarin active compound isolated from <i>Aegle marmelos</i> Correa.	The inhibitory effect of marmin on the histamine release from mast cells depends on the type of mast cell and also involves mechanisms related to intracellular Ca ²⁺ signaling events by blocking Ca ²⁺ influx into mast cells.	Nugroho et al., 2011
<i>Bauhinia variegata</i> (Caesalpinaceae)	Ethanol extracts of stem bark possessed potent mast cell stabilizing activity, suggesting potential for use in the treatment of asthma.	Mali and Dhake, 2011
<i>Strychnos potatorum</i> Linn	Chloroform, petroleum ether, and methanolic extracts of seed were shown potent inhibitory effects on compound 48/80 induced anaphylactic reaction and mast cell activation.	Patil et al., 2011
<i>Cordia verbenacea</i>	Ethanol extract of leaves (30 µg/ml) reduced the in vitro secretion of histamine from rat mast cells induced by ionophore A23187, concanavalin A and compound 48/80	Costa et al., 2011
<i>Calotropis gigantean</i> (Linn.) R.Br. (Asclepiadaceae)	Methanolic extract of root showed significant percentage protection in compound 48/80 induced mast cell degranulation in rats.	Bulani et al., 2011
<i>Lindera obtusiloba</i>	Water extract reduced histamine release from various types of mast cells activated by immunoglobulin E (IgE) or phorbol 12-myristate 13-acetate and calcium ionophore A23187 (PMACI). Inhibitory effect was mediated by calcium signal.	Suh et al., 2011
<i>Taxus baccata</i> Linn.	Alcoholic extract of leaves dose dependently protected the mast cell disruption induced by compound 48/80.	Patel et al., 2011
<i>Baliospermum montanum</i> Mill. Arg. (Euphorbiaceae)	Ethanol extract of leaves was found to be effective against degranulation and release of histamine from mast cells.	Venkatesh et al., 2010
<i>Thespesia populnea</i>	Significant reduction of % mast cell degranulation was observed at 60 mg/ml dose of ethanolic extract of bark.	Patel et al., 2010
<i>Solanum xanthocarpum</i> Schrad. (Solanaceae)	Ethanolic extract of leaves protected mast cells from compound 48/80-provoked degranulation.	Parmar et al., 2010
<i>Prunus persica</i> (L) Batsch	Histamine releasing from mast cells was reduced by ethanol extract of fruits, which was mediated by modulation of intracellular calcium. Extract attenuated the phorbol 12-myristate 13-acetate and calcium ionophore A23187 (PMACI)-stimulated expression and secretion of pro-inflammatory cytokines in human mast cells.	Shin et al., 2010

Chinese propolis	This inhibitory effect of extract on pro-inflammatory cytokines was nuclear factor (NF)- κ B dependent. This provide evidence that extract inhibits mast cell-derived allergic inflammation.	Nakamura et al., 2010
<i>Gleditsiae Spina</i> (WGS) (Leguminosae)	The ethanol extract is the strongest inhibitor of mast cell degranulation which contains chrysin, kaempferol and its derivative.	Shin, 2010
<i>Nelumbo nucifera</i>	Water extract reduced histamine release from HMC-1 cells.	Mukherjee et al., 2010
<i>Rhododendron anthopogonoides</i>	Rhizome extract protected mast cells from degranulation against compound 48/80.	Mukherjee et al., 2010
<i>Paeonia suffruticosa</i> Andrews	Chromane derivatives, anthopogochromane and anthopogochromene A inhibited compound 48/80-induced histamine release from rat peritoneal mast cells.	Iwata and Kitanaka, 2010
<i>Ulmus davidiana</i> var. japonica	Ethanol extract of root cortex suppressed the release of histamine from rat peritoneal mast cells induced by compound 48/80.	Hong et al., 2010
<i>Vitex nigundo</i> Linn.	Compounds 11, 12, 13, 15 and 19 isolated from the root bark inhibited β -hexosaminidase release, a marker of mast cell degranulation reaction, from bone marrow-derived mast cell that suggest that the anti-inflammatory activity.	Zheng et al., 2010
<i>S. baicalenesis</i> and <i>P. edulis</i>	Alcoholic extract of leaves dose dependently protected the mast cell disruption induced by compound 48/80. This activity is may be due to flavonoids and phenolic compounds present in extract.	Patel et al., 2010
<i>Butea monosperma</i>	Combined standardized herb composition of <i>S. baicalenesis</i> and <i>P. edulis</i> reduce degranulation during mast cell activation and could be a promising candidate for the treatment of immune/allergic diseases related to mast cells.	Kim et al., 2010
<i>Zanthoxylum piperitum</i> DC	Butrin, isobutrin, and butein isolated from <i>B. monosperma</i> flower extract significantly reduced the phorbol 12-myristate 13-acetate and calcium ionophore A23187-induced inflammatory gene expression and production of TNF- α , IL-6, and IL-8 in HMC-1 cells by inhibiting the activation of NF- κ B. This indicates potential therapeutic value for the treatment of inflammatory and other diseases in which activated mast cells play a role.	Rasheed et al., 2010
<i>Clinopodium gracile</i> Matsum var. multicaule	Isolated glycoprotein from fruit inhibited interleukin-4, immunoglobulin E, and histamine are released in mouse serum. Also, it attenuated the degranulation of mast cells, intracellular Ca^{2+} levels, and the activities of phosphorylation of p^{38} mitogen-activated protein kinase, nuclear factor- κ B (p^{50} and p^{65}), and cyclooxygenase-2 in the HMC-1 cells. The glycoprotein can prevent dysfunction in the immune system caused by several different allergens.	Lee and Lim, 2010
<i>Cynodon dactylon</i>	The water extract dose-dependently reduced histamine release from rat peritoneal mast cells and human mast cells. In addition, it attenuated the phorbol 12-myristate 13-acetate and calcium ionophore A23187-stimulated gene expression and secretion of proinflammatory cytokines such as tumor necrosis factor- α and interleukin-6 in human mast cells. WECG inhibits mast cell-derived allergic inflammation through involvement of calcium and NF- κ B in these effects.	Park et al., 2010
<i>Aralia cordata</i>	Extract has significant rat peritoneal mast cells stabilization activity induced by compound 48/80.	Savali et al., 2010
<i>Ailanthus altissima</i> swingle	7-oxosandaracopimaric acid isolated from the ether fraction of <i>Aralia cordata</i> methanol root extract significantly inhibited compound 48/80-induced histamine release from rat mast cells.	Kim et al., 2010
<i>Aristolochia bracteolata</i>	Extract inhibited histamine release from rat peritoneal mast cells in a dose-dependent manner. In activated HMC-1 cells, the expression level of NF- κ B/Rel A protein increased in the nucleus, whereas the level of NF- κ B/Rel A in the nucleus was decreased by extract treatment. In conclusion, the extract has potent anti-anaphylactic and anti-inflammatory properties.	Kang et al., 2010
<i>Curculigo orchioides</i>	Chloroform extract showed mast cell membrane stabilization activity in compound 48/80 induced mast cell activation. The extract possess potent antiallergic activity, possibly through mast cell membrane stabilization.	Chitme et al., 2010
	Extract of rhizomes stabilized the mast cell degranulation.	Venkatesh et al., 2009

Gaertn. (Fam. Amaryllidaceae) <i>Eriobotrya japonica</i> Lindl. (Rosaceae)	Extract of leaves dose-dependently decreased histamine release from mast cells. Furthermore, it decreased the production of tumor necrosis factor- α in phorbol 12-myristate 13-acetate and A23187-stimulated human mast cells. Thus it can be used as an anti-allergic agent.	Kim et al., 2009
<i>Tinospora cordifolia</i> (Willd.) Miers (Menispermaceae)	Aqueous extract of stem significantly inhibited the histamine release from rat peritoneal mast cells activated by compound 48/80. It also significantly inhibited the secretion of tumor necrosis factor- α (TNF- α) in antidinitrophenyl (DNP) IgE-stimulated rat peritoneal mast cells. Thus it may be beneficial in the treatment of acute and chronic allergic disorders.	Zalawadia et al., 2009
<i>Centella asiatica</i>	Extract significantly inhibited the histamine release from rat peritoneal mast cells activated by compound 48/80.	George et al., 2009
<i>Pithecellobium clypearia</i> Benth	Polyphenols from ethanol extract (-)-epigallocatechin-7-gallate, (-)-5, 7, 3', 4', 5'-pentahydroxyflavan and (-)-tetra hydroxyflavan-7-gallate showed significant inhibition effect on histamine release from rat peritoneal mast cells in vitro stimulated by compound 48/80.	Bao et al., 2009
<i>Rubus coreanus</i> Miq. (Rosaceae)	Extract of ripe fruits decreased the gene expression and production of tumor necrosis factor- α (TNF- α) and interleukin (IL)-6 in phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore A23187 (A23187)-stimulated human mast cells. Thus it could be a candidate as an anti-allergic agent.	Shin, 2009
<i>Urtica dioica</i>	Extract causes inhibition of mast cell tryptase preventing degranulation and release of a host of pro-inflammatory mediators that cause the symptoms of hay fevers.	Roschek Jr. et al., 2009
<i>Allium cepa</i> (Liliaceae)	An herbal fraction (ALC-02) from (bulb) inhibited histamine release and attenuated intracellular calcium levels in Compound 48/80-induced rat peritoneal mast cells.	Kaiser et al., 2009
<i>Sphaeranthus indicus</i>	Ethanol and ethyl acetate extracts showed better protection of mast cell degranulation against compound 48/80 and sheep serum induced mast cell degranulation.	Mathew et al., 2009
<i>Sophora flavescens</i> Aiton	Extract of dried roots inhibited the mast cell-mediated passive cutaneous anaphylaxis reaction in vivo and the release of histamine from rat peritoneal mast cells by compound 48/80. In addition, the expression levels of phorbol 12-myristate 13-acetate (PMA) and calcium ionophore A23187-stimulated TNF- α , IL-6, and IL-8 were also decreased. Thus it could be used as a treatment for mast cell-derived allergic inflammatory diseases.	Hong et al., 2009
<i>Teucrium japonicum</i> Houttuyn (Labiatae)	Aqueous extract reduced histamine release and intracellular calcium from rat peritoneal mast cells activated by compound 48/80. In addition, extract attenuated activation of nuclear factor (NF)- κ B, and downstream tumor necrosis factor (TNF)- α expression in phorbol 12-myristate 13-acetate and calcium ionophore A23187-stimulated human mast cells.	Kim et al., 2009
Natsudaidain, a polymethoxyflavone isolated from Citrus plants	Natsudaidain hardly affects histamine release from RBL-2H3 cells, except at high concentrations.	Matsui et al., 2009
<i>Vitex negundo</i>	Ethyl acetate, ethanolic and aqueous extracts of leaves showed significant protection of rat mesenteric mast cells from disruption caused by compound 48/80.	Patel et al., 2009
<i>Schinus terebinthifolius</i> (Anacardiaceae)	Ethyl acetate fraction preventing mast cell degranulation and, consequently, histamine release in Wistar rat peritoneal mast cells induced by C 48/80. This histamine inhibition was also observed after mast cell pre-treatment with both methyl gallate and 1,2,3,4,6-pentagalloylglucose, the isolated compounds from the ethyl acetate fraction.	Cavalher-Machado et al., 2008
PentaHerbs formula (PHF) containing Cortex Moutan, root	PHF, Cortex Moutan and Herba Menthae significantly attenuated histamine release and prostaglandin D2 synthesis from RPMC activated by anti-IgE and compound 48/80. Flos Lonicerae and	Chan et al., 2008

bark of <i>Paeonia suffruticosa</i> Andr. (Ranunculaceae), <i>Cortex Phellodendri</i> , bark of <i>Phellodendron chinensis</i> Schneid. (Rutaceae), Flos Lonicerae, flower of <i>Lonicera japonica</i> Thunb. (Caprifoliaceae), <i>Herba Menthae</i> , aerial part of <i>Mentha haplocalyx</i> Briq. (Labiatae) and Rhizoma <i>Atractylodis</i> , rhizome of <i>Atractylodes lancea</i> (Thunb.) DC. (Compositae)	Rhizoma <i>Atractylodis</i> suppressed only mediator release from compound 48/80 activated RPMC.	
<i>Piper nigrum</i>	Methanolic extract of leaf exhibited in vitro inhibitory effect on compound 48/80-induced histamine release from rat peritoneal mast cells. Two lignans of extract, (-)-cubebin and (-)-3,4-dimethoxy-3,4-desmethylenedioxcubebin, were identified as major active principles having histamine release inhibitory activity.	Hirata et al., 2008
<i>Mosla dianthera</i> (M. <i>dianthera</i>)	Aqueous extract attenuated histamine release from mast cells and decreased the gene expression and production of tumor necrosis factor (TNF)- α in phorbol 12-myristate 13-acetate (PMA) and calcium ionophore A23187-stimulated human mast cells. It could be an antiallergic agent.	Kim et al., 2008
<i>Albizia lebbek</i>	Methanolic extract of leaf and methanolic and water extracts of bark showed in vitro mast cell stabilizing effect against compound 48/80.	Shashidhara et al., 2008
<i>Rubus suavissimus</i> S. Lee	Extract inhibited the release of histamine in rat peritoneal mast in vitro, a dose-dependent manner. Thus it exerts potential anti-allergy effect may be partly related to its inhibitory effect on the release of histamine from mast cells.	Fang et al., 2008
<i>Dictamnus dasycarpus</i> Turcz	70% ethanol extract was effective in antagonizing certain pharmacological effects induced by compound 48/80 that occurred via both histamine and serotonin released from mast cells. Thus it may be effective in the relief of symptoms of allergic atopic dermatitis and other allergy-related diseases.	Jiang et al., 2008
Selinidin, one of the coumarin derivatives isolated from <i>Angelica keiskei</i>	Selinidin attenuates the release of β -hexosaminidase, synthesis of leukotriene C ₄ , and production of tumor necrosis factor- α without affecting IgE-Fc ϵ RI binding. Furthermore, biochemical analyses of the Fc ϵ RI-mediated signaling pathway demonstrated that selinidin decreases phosphorylation of phospholipase C- γ 1, p ³⁸ mitogen-activated protein kinase, and I κ B- α upon Fc ϵ RI stimulation. These results suggest that this compound suppresses IgE-mediated mast cell activation by inhibiting multiple steps of Fc ϵ RI-dependent signaling pathways and would be beneficial for the prevention of allergic inflammation.	Kishiro et al., 2008
<i>Phlomis umbrosa</i> Turcz. (Labiatae)	Aqueous extract of root dose-dependently inhibited the histamine release from rat peritoneal mast cells activated by compound 48/80 or anti-DNP IgE. Extract inhibited the secretion of interleukin (IL)-1 β in phorbol 12-myristate 13-acetate plus calcium ionophore A23187-stimulated human mast cell line (HMC-1) cells. Extract inhibited the gene expression and production of the main inflammatory cytokine, TNF- α , in HMC-1 cells. These results provide evidence that extract may be beneficial in the treatment of allergic diseases.	Shin et al., 2008
<i>Vitis amurensis</i> Rupr. (Vitaceae)	Methanol extract of fruits dose-dependently reduced histamine release from mast cells activated by compound 48/80 or IgE. The inhibitory effect of extract on histamine release was mediated by	Kim et al., 2008

	the modulation of intracellular calcium. In addition, extract attenuated the phorbol 12-myristate 13-acetate and calcium ionophore A23187 (PMACI)-stimulated secretion of tumor necrosis factor- α , interleukin-6 (IL-6), and IL-8 in human mast cells. The inhibitory effect of extract on these proinflammatory cytokines was p38 mitogen-activated protein kinase and nuclear factor- κ B (NF- κ B) dependent. Our findings provide evidence that extract inhibits mast cell-derived immediate-type allergic reactions.	
<i>Salvia miltiorrhiza</i>	Mast cell degranulation is blunted by cryptotanshinone and 15,16-dihydrotranshinone I isolated from root extract.	Han et al., 2008
<i>Angelicae dahuricae</i>	Isoimperatorin (4-[(3-Methyl-2-butenyl)oxy]-7H-furo[3,2-g][1]benzopyran-7-one) isolated from roots inhibit the cyclooxygenase-2 (COX-2) and COX-1-dependent phases of prostaglandin D2 (PGD2) generation in bone marrow-derived mast cells (BMMC) in a concentration-dependent manner therefore may provide the basis for novel anti-inflammatory drugs.	Moon et al., 2008
<i>Lithospermi radix</i> (Borraginaceae)	Root extract inhibited the release of histamine from rat peritoneal mast cells by compound 48/80 in a dose-dependent manner. Extract inhibited the PMA plus A23187-induced increase in IL-6, IL-8, and TNF- α expression in HMC-1 cells. These results show that extract had an inhibitory effect on the atopic allergic reaction.	Kim et al., 2007
<i>Amomum xanthiodes</i> (Zingiberaceae)	Aqueous extract reduced histamine release and intracellular calcium from rat peritoneal mast cells activated by compound 48/80. Furthermore, it decreased the activation of p38 mitogen-activated protein kinase (MAPK) but not extracellular signal-regulated kinase and c-jun N-terminal kinase, and downstream tumor necrosis factor (TNF)- α production in phorbol 12-myristate 13-acetate and calcium ionophore A23187-stimulated human mast cells. It can be concluded that extract inhibits mast cell-derived allergic reactions, and that intracellular calcium, TNF- α , and p38 MAPK are involved in these effects.	Kim et al., 2007
<i>Moringa oleifera</i> Lam (Moringaceae)	Ethanol extract of seeds decreases the mast cell-mediated immediate type hypersensitivity reaction. When extract was given as pretreatment, the histamine release from the mast cells that was induced by the 48/80 was reduced in a dose-dependent manner. These results suggest a potential role for extract as a source of anti-anaphylactic agents for use in allergic disorders.	Mahajan and Mehta, 2007
<i>Glycine max</i> Men. (Leguminosae)	Extract decreased the phorbol 12-myristate 13-acetate plus calcium ionophore A23187-stimulated tumor necrosis factor (TNF)- α and interleukin (IL)-8 secretion in human mast cells. It indicates that extract may be beneficial in the treatment of mast cell-mediated immediate-type allergic reactions.	Shin et al., 2007
<i>Moutan cortex</i>	Ethanol extract inhibited histamine release from rat peritoneal mast cells induced by compound 48/80. In conclusion, it may be useful for the relief of symptoms of atopic dermatitis and other allergy-related diseases.	Jiang et al., 2007
<i>Forsythia koreana</i>	Methanol extract inhibited histamine release from the RPMCs by and TNF- α , IL-6, and IL-8 production from HMC-1 cells.	Choi et al., 2007
<i>Prunella vulgaris</i> (Labiatae)	Aqueous extract attenuated phorbol 12-myristate 13-acetate (PMA) and calcium ionophore A23187-stimulated TNF- α , IL-6, and IL-8 secretion in human mast cells. Thus extract inhibits mast cell-derived immediate-type allergic reactions	Kim et al., 2007
<i>Tridax procumbens</i>	Flavone glucoside 5,3',4'-trihydroxy-7,5'-dimethoxy-5-O- α -L-methyl pyranoside inhibited histamine release from mast cells.	Nagina et al., 2007
<i>Schizandra chinensis</i> BAILL (Magnoliaceae)	Schizandrin isolated from fruit also inhibited the in vitro degranulation of compound 48/80-induced rat peritoneal mast cells and IgE-induced RBL 2H3 cells. Schizandrin reduced the protein expressions of TNF- α and IL-4 in IgE-induced RBL 2H3 cells.	Lee et al., 2007
<i>Meliae cortex</i>	Ethanol extract inhibited the expression of the proinflammatory mediator TNF- α through suppressing the activating phosphorylation of Syk, a key enzyme in mast-cell signaling	Lee et al., 2007

<i>Bidens parviflora</i>	processes and that of Akt in a dose-dependent manner. It also inhibited the MAP kinase ERK1/2, which is critical for the production of inflammatory cytokines in mast cells, as indicated by the suppression of the activating phosphorylation of ERK1/2. Taken together, these results suggest that the anti-allergic activity of extract may be due to the inhibition of histamine secretion and cytokine expression through the Syk inhibition in mast cells.	Wang et al., 2007
<i>Glycyrrhiza glabra</i> L., Leguminosae	Compounds guaiacyl glycerol 8-O- β -D-glucoside, syringin, 4-allyl-2-methoxyphenol-O- (6-O- β -D-apiofuranosyl)- β -D-glucoside, and 5, 7-dihydroxy chromone 7-O- β -D-glucoside isolated from plant extract exhibit the activities of anti-histamine release from rat mast cell stimulated by antigen-antibody reaction.	Shin et al., 2007
<i>Syzygium cumini</i> (L.) Skeels (Myrtaceae)	Liquiritigenin and 18 β -glycyrrhetic acid isolated from plant extract most potently inhibited the degranulation of rat peritoneal mast cells induced by compound 48/80.	Brito et al., 2007
<i>Mosla dianthera</i> (Maxim.)	Aqueous leaf extract prevented mast cell degranulation and the consequent histamine release in Wistar rat peritoneal mast cells induced by compound 48/80 indicating its anti-edematogenic effect.	Lee et al., 2006
<i>Artemisia iwayomogi</i>	Aqueous extract attenuated intracellular calcium level and release of histamine from rat peritoneal mast cells activated by compound 48/80. Furthermore, it attenuated the phorbol 12-myristate 13-acetate (PMA) and calcium ionophore A23187-stimulated TNF- α , IL-8 and IL-6 secretion in human mast cells. Thus it inhibits mast cell-derived immediate-type allergic reactions.	Shin et al., 2006
<i>Rubus coreanus</i> Miq. (Rosaceae)	Extract dose-dependently reduced histamine release from rat peritoneal mast cells activated by compound 48/80 or anti-DNP IgE. Furthermore, it attenuated the phorbol 12-myristate 13-acetate plus calcium ionophore A23187-stimulated tumor necrosis factor- α and interleukin-6 secretion in human mast cells. Thus it may be beneficial in the treatment of allergic diseases.	Shin et al., 2006
<i>Agaricus blazei</i>	Extract of unripe fruits reduced histamine release from rat peritoneal mast cells activated by compound 48/80 or IgE. Furthermore, it decreased the phorbol 12-myristate 13-acetate plus calcium ionophore A23187-stimulated tumor necrosis factor (TNF)- α and interleukin (IL)-6 secretion in human mast cells. Thus it may inhibit mast cell-derived immediate-type allergic reactions.	Choi et al., 2006
<i>Japanese butterbur</i>	Water extract dose-dependently inhibited compound 48/80-induced or anti-DNP IgE-mediated histamine release from rat peritoneal mast cells.	Shimoda et al., 2006
<i>Rubiae Radix</i>	Aqueous ethanol extract from aerial parts inhibited mast cell degranulation by inhibition of β -hexosaminidase release. Fukinolic acid, a principal polyphenol constituent, showed potent inhibitory activity. Thus it suppress the type I allergic reaction.	Lee et al., 2006
<i>Euphorbia hirta</i>	Extract suppresses the activation of mast cells through the inhibition of Syk for anti-allergic activity.	Singh et al., 2006
<i>Dracocephalum argunense</i> FISCH. (Labiatae)	95% Ethanol extract from whole aerial parts inhibited rat peritoneal mast cell degranulation triggered by compound 48/80.	Kim et al., 2006
<i>Mangifera indica</i> L.	Aqueous extract of dose-dependently reduced IgE-induced histamine release from mast cells. The level of cAMP was transiently increased by treatment of extract. Extract specifically blocked the phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore A23187-induced p38 mitogen-activated protein kinase (MAPK) activation. Extract decreased the secretion of pro-inflammatory cytokines, such as tumor necrosis factor- α and interleukin-6 in mast cells.	García Rivera et al., 2006
<i>Saururus chinensis</i>	Extract and mangiferin, the major compound isolated from extract had an effect on an in-vivo model of inflammatory allergy mediated by mast cells.	Lee et al., 2006
<i>Dracocephalum</i>	Ethanol extract inhibited rat peritoneal mast cell degranulation.	Kim and Shin, 2006
<i>Dracocephalum</i>	Aqueous extract dose-dependently reduced histamine release from	Kim and Shin, 2006

<i>argunense</i> Fisch. (Labiatae)	mast cells activated by compound 48/80 or IgE. The inhibitory effect of extract on histamine release was mediated by the modulation of intracellular calcium. In addition, extract decreased TNF- α and IL-6 gene expression and production in human mast cells stimulated by phorbol-12-myristate-13-acetate (PMA) plus calcium ionophore A23187.	
<i>Lycopus lucidus</i> Turcz. (Labiatae)	Aqueous extract dose-dependently reduced histamine release from rat peritoneal mast cells activated by compound 48/80 or anti-DNP IgE. Furthermore, it decreased the secretion of TNF- α and IL-6 in phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore A23187-stimulated human mast cells. Thus it inhibits mast cell-derived immediate-type allergic reactions and involvement of pro-inflammatory cytokines, p38 MAPK, and NF- κ B in these effects.	Shin et al., 2005
<i>Selaginella tamariscina</i>	70% ethanol extract of herb can reduce histamine release from rat peritoneal mast cells triggered by compound 48/80 and an antigen in vitro. When incubated with rat mast cells, the extract can significantly elevate the intracellular cAMP levels. Thus it inhibits mast cell-dependent immediate allergic reactions.	Dai et al., 2005
<i>Houttuynia cordata</i>	Water extract reduced the compound 48/80-induced mast cell degranulation and colchicine-induced deformation of rat peritoneal mast cells. Moreover, HCWE dose-dependently inhibited histamine release and calcium uptake of RPMC induced by compound 48/80 or anti-DNP IgE. Extract increased the level of intracellular cAMP and inhibited significantly the compound 48/80-induced cAMP reduction in RPMC. Thus extract may be beneficial in the treatment of mast cell-mediated anaphylactic responses.	Li et al., 2005
<i>Morus alba</i>	Hot-water extract from the root bark dose-dependently inhibited mast cell degranulation, histamine release and calcium uptake into RPMC induced by the compound 48/80 or anti-CGG IgE. When extract was added, the level of intracellular cAMP in RPMC showed a transient and significant increase (5-fold) compared with that of control cells. Extract also inhibited significantly the compound 48/80-induced cAMP reduction in RPMC. These results suggested that extract inhibits the compound 48/80- or anti-CGG IgE-induced mast cell activation and its inhibitory effects on mast cell activations were favorably comparable to disodium cromoglycate. And extract is a candidate for effective therapeutic tools of allergic diseases.	Chai et al., 2005
<i>Amomum xanthiodes</i> (Zingiberaceae)	Extract dose-dependently attenuated the release of histamine from rat peritoneal mast cells (RPMC) activated by compound 48/80 or IgE. Extract increased the cAMP levels and decreased the compound 48/80-induced intracellular Ca ²⁺ . Furthermore, it attenuated the phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore (A23187)-stimulated tumor necrosis factor- α (TNF- α) and interleukin (IL)-6 secretion in human mast cells. Thus it inhibits mast cell-derived immediate-type allergic reactions, and that cAMP, intracellular Ca ²⁺ , proinflammatory cytokines, and NF- κ B are involved in these effects.	Kim and Shin, 2005
<i>Siraitia grosvenori</i> Swingle	Both the extract and glycoside isolated from the extract inhibited the histamine release induced by compound 48/80.	Hossen et al., 2005
<i>Sargassum hemiphyllum</i>	Extract significantly inhibited compound 48/80-induced histamine and β -hexosaminidase release from rat peritoneal mast cells. It inhibited interleukin (IL)-8 and tumor necrosis factor (TNF)- α release induced by phorbol 12-myristate 13-acetate and A23187 from HMC-1 this may be useful in the treatment of allergic inflammatory diseases, such as atopic dermatitis.	Na et al., 2005
<i>Artemisia iwayomogi</i> (Compositae)	Extract dose dependently attenuated histamine release from rat peritoneal mast cells activated by compound 48/80 or IgE. It decreased the compound 48/80-induced intracellular Ca ²⁺ . Furthermore, it decreased the phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore A23187-stimulated tumor necrosis factor- α and interleukin-6 gene expression and production in	Kim et al., 2005

Clove and Magnoliae Flos	human mast cells. Thus extract inhibits mast cell-derived immediate-type allergic reactions. It is depicted that the survival of animals even after administration of the fatal dose of compound 48/80 might result from the decreased number of mast cells by eugenol pretreatment isolated from volatile oil. Eugenol induces apoptosis in mast cells via translocation of phospho-ser 15-p53 into mitochondria.	Park et al., 2005
<i>Chrysanthemi sibirici</i>	Ethanol extract exerted the potent inhibitory activity on antigen-induced degranulation in RBL-2H3 mast cells. It dose-dependently inhibited DNP-BSA or compound 48/80-induced degranulation in RBL-2H3 mast cells. It also inhibited the expression of TNF- α and the activation of the MAP kinase, ERK1/2, which is critical for the production of inflammatory cytokines in mast cells, as indicated by the suppression of activating phosphorylation of ERK1/2. Thus it may be used clinically to treat various allergic diseases.	Lee et al., 2004
<i>Stachys riederi</i> var. <i>japonica</i> Miq. (Labiatae)	Aqueous extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE. Moreover, it inhibited the secretion of tumor necrosis factor- α (TNF- α) and interleukin (IL)-6 in phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore A23187-stimulated human mast cells (HMC-1 cells). Thus it may be beneficial in the treatment of acute and chronic allergic diseases.	Shin, 2004
<i>Isodon japonicus</i> Hara (Labiatae)	Extract dose-dependently reduced histamine release from rat peritoneal mast cells activated by compound 48/80 or anti-DNP IgE. Furthermore, it decreased the production of TNF- α in phorbol 12-myristate 13-acetate plus calcium ionophore A23187-stimulated human mast cells. Thus it inhibits mast cell derived immediate-type allergic reactions.	Shin et al., 2004
<i>Rubus croceacanthus</i> Leveille	When methanol extract was given as pre-treatment, the histamine release from rat peritoneal mast cells induced by compound 48/80 or antidinitrophenyl (DNP) immunoglobulin E (IgE) was reduced in a dose-dependent manner. In addition, it inhibited phorbol 12-myristate 13-acetate and A23187-induced tumor necrosis factor- α secretion from human mast cell line HMC-1 cells. Thus it may possess a strong anti-anaphylactic activity.	Moon et al., 2004
<i>Cissus sicyoides</i> L. (Bejuco caro)	Methanolic extract of Bejuco and its isolated constituent hydroxystilbene resveratrol showed inhibition in histamine release from rat peritoneal mast cells.	Quilez et al., 2004
<i>Protium heptaphyllum</i>	The compound 48/80-elicited degranulation of rat peritoneal mast cells (ex vivo) was also markedly reduced in animals pretreated with α,β -amyrins, the pentacyclic triterpenes isolated from the resin.	Oliveira et al., 2004
5-O- α -D-(3-C-hydroxymethyl)lyxofuranosyl- β -D-(2-C-hydroxymethyl)arabino furanose <i>Arecae semen</i>	The natural disaccharide inhibited histamine release evoked by both compound 48/80 and calcium ionophore A23187 in rat peritoneal mast cells indicating that mast cell stabilization is the major mechanism of action for its antiallergic activity.	Kwan et al., 2004
	Extract was the most potent inhibitor of antigen-induced degranulation in RBL-2H3 mast cells. It inhibited DNP-BSA- and compound 48/80-induced degranulation in RBL-2H3 mast cells. It also inhibited the expression of TNF- α and the activation of mitogen activated protein kinase, ERK1/2, which is critical for the production of inflammatory-cytokines in mast cells, as indicated by the suppression of the activating phosphorylation of ERK1/2. Thus it may be useful for the treatment of various immediate and delayed allergic diseases.	Lee et al., 2004
<i>Rhododendron dauricum</i>	Four new prenylated orcinol derivatives, daurichromenes A-D, along with two known compounds, confluentin and grifolin significantly inhibited compound 48/80-induced histamine release from rat peritoneal mast cells.	Iwata et al., 2004
<i>Cimicifuga racemosa</i>	Extract showed inhibitory potential on the compound 48/80-induced histamine release from rat peritoneal mast cells. In addition, it inhibited the IL-4, IL-5 and TNF- α mRNA induction	Kim et al., 2004

<i>Isodon japonicus</i> Hara (Labiatae)	by PMA and A23187 in human leukemia mast cells, HMC-1. Thus it has anti-allergic potential. Aqueous extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE. It inhibited the secretion of tumor necrosis factor- α (TNF- α) and interleukin (IL)-6 in phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore A23187-stimulated human mast cell line (HMC-1) cells. In addition, the expression of TNF- α mRNA in HMC-1 cells was inhibited by extract. Thus it may be beneficial in the regulation of immediate-type allergic reaction.	Kim et al., 2004
<i>Anthriscus sylvestris</i>	Deoxydopodophyllotoxin (Anthriscin) isolated from plant inhibits cyclooxygenase-2 (COX-2) and COX-1-dependent phases of prostaglandin D2 (PGD2) generation in bone marrow-derived mast cells (BMMC) in a concentration-dependent manner. Thus this compound might provide a basis for novel anti-inflammatory drugs.	Lee et al., 2004
indolin-2-one	The alkaloids indolin-2-one inhibits histamine release from the mast cell.	Ruster et al., 2004
<i>Plumbago zeylanica</i>	70% ethanol extract of stem inhibits mast cell-dependent immediate allergic reactions, which is probably mediated by reducing the release of mediators such as histamine from mast cells via elevating intracellular cAMP level and weakening the inflammatory action of mediators.	Dai et al., 2004
<i>Artemisia iwayomogi</i> (Compositae)	Aqueous extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80. Moreover, it inhibited the secretion of interleukin (IL)-6 in phorbol 12-myristate 13-acetate (PMA) plus calcium ionophore A23187-stimulated human mast cell line (HMC-1) cells. Thus it may be beneficial in the treatment of allergic diseases.	Shin et al., 2004
Aller-7, a botanical formulation of combination of extracts from <i>Phyllanthus emblica</i> , <i>Terminalia chebula</i> , <i>T. bellerica</i> , <i>Albizia lebbek</i> , <i>Piper nigrum</i> , <i>Zingiber officinale</i> and <i>P. longum</i>	Aller-7 inhibited histamine release from the mast cell induced by compound 48/80.	Amit et al., 2003
Chamomile, saffron, anise, fennel, caraway, licorice, cardomom and black seed mixture.	The herbal water-extract and quercetin inhibited histamine release from chemically-and immunologically-induced cells.	Haggag et al., 2003
<i>Xanthii fructus</i>	Aqueous extract dose-dependently inhibited histamine release from rat peritoneal mast cells (RPMC) by compound 48/80.	Hong et al., 2003
<i>Gleditsia sinensis</i> Lam.	n-Butanol fraction from the anomalous fruits significantly reduced in vitro histamine release from rat peritoneal mast cells triggered by compound 48/80.	Fu et al., 2003
<i>Forsythia fructus</i>	Extract dose-dependently inhibited the histamine release induced by compound 48/80 from RPMCs.	Kim et al., 2003
<i>Isodon japonicus</i> Hara (Labiatae)	Aqueous extract dose-dependently inhibited histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80. The level of cAMP in human mast cell line (HMC-1) cells, when extract was added, significantly was increased, compared with that of normal control. Thus it will be beneficial in the treatment of immediate-type allergic reaction.	Kim et al., 2003
<i>Euonymus alatus</i>	70% Ethanolic extract had a dose dependent restraint-effect to release the histamine from rat peritoneal mast cells.	Huang, 2003
<i>Mentha arvensis</i> L. var. <i>piperascens</i> Malinv. (Labiatae)	Aqueous extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE.	Shin, 2003
<i>Stachys riederi</i> var.	Aqueous extract inhibited the histamine release induced by	Kim et al., 2003

<i>japonica</i> Miq. (Labiatae)	compound 48/80 in RPMC. The level of cAMP in human leukemia cell line, HMC-1, when extract was added, significantly increased compared with that of basal cells. Thus it may be beneficial in the treatment of immediate-type allergic reaction.	
<i>Pinus pinaster</i>	Extract produced a concentration dependent inhibition of histamine release induced from mast cells.	Sharma et al., 2003
Dodutang, Korean traditional medicine.	Dodutang significantly inhibited the histamine release from rat peritoneal mast cells activated by compound 48/80. In addition, it potently inhibited the secretion of tumor necrosis factor- α (TNF- α), interleukin (IL)-1 β in phorbol 12-myristate 13-acetate plus calcium ionophore A23187-stimulated human mast cells. Thus it may be beneficial in the treatment of acute and chronic allergic diseases.	Shin et al., 2002
<i>Sanguisorba officinalis</i> L. (Rosaceae)	aqueous extract of root dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE. The level of cyclic AMP (cAMP) in RPMC, when extract was added, transiently and significantly increased compared with that of basal cells. Thus it may be beneficial in the treatment of allergic diseases.	Kim et al., 2002
<i>Mallotus philippensis</i>	Two new phloroglucinol derivatives, mallotophilippen A (1) and B inhibited histamine release from rat peritoneal mast cells induced by Compound 48/80. Thus it have anti-inflammatory effects.	Daikonya et al., 2002
<i>Vitex trifolia</i>	Vitexicarpin isolated from n-hexane extract is able to block effects of histamine released from sensitized mast cells possibly by stabilizing the mast cells membrane function.	Alam et al., 2002
<i>Rubus coreanus</i> Miq. (Rosaceae)	Aqueous extract of fruits dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE. The level of cAMP in RPMC, when extract was added, significantly increased, compared with that of the normal control. Moreover, extract had a significant inhibitory effect on anti-DNP IgE-induced tumour necrosis factor- α production from RPMC. Thus it may possess antianaphylactic action.	Shin et al., 2002
<i>Gleditsia sinensis</i>	70% Ethanol extract from the anomalous fruits significantly reduced histamine release from rat peritoneal mast cells triggered by compound 48/80.	Dai et al., 2002
<i>Bupleurum falcatum</i>	saikosaponin-A, a triterpenoid glycoside isolated from extract possesses inhibitory activity on histamine release induced by A-23187 in rat mast cells.	Park et al., 2002
<i>Salvia plebeia</i> R. Brown (Labiatae)	Aqueous extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE. The level of cyclic AMP in RPMC, when extract was added, significantly increased compared with that of basal cells.	Shin and Kim, 2002
<i>Acanthopanax senticosus</i>	Stem extract inhibited histamine release from mast cells in a dose-dependent manner. Moreover, it had an inhibitory effect on anti-dinitrophenyl IgE-induced tumor necrosis factor- α (TNF- α) production from mast cells.	Yi et al., 2002
<i>Magnolia obovata</i>	Crude bark extract and magnolol and honokiol isolated from the methanol fraction inhibited compound 48/80-induced histamine release from mast cells in a concentration-dependent manner.	Ikarashi et al., 2001
<i>Acanthopanax senticosus</i>	When root extract was given as pre-treatment, the histamine release from rat peritoneal mast cells induced by compound 48/80 was reduced in a dose-dependent manner.	Yi et al., 2001
<i>Bidens parviflora</i> WILLD.	Five new polyacetylene glucosides, bidensyneosides A1, A2, B, C, and 3-deoxybidensyneoside B, have been isolated from the air-dried whole plant, inhibited histamine release from rat mast cells stimulated by the antigen-antibody reaction.	Wang et al., 2001
<i>Bacopa monnieri</i>	The methanolic fraction inhibited histamine release from rat mast cells.	Samiulla et al., 2001
<i>Angelica keiskei</i>	Six chalcones isolated from the EtOAc extract of the dried roots,	Nakata and Babu, 2001

<i>Chaenomeles sinensis</i>	Xanthoangelol B, xanthoangelol C, and xanthoangelol E inhibited the compound 48/40-induced histamine release.	Osawa et al., 2001
<i>Gleditsia sinensis</i> thorns (Leguminosae)	5-O-p-coumaroylquinic acid butyl ester isolated from 90% EtOH extract of fruits inhibited the compound 48/40-induced histamine release.	
<i>Vitex rotundifolia</i> (L.) (Verbenaceae)	Aqueous extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE. The level of cyclic AMP in RPMC, When extract was added, transiently and significantly increased about fourfold compared with that of basal cells. Moreover, it had a significant inhibitory effect on anti-DNP IgE-induced tumor necrosis factor- α production from RPMC.	Shin and Kim, 2000
<i>Perilla frutescens</i> (Labiatae)	Aqueous extract of fruits dose-dependently inhibited the histamine release from the rat peritoneal mast cells (RPMC) by compound 48/80 or anti-DNP IgE. Moreover, it had a significant inhibitory effect on anti-DNP IgE-induced tumor necrosis factor- α production from RPMC.	Shin et al., 2000
<i>Sinomenium acutum</i>	Aqueous extract dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP IgE. The level of cyclic AMP in RPMC, When extract was added, transiently and significantly increased about 4-fold compared with that of basal cells.	Shin et al., 2000
<i>Tephrosia purpurea</i> Linn.	Aqueous extract of stem dose-dependently inhibited histamine release from the rat peritoneal mast cells (RPMCs) activated by compound 48/80 or anti-DNP IgE.	Kim et al., 2000
<i>Aglaia roxburghiana</i>	Ethanol extract showed a dose-dependent inhibition of rat mast cell degranulation induced by compound 48/80 and egg albumin.	Gokhale et al., 2000
<i>Solanum nigrum</i> Linn (Solanaceae)	Ethanol extract of the leaves protected mast cell degranulation by compound 48/80.	Janaki and Vijayasekaran, 2000
<i>Nyctanthes arbortristis</i> Linn (Oleaceae)	Petroleum ether extract of berries protected mast cell degranulation by clonidine.	Nirmal et al., 2012
<i>Nyctanthes arbortristis</i> Linn (Oleaceae)	The petroleum ether extract of bark showed maximum protection against mast cell degranulation by clonidine.	Nirmal et al., 2012
<i>Ficus bengalensis</i> Linn (Moraceae)	The petroleum ether extract of leaves showed maximum protection against mast cell degranulation by clonidine.	Nirmal et al., 2011
	Aqueous extract, ethyl acetate extract and methanol extract significantly protect mast cell from degranulation challenged by clonidine.	Taur et al., 2010

Conclusion:

In summary, the mast cell has emerged as a unique immune cell that could be activated by many non-immune processes and could participate in a variety of inflammatory diseases and various allergic conditions. Many plant extracts and isolated compounds showed promising mast cell degranulation effect, which is beneficial for the treatment of allergy and inflammatory diseases associated with mast cell. These plants can be a potential source of new lead compounds against mast cell degranulation and associated pathological condition.

Conflict of Interest statement

The authors declare no conflict of interest.

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