



## The Use of Herbal Medicines for Allergic Rhinitis

Prisyadhibha Ramadhani<sup>1\*</sup>

<sup>1</sup> Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

### ARTICLE INFO

#### Keywords:

Herbal medicine  
Allergic rhinitis  
Corticosteroid

#### Corresponding author:

Prisyadhibha Ramadhani

E-mail address:

[prisyardhibha.ramadhani@gmail.com](mailto:prisyardhibha.ramadhani@gmail.com)

The author has reviewed and approved the final version of the manuscript.

<https://doi.org/10.37275/ehi.v3i2.48>

### ABSTRACT

Allergic rhinitis (AR) is an immunoglobulin E-mediated illness that causes inflammation of the nasal mucosa. In recent years, the global incidence and prevalence of AR has been increased. AR has been treated with antihistamines, intranasal corticosteroids, decongestants, intranasal anticholinergics, intranasal cromolyn, leukotriene receptor antagonists, and immunotherapy. However, because many of the present medicines have documented negative side effects, there is a need to look for more effective and safer alternatives. Herbal therapy has long been used to treat the symptoms of AR, but its usefulness and safety have not been validated scientifically. In this review, recent research on the use of herbal medicine as a treatment for allergic rhinitis is collated and critically analyzed. From 2016 to 2021, the data was gathered mostly from English language publications published in journals or research from Pubmed databases. "Herbal medication" and "Allergic Rhinitis" were the terms or keywords used to discover relevant studies. This literature study may be useful in determining the potential utility of herbal medicine as a treatment for allergic rhinitis, determining the underlying mechanisms of action, and identifying natural product candidates for the development of innovative anti-allergic rhinitis drugs in the future.

## 1. Introduction

Allergic rhinitis (AR) is an immunoglobulin E-mediated illness that causes inflammation of the nasal mucosa which affecting 30% of the world population<sup>1</sup>. AR is defined as the occurrence of two or more of the following symptoms: nasal discharge, sneezing, nasal itching, and congestion, all of which interfere with everyday activities, interrupt typical sleep patterns, or negatively impact the patient's social life or intellectual performance<sup>2</sup>. Although AR is not a life-threatening condition, it has a substantial impact on quality of life and causes social and economic hardship. Asthma, rhinosinusitis, nasal polyps, otitis media, and allergic conjunctivitis are all linked to untreated AR<sup>3</sup>. In recent years, the global incidence and prevalence of AR has been increased. In recent years, the global incidence and prevalence

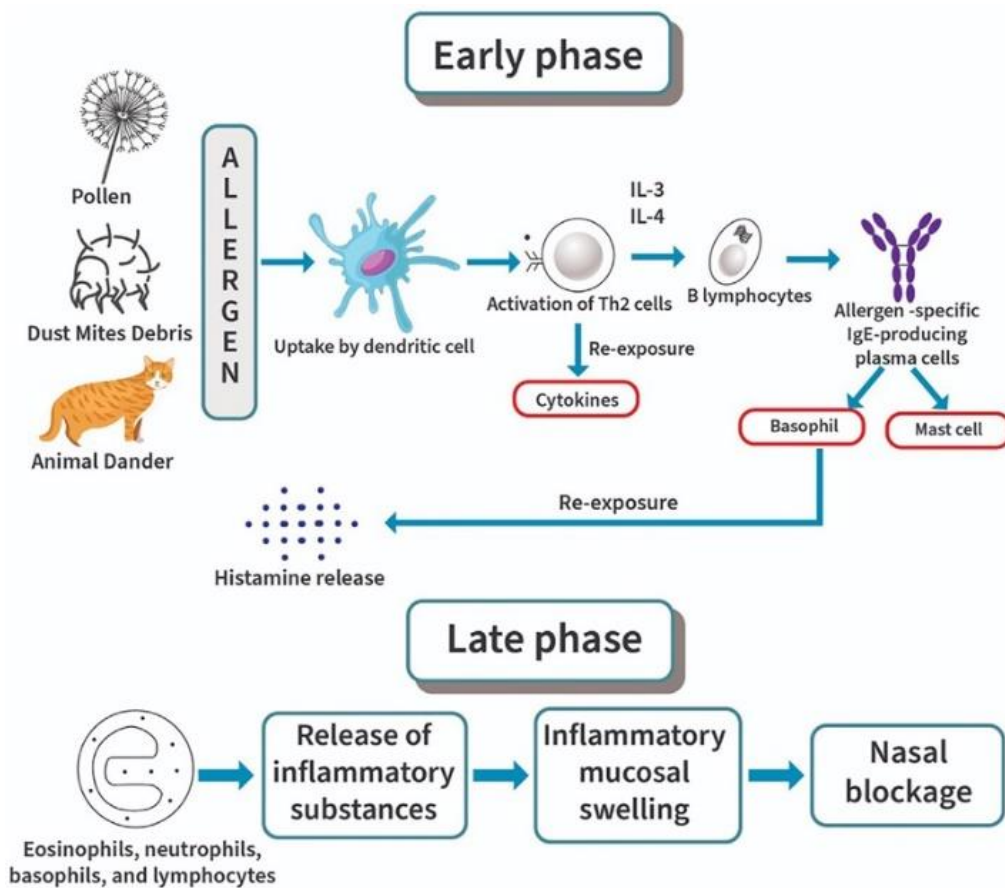
of AR has been increased. According to epidemiological research, the prevalence of AR has steadily increased in more industrialized countries, and it now affects 10–40% of adults and 2–25% of children<sup>1</sup>.

AR is induced by allergens, and it involves mucosal inflammation mediated by type 2 helper T (Th2) cells (Figure 1)<sup>1</sup>. Animal dander, dust mites, shellfish, and cigarette smoke are among allergens that can cause AR symptoms. Treatment of symptoms with traditional or alternative medicine may be effective, but identifying the triggers or allergies is necessary to avoid recurrence. It may be impossible to avoid potential allergen exposure, thus medication may be required to provide immediate relief. The usage of conventional treatment is on the

rise, as the number of people suffering from this condition rises.

When exposed to an inciting allergen, inflammatory cells such as mast cells, CD4-positive T cells, B cells, macrophages, and eosinophils invade the nasal lining (most commonly airborne dust mite fecal particles, cockroach residues, animal dander, molds, and pollens). T cells invading the nasal mucosa are largely T helper 2 (Th2), and they release cytokines (e.g., interleukin [IL]-3, IL-4, IL-5, and IL-13) that stimulate plasma cell IgE production. The

release of mediators such as histamine and leukotrienes, which cause arteriolar dilatation, increased vascular permeability, itching, rhinorrhea, mucous secretion, and smooth muscle contraction in the lung is triggered by allergens cross-linking IgE linked to mast cells<sup>4</sup>. This process consist of 2 main phases : early phase and late phase as described in Figure 1.



**Figure 1. Pathophysiology of allergic rhinitis: early phase and late phase.<sup>1</sup>**

The overall therapy and management of AR seeks to relieve symptoms as early as possible by avoiding allergen sources and controlling symptoms to prevent recurrence. However, due to industrialization, modernity, and urbanization, most people are unable to totally avoid allergies. Antihistamines, decongestants,

and glucocorticoids are commonly used to manage AR symptoms, although there are concerns of side effects with long-term usage, and the effects do not last once the medicine is stopped<sup>5</sup>. Furthermore, some AR sufferers are unable to take medicine due to its negative effects. Antihistamines, intranasal corticosteroids,

decongestants, intranasal anticholinergics, intranasal cromolyn, leukotriene receptor antagonists and immunotherapy have been used to treat AR<sup>1</sup>. However, because many of the present medicines have documented negative effects, there is a need to look for more effective and safer alternatives. Herbal therapy has long been used to treat the symptoms of AR. In a 2018 study, for example, Chinese herbal medicine (CHM) was found to be more efficient than placebo in treating allergic rhinitis in children. In comparison to controls, CHM may reduce the recurrence and amount of immunoglobulin E, as well as alleviate symptoms including sneezing, running nose, and nasal congestion<sup>4</sup>. Herbal medicine's efficacy and safety, on the other hand, have not been scientifically verified.

## 2. Methods

PubMed was used as the search engine of this study. The search was conducted using the keywords "Herbal medicine" and "Allergic Rhinitis" up until August 17, 2021. All of the articles chosen were published during the last five years. Duplicates articles that were published were removed. A total of 15 findings were gathered from PubMed and included in the review.

## 3. Result and Discussion

We discovered some relevant facts about the use of herbal medicine as a treatment for allergic rhinitis based on the findings of the review research (Table 1). Herbal medication and its bioactive metabolites work in several ways to fight immune system mediators implicated in AR inflammatory cascades or allergic reaction pathways. Several cellular, animal, and clinical investigations have been conducted to assess the anti-allergic and anti-inflammatory characteristics of medicinal plants, notably in the treatment of AR, employing AR-induced models or patients. In the pathophysiology of AR, a large variety of mediators are implicated. These various targeted cells or mediators are critical vital components for various phytochemicals identified in a variety of herbal medicines. The immune system may be suppressed by suppression of IgE, inhibition of cytokine

synthesis, inhibition of histamine release, and suppression of eosinophil production when medicinal plants and their bioactive metabolites have anti-allergic rhinitis effects<sup>1</sup>.

### Suppression of immunoglobulin E

The suppressive impact of medicinal herbs on IgE in an AR-induced paradigm has been investigated in a number of cellular and animal investigations. In an ovalbumin (OVA)-induced AR mouse model, the effect of *Bupleurum chinense* extract on allergic inflammatory responses was investigated by measuring anti-OVA specific IgE, IgG1, and IgG2a levels in the serum. This study found that taking *B. chinense* orally can help with allergic inflammatory responses in the early stages of AR, as the IgE antibody is the essential component that triggers the hypersensitive reaction. In an OVA-induced animal model, *Cinnamomum verum* bark extract was tested for its ability to reduce IgE levels. The extracts from the bark of *C. verum* demonstrated prophylactic potential against an OVA-induced model by suppressing IgE and histamine production, according to this study. Another in vivo investigation in OVA-induced AR treatment with a methanol extract of *Ostericum grosseserratum* found that *O. grosseserratum* extract inhibited IgE formation in allergy responses by regulating the IL-4/IFN- ratio. Shikonin, a naphthoquinone derivative derived from the roots of *Symphytum officinale* L., was tested in an OVA-induced AR rat model for its ability to reduce IgE production during allergic reactions. The findings revealed that Shikonin, in addition to its modulation of GATA-3 and T-bet protein expression in nasal mucosa tissue and anti-oxidative stress actions, could reduce AR in the rat model via suppressing IgE levels. *Camellia japonica* L. has yielded okicamelliaside, a ellagic acid glucoside. It is an anti-degranulation agent with the ability to decrease allergy reactions in vivo<sup>1</sup>.

### Inhibition of histamine release

Histamine has been a possible target in controlling AR disease since it is one of the most significant critical components in the early stages of AR pathogenesis and

causes acute symptoms within minutes of allergen exposure. In vivo studies on phorbol myristate acetate (PMA)-induced or histamine-induced upregulation of H1 receptor messenger ribonucleic acid (mRNA) expression in human epithelial cells were undertaken using wild grape or *Ampelopsis glandulosa* var. *brevipedunculata* hot water extract. The study found that it had a high level of effectiveness in decreasing histamine release in an AR-induced model, suggesting that it could be useful in reducing the symptoms of AR. *Wurfbainia villosa* var. *xanthioides* extract from the *Zingiberaceae* family decreased systemic allergy reactions and histamine production considerably. Because there was not much of a meaningful change when a greater dose of *W. villosa* extract was applied, the activity of *W. villosa* in suppressing histamine release was moderate. The anti-allergic activity of a hydroalcoholic extract of *Cinnamomum verum* standardized to type-A procyanidines polyphenols (CZ-TAPP) in mice with OVA-induced AR was investigated. When compared to AR control mice, treatment with *C. verum* extracts resulted in a significant reduction in IgE serum and histamine release, as well as a reduction in symptoms such as sneezing and rubbing. In comparison to control mice given OVA alone, oral treatment of *Ostericum grosseserratum* methanol extract significantly decreased OVA-specific IgE production in OVA-sensitized mice. According to this research, *O. grosseserratum* shows a high level of activity in an AR-induced model. *Artemisia abrotanum* L., produced as a nasal spray, was another plant that had a histamine-suppressing action. Within minutes of application, nasal spray preparations have shown a rapid beginning of action and alleviation of nasal symptoms such as congestion, rhinorrhea, and sneezing. Peppermint or *Mentha piperita* L., a 50 percent ethanol extract, has been shown to suppress histamine release from peritoneal mast cells in actively sensitized rats<sup>1</sup>.

### **Inhibition of cytokines release**

Mast cells stimulated by an IgE-mediated mechanism

produced cytokines, mainly cysteinyl-leukotrienes, in AR. Eosinophils produce and release cytokines like IL-3, IL-5, and GM-CSF, which are important in the late stages of allergic inflammation. Several herbal treatments have been utilized to treat AR in Korea. SCRT, also known as Sho-seiryoto or Xiao-Qing-Long-Tang, is a combined herbal preparation that has been utilized in Asian countries for hundreds of years. In an ovalbumin-induced AR model, SCRT has been shown to have antiallergic effects by reducing Th2 cytokine release and decreasing infiltration of inflammatory cells into the nasal mucosa<sup>2</sup>. Traditional Chinese herb *Saposhnikovia divaricata* is often used to treat allergic rhinitis. According to a study, *S. divaricata* reduces the levels of inflammatory cytokines<sup>5</sup>. In OVA-sensitized mice, 10mg/kg of *Allium hookeri* thanol extract significantly reduced the elevated rubs scores, IgE, and IL 4 levels. When OVA-induced mice were given 100 mg/kg/day of *Piper nigrum* L. extract, the level of Th1 related cytokines such as IL-12 was significantly reduced, whereas IFN- was significantly increased. *P. nigrum* may be a promising immunotherapy technique for airway illnesses like AR since it has numerous mechanisms that act against the AR model's cascades to alleviate symptoms through a subsequent set of pathways in the pathophysiology of AR. In a randomized therapeutic experiment, 43 people with a history of seasonal AR were given a syrup version of *Zataria multiflora* and tested it. When compared to the control group, the multiflora syrup formulation significantly reduced IL-17 expression. Ze339 is a herbal extract from *Petasites hybridus* L. called Petasol butenoate complex. leaves has been shown to be beneficial in the treatment of rheumatoid arthritis. Ze339 and its components, isopetasin and neopetasin, are viable candidates for developing medicines to address immunological aberrations caused by chronic cytokine-induced inflammation<sup>1</sup>.

Plant name	Family	Plant part used	Isolated compound/ extract used	Assay type/Type of model or cells	Mechanism of action	References
<i>Acanthus ilicifolius L</i>	Acanthaceae	Ariel	95% ethanol extract	In vivo blood from toluene 2, 4-diisocyanate (TDI)-induced allergic mice model	Decreased the expression of leukocytes, eosinophils, monocytes and basophils	Sarder et al. (2018)
<i>Allium hookeri thwaites</i>	Amaryllidaceae	Not stated	Ethyl alcohol extract	In vivo stimulated human mast cell line (HMC) 1 cells, and nasal mucosa of ovalbumin (OVA) sensitized mouse model or AR	it reduced IL-4, VEGF expression and inhibited TNF $\alpha$ in nasal mucosa tissue	Kim et al (2019)
<i>Wurfbainia villosa var.xanthioides (Wall, ex Baker) Skomick. And A.D. Poulsen</i>	Zingiberaceae	Fruit	Aqueous extract	In vivo blood samples from heart was taken for histamine serum measurement from male mice	Reduced histamine release and calcium ionophore-mediated expression of TNF- $\alpha$	Kim et al (2007)
<i>Ampelopsis glandulosa var.brevipedunculata (Maxim.) Momly</i>	Vitaceae	Fruit	Hot water extract	In vivo nasal mucosa and protein serum from toluene-2,4 diisocyanate (TDI)-sensitized rats	Reduced H1R and IL-9 gene expression in the nasal mucosa	Islam et al (2018)
<i>Asarum sieboldii Miq</i>	Aristolochiaceae	Root	Essential oil	In vivo Blood and serum sample from fundus venous plexus and nasal mucosa of OVA induced sixty male Sprague-Dawley rats	Reduced IgE and histamine levels. Reduced IL-17 and increased IFN- $\gamma$ levels	Zhang and Kang (2020)
<i>Bupleurum chinense DC.</i>	Apiaceae	Not stated	Dissolved saline Bupleurum chinense DC extract powder	In vivo blood serum BALB/c mice	It suppressed mast cell infiltration and down-regulated IL-4, IL-5 and IL-13 levels compared to the levels. Besides it also decreases the IgE and IgG1 expression	Bui et al (2019c)
<i>Chamaecyparis obtuse (Siebold and Zucc.) Endl</i>	Cupressaceae	Leaves	Essential oil	In vivo IgE levels, nasal lavage fluid (NLF), splenocytes and sinonasal mucosa of OVA induced BALB/c mice	Inhibited the production of IgE, reduces the inflammatory mediators level (IL-4, IL-10, IFN- $\gamma$ , and TNF- $\alpha$ ) in NLF. It also inhibits the IL-4, GATA-3 expressions as well as IL-10 and Foxp3 Mrna expressions in sinonasal mucosa prevented the elevation of histamine and IgE level	Shin et al. (2020)
<i>Cinnamomum verum J.Presl</i>	Lauraceae	Bark	Standardized hydroalcoholic extract	In vivo OVA induced male BALB/c mice (histamine challenge based on effects on nasal sign)	Prevented the elevation of histamine and IgE levels	Aswar et al (2015)
<i>Cissampelos sympodials Eichier</i>	Menispermaceae	Root	Warifleine (3) and methywariflene (4)	In vivo nasal lavage fluids (BALF) of OVA induced isogenic female BALB/c mice (20-25 g)	Reduced the number of inflammation cells, eosinophils, IgE, and cytokines (IL-4, IL-13, IL-5 and IL-17)	Cavalcanti et al (2020)
-	-	leaves	Okicamelliaside (2) (OCS)	In vivo blood samples from heart was taken for IgE measurement from Japanese cedar pollen induced male BALB/c mice	Suppressing degranulation as it has shown no significant differences in IgE levels	Kuba et al (2008)
<i>Citrus deliciosa Ten</i>	Rutaceae	Fruit	50% methanol extract from MEC (Citrus unshiu Powder)	In vivo basophils of patients with seasonal allergic rhinitis to pollen and rat basophilic leukemia RBL-2H3 cells	Inhibited histamine release and decrease the release of $\beta$ -hexosaminidase	Kobayashi and Tanabe (2006)
<i>Cryptomeria japonical (Thunb.ex L.f.) D.Don</i>	cupressaceae	Pollen	Transgenic rice containing the hypoallergenic pollen of the plant	In vivo blood samples of 4 Japanese monkey with Japanese Cedar Polinosis and 2 healthy monkey fed with 20 g of raw polished transgenic rice seeds containing destructured Cry j1 and Cry j2 derivatives (10-25 mg antigens/ 20g	Reduced IgE antibody and peripheral blood mononuclear cell (PBMC) Proliferation by inducing the oral immune tolerance against Japanese cedar allergens	Saito et al (2020)

<i>Eupetorium cannabinum L</i>	Asteraceae	Arial	60% ethanol extracts	seeds) In vivo Lipopolysaccharides (LPS) stimulated human neutrophils	Inhibited IL-8 and TNF $\alpha$ production in LPS-stimulated human neutrophils	Michalak et al (2019)
<i>Lonicera japonica thymb</i>	Caprifoliaceae	Flowe	95% ethanol extracts	In vivo nasal septum mucosal tissue	Inhibited airway eosinophilia, IgE production and cytokines expression	Bai et al (2020)
<i>Mangifera indica L</i>	Anacardiaceae	Tree	Mangiferin (8)	In vivo nasal, lung tissue and nasal lavage fluid of OVA-induced AR model	Reduced eosinophil, IgE, igG, histamine levels, IL-4, IL-5, IL-13, IL-17, IL6, GATA-3, ROR $\gamma$ , TNF $\alpha$ and increase in IFN $\gamma$ level	Piao et al (2020)
<i>Mentha x piperita L</i>	Lamiaceae	Arial	Luteolin-7-O-rutinoside (5)	In vivo rat peritoneal mast cells	Protection from mast cell degranulation	Inoue et al (2011)
<i>Ostericum grosserratum (Maxim.) kitag</i>	Apiaceae	Root	methanol extracts	In vivo blood samples from Balb/c mice (10 weeks old)	Decreased histamine release and have immunosuppressive effects on mast cells and meaningfully inhibited the antigen-induced mRNA expression and production of inflammatory cytokines related to allergic reactions, Also inhibits the IgE production	Jung et al (2011)
<i>Petasites hybridus (L) G.Gaertn., B.Mey, and Schreb</i>	Asteraceae	leaves	Petasin (7)	In vivo primary human nasal epithelial cell	Inhibited the IL-8 expression following PolyIC stimulation	Steirt et al (2017)
<i>Pleum pratense L</i>	Poaceae	Leaves	Aqueous grass pollen allergen extract	In vitro cultures of house dust mite stimulated peripheral blood mononuclear cells from patient with history of severe summer hay fever	Reduced the production of IL-5	Till et al (1997)
<i>Piper nigrum L</i>	Piperaceae	Fruit	70% ethanol extracts	In vivo nasal lavage fluid (NALF) from male six-week-old BALB/c mice	Decreased the production of eosinophils, neutrophils and macrophages cells in NALF. Inhibits the phosphorylation of NF $\kappa$ Bp65-free and bN $\kappa$ BP65, I $\kappa$ B $\alpha$ . It also may down regulates the Th17-related cytokines such as factor ROR $\gamma$ , IL 17A and Th2-related cytokineslike IL-5, IL-13 and IL-6	Bui et al (2019a)
-	-	Fruit	70% ethanol extracts	In vivo cell count for nasal mucosa and blood sample of OVA-induced BALB/c mice	Suppressed the OVA-specific antibodies, serum histamine release and inflammatory cells accumulation. It enhanced the activation of Nrf2/HO-1 signaling	Bui et al (2020)
<i>Rosa multiflorae</i>	Rosaceae	-	Standardized extract from Rosae multiflorae extract powder (RMFE)	In vivo NALF, nasal tissue, spleen and nasal-associated lymphoidtissue (NALT) from OVA-induced AR mouse model	Inhibited the accumulation of eosinophils in the nasal mucosa, nasal lavage fluid (NALF) and goblet cells in the nasal epithelium, and mast cell in the respiratory region of the nasal cavity. It also suppressed Th2-related cytokines in NALF, NALT and splenocytes, whereas the Th1- associated cytokine IL-12 was	Bui et al (2019b)

					upregulated by RMFE.	
<i>Symphytum officinate L</i>	Boraginaceae	Root	Shikonin (1)	In vivo nasal mucosa tissue from AR model rats	Decreased Ig-E and IL-4 and GATA-3 expression level. Increase level of IFN- $\gamma$ , superoxide dismutase and malondialdehyde	Wang et al (2017)
<i>Stephania tetrandia S.Moore</i>	Menispermaceae	Root	Hot water extract and 99% ethanol extracts	In vivo and vitro plasma samples of 26 week old BALB/c female mice (in vivo) RBL-2H3 cells (In vitro) RBL-2H3 cells (In vitro)	Decreased plasma Ig-E concentration and degranulation levels	Maeta et al (2017)
<i>Tussifago farfara L</i>	Asteraceae	Fruit	Tusilagone (6)	In vivo and vitro nasal mucosa tissue of OVA sensitized guinea pig (In vivo) RBL-2H3 cells (In vitro)	Reduced the production of IgE, histamine, and IL-6. it also inhibits Lyn/Syk, NF- $\kappa$ B and p38 MAPK signaling pathways in activated mast cells	Jin et al (2020)
<i>Xanthium strumarium L</i>	Asteracea	Flower	75% aqueous ethanol extracts	In Vivo nasal mucosa of allergic rhinitis model rats.	Inhibited the releases of histamine in bone marrow-derived mast cell. It also decreased the serum levels of IgE, IL-1, IL-4 and IL-5 of AR rats, whereas increased the IFN-level in serum	Peng et al (2019)

**Table 1: Herbal medicine used as treatment for allergic rhinitis<sup>1</sup>**

### Suppression of eosinophil production

In allergic inflammation, eosinophils and mast cells are the main inflammatory cells. Eosinophil infiltration has long been thought to be the most important feature of AR mucosal inflammation. The use of an oral dose of ethanolic extract of *Acanthus ilicifolius L.* could reduce the number of these inflammatory cells. With medium activity, ethanol extracts of *A. ilicifolius* considerably reduced sneeze and nasal scoring. Eosinophil suppression was shown to be considerable when given with a standardized extract of *Rosa multiflora* in another in vivo investigation. In a patient given an Urtidin F. C tablet containing 150 mg of *Urtica dioica L.*, there was also a statistically significant reduction in mean nasal smear eosinophil count. When compared to the OVA group administered at doses of 5 and 20 mg/kg, Mangiferin extracted from *Mangifera indica L.* demonstrated a substantial decrease in eosinophil levels. The animal models treated with 2.5 mg/kg dexamethasone exhibited a similar substantial difference in eosinophil levels<sup>1</sup>.

### Toxicology

The herbal medicine presented in this review could be developed as an alternative to treat the symptoms of AR. However, more research is needed to determine their level of safety for human use in the treatment of AR. When it comes to developing pharmaceutical or health products, the most crucial consideration is safety. As a result, toxicity studies of herbal medicine and their bioactive metabolites should be conducted and analyzed in order to discover any potential acute or chronic toxicity that may occur when they are used to treat allergy illnesses like AR. Some of these possible herbal medicines have been subjected to toxicity tests.

### 4. Conclusion

The reduction of histamine release is one of the most common possible targets in treating AR since histamine is one of the most significant crucial components in the early stages of AR pathogenesis and causes symptoms within minutes after allergen contact. Antihistamine medications are currently used as first-line therapy in traditional treatment.

Other mechanistic effects, such as IgE suppression, cytokine inhibition, and eosinophil suppression, have also been employed as targets in efforts to find bioactive principles from herbal medicine that have substantial anti-allergic rhinitis benefits.

rhinitis: A study protocol for a randomized, open-label, cetirizine controlled, clinical trial. *Medicine (Baltimore)*. 2018; 97(34): e11812.doi:10.1097/MD.00000000000011812.

## 5. References

1. Rahim NA, Jantan I, Said MM, Jalil J, Abd Razak AF, Husain K. Anti-Allergic Rhinitis Effects of Medicinal Plants and Their Bioactive Metabolites *via* Suppression of the Immune System: A Mechanistic Review. *Front Pharmacol*. 2021; 12:660083. Published 2021 Apr 13. doi:10.3389/fphar.2021.660083.
2. Zheng Z, Sun Z, Zhou X, Zhou Z. Efficacy of Chinese herbal medicine in treatment of allergic rhinitis in children: a meta-analysis of 19 randomized controlled trials. *J Int Med Res*. 2018; 46(10): 4006-4018. doi:10.1177/0300060518786905.
3. Kim MH, Ko Y, Ahn JH, et al. Efficacy and safety of So-Cheong-Ryong-Tang in treatment of perennial allergic rhinitis: study protocol for a double-blind, randomised, parallel-group, multicentre trial. *BMJ Open*. 2017; 7(9): e016556. Published 2017 Sep 27. doi:10.1136/bmjopen-2017-016556.
4. Liao Y, Zhong J, Liu S, et al. Yu ping feng san for pediatric allergic rhinitis: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*. 2021; 100(13): e24534. doi:10.1097/MD.00000000000024534.
5. Kim YE, Son MJ, Jung SY, Kwon O, Lee JH, Lee DH. Socheongryong-tang for improving nasal symptoms associated with allergic