

# A Review of Acupuncture for Allergic Disorders: Modulation of Mast Cell Regulation via Inflammatory Pathway Suppression and Cytokine Balance

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**Objective:** Mast cells drive allergic diseases (asthma, rhinitis, dermatitis) via degranulation and pro-inflammatory mediator release. This review explores acupuncture's role in modulating mast cells to alleviate allergic symptoms.

**Methods:** We screened PubMed and Embase databases from January 2010 to January 2025 to search for published studies. The search keywords used are as follows: ["acupuncture" or "electroacupuncture"], ["allergic disease" or "asthma" or "allergic rhinitis" or "dermatitis" or "urticaria"], ["mast cell"]. 365 peer-reviewed studies on human/animal models were included, and articles that did not meet the requirements were excluded.

**Results:** Acupuncture inhibited mast cell degranulation, reducing histamine and IgE levels. It downregulated pro-inflammatory cytokines (TNF- $\alpha$ , IL-4, IL-5, IL-13) and upregulated anti-inflammatory IL-10, via suppressing NF- $\kappa$ B, MAPK (p38, ERK), and TLR4/MyD88 pathways. Clinically, it improved asthma (FEV1/PEF elevation), allergic rhinitis, and atopic dermatitis. Preclinically, it reduced eosinophil infiltration and inhibited NLRP3/caspase-1-mediated pyroptosis, further mitigating inflammation.

**Conclusion:** Acupuncture alleviates allergic disorders by targeting mast cells and inflammatory cascades, supporting its potential as a safe, effective therapeutic option.

**Keywords:** acupuncture, mast cells, allergic diseases, allergic asthma, traditional Chinese medicine, immune system

## Introduction

Allergic diseases refer to a category of disorders caused by abnormal immune responses, typically characterized by hypersensitivity to common environmental substances such as mold, insects, pollen, dust mites, and food.<sup>1</sup> These diseases primarily include allergic rhinitis, allergic asthma, atopic dermatitis, food hypersensitivity, and others. The pathogenesis of allergic diseases is complex, involving multiple factors such as genetic, environmental, and immunological influences.<sup>2</sup> With changes in modern lifestyle, the incidence of allergic diseases has shown an upward trend, significantly impacting patients' quality of life. These conditions not only cause physical discomfort but may also trigger psychological issues such as anxiety and depression, further affecting patients' daily life and social capabilities.<sup>3,4</sup>

The pathogenesis of allergic diseases primarily involves immunoglobulin E (IgE)-mediated allergic reactions and non-IgE-mediated responses. IgE-mediated reactions typically involve mast cell activation and degranulation, leading to the release of histamine and other inflammatory mediators, which trigger a series of allergic symptoms.<sup>5</sup> Additionally, mast cells contribute to the maintenance of chronic inflammation in allergic reactions, promoting the chronicity of allergic diseases.<sup>6,7</sup> Abnormal activation of mast cells is not only associated with the development of allergic diseases but

may also exacerbate other immune system disorders. Therefore, targeting mast cell regulation has become a key direction in the treatment of allergic diseases.

Acupuncture, a traditional Chinese medical therapy with a long history, has increasingly gained recognition in modern medicine.<sup>8</sup> Its fundamental theory involves stimulating specific acupoints to regulate the body's qi and blood, thereby achieving the goal of disease treatment.<sup>9</sup> In recent years, a growing body of research has demonstrated that acupuncture exhibits significant effects in modulating immune responses and reducing inflammation. Especially in the treatment of allergic diseases, acupuncture is believed to alleviate allergic symptoms by regulating mast cell function and reducing their degranulation response.<sup>10,11</sup> Needling Yingxiang (LI20) or sphenopalatine ganglion acupuncture alleviates AR's nasal symptoms and reduces recurrence, while its anti-allergic mechanisms involve rebalancing Th1/Th2 cytokines (upregulating IFN- $\gamma$ , downregulating IL-4/IL-5), lowering serum IgE (inhibiting mast cell activation), and suppressing NF $\kappa$ B-mediated inflammation.<sup>12–16</sup>

Current research on acupuncture and allergic diseases indicates that acupuncture not only improves symptoms of conditions such as allergic rhinitis and allergic asthma but may also exert anti-allergic effects by regulating the number and function of mast cells and influencing the expression of related cytokines.<sup>7,17</sup> For example, studies have found that acupuncture can significantly reduce serum IgE levels in patients with allergic diseases and inhibit mast cell degranulation, providing strong scientific evidence for its application in treating allergic conditions.<sup>6,18</sup> However, despite the growing recognition of acupuncture's potential in allergic disease therapy, more clinical trials and mechanistic studies are still needed to further validate its efficacy and safety.

## Method

### Search Strategy

We screened PubMed and Embase databases from January 2010 to January 2025 to search for published studies. The search keywords used are as follows: ["acupuncture" or "electroacupuncture"], ["allergic disease" or "asthma" or "allergic rhinitis" or "dermatitis" or "urticaria"], [{"mast cell"}]. We only search for English publications. Preliminary screening is conducted using search engines provided by various databases. After deleting 128 duplicate records, we identified 1025 related articles.

### Study Selection

Before reading the full texts of the selected papers, we used Endnote software to identify references relevant to the topic. Among them, 32 articles lacked full-text abstracts, 156 were irrelevant to acupuncture and allergic diseases, 253 were reviews or meta-analyses, and 219 clinical research articles. Finally, 365 full-text original research papers relevant to the topic were included. The flowchart of the search process is shown in [Supplementary Figure 1](#).

### Data Extraction

Given the overlapping nature of the research content, this study adopted a targeted approach to select representative literature and focused on extracting key data on how acupuncture treats allergic diseases through mast cell regulation. A predefined data extraction form was used to systematically collect information, which included the types of allergic diseases, intervention details (treatment protocols, acupoint selection, and acupuncture parameters), and outcome metrics (inflammatory phenotypes and mechanism-specific assays). Data extraction was first conducted by the primary author and then cross-checked by other authors. Through double verification, we ensured data integrity and reliability, laying the foundation for subsequent analyses of efficacy and mechanisms.

### Pathophysiological Mechanisms of Allergic Diseases

The pathophysiological mechanisms of allergic diseases involve complex immune responses and the participation of multiple cell types. An allergic reaction is typically triggered by the immune system's excessive response to harmless environmental substances such as Mold, insects, pollen and dust mites.<sup>19</sup> Allergic reactions can be classified into four types, with the IgE-mediated type I reaction being the most common. This reaction involves the production of specific

IgE antibodies, which bind to mast cells and basophils, leading to the release of histamine and other inflammatory mediators from these cells upon re-exposure to allergens, thereby triggering allergic symptoms.<sup>20</sup>

The immune system plays a central role in allergic reactions, particularly involving immune cells such as T cells, B cells, mast cells, and basophils.<sup>21</sup> When an allergen first enters the body, B cells produce specific IgE antibodies that bind to high-affinity IgE receptors (FcεRI) on the surface of mast cells. Upon re-exposure to the same allergen, the allergen cross-links these IgE antibodies, triggering mast cell degranulation and the release of histamine, leukotrienes, and other inflammatory mediators, which in turn initiate allergic reactions.<sup>20,22</sup> Additionally, cytokines such as IL-4 and IL-13 play critical roles in promoting T cell differentiation into Th2 cells and regulating IgE synthesis, further exacerbating the development of allergic responses.<sup>23</sup>

In allergic reactions, mast cells and basophils serve as the primary mediator cells.<sup>24</sup> Through binding IgE via their surface FcεRI receptors, mast cells act as the primary effector cells in allergic reactions. Upon exposure to allergens, they rapidly release various bioactive substances such as histamine, peptides, and cytokines, leading to vasodilation, smooth muscle contraction, and recruitment of inflammatory cells.<sup>25,26</sup> Basophils also participate in allergic reactions, releasing mediators that exacerbate inflammatory responses and cause tissue damage. Additionally, dendritic cells initiate allergic reactions by capturing and presenting allergens to activate T cells during the early stage, further driving the progression of allergic responses.<sup>27</sup>

The clinical manifestations of allergic diseases are diverse, commonly including allergic rhinitis, asthma, atopic dermatitis, and food hypersensitivity.<sup>28</sup> Symptoms of these conditions can range from mild manifestations such as nasal congestion, runny nose, and sneezing to severe symptoms like dyspnea, skin itching, and abdominal pain.<sup>29,30</sup> Based on the duration and severity of symptoms, allergic diseases are classified into acute and chronic categories. Acute allergic reactions typically present with rapidly emerging symptoms such as urticaria and anaphylactic shock, whereas chronic allergic conditions like allergic rhinitis and asthma are characterized by long-term symptoms and recurrent episodes.<sup>31,32</sup> Management of these conditions typically requires comprehensive consideration of patients' allergens, symptoms, and their severity to develop individualized treatment plans.

### Biological Characteristics of Mast Cells

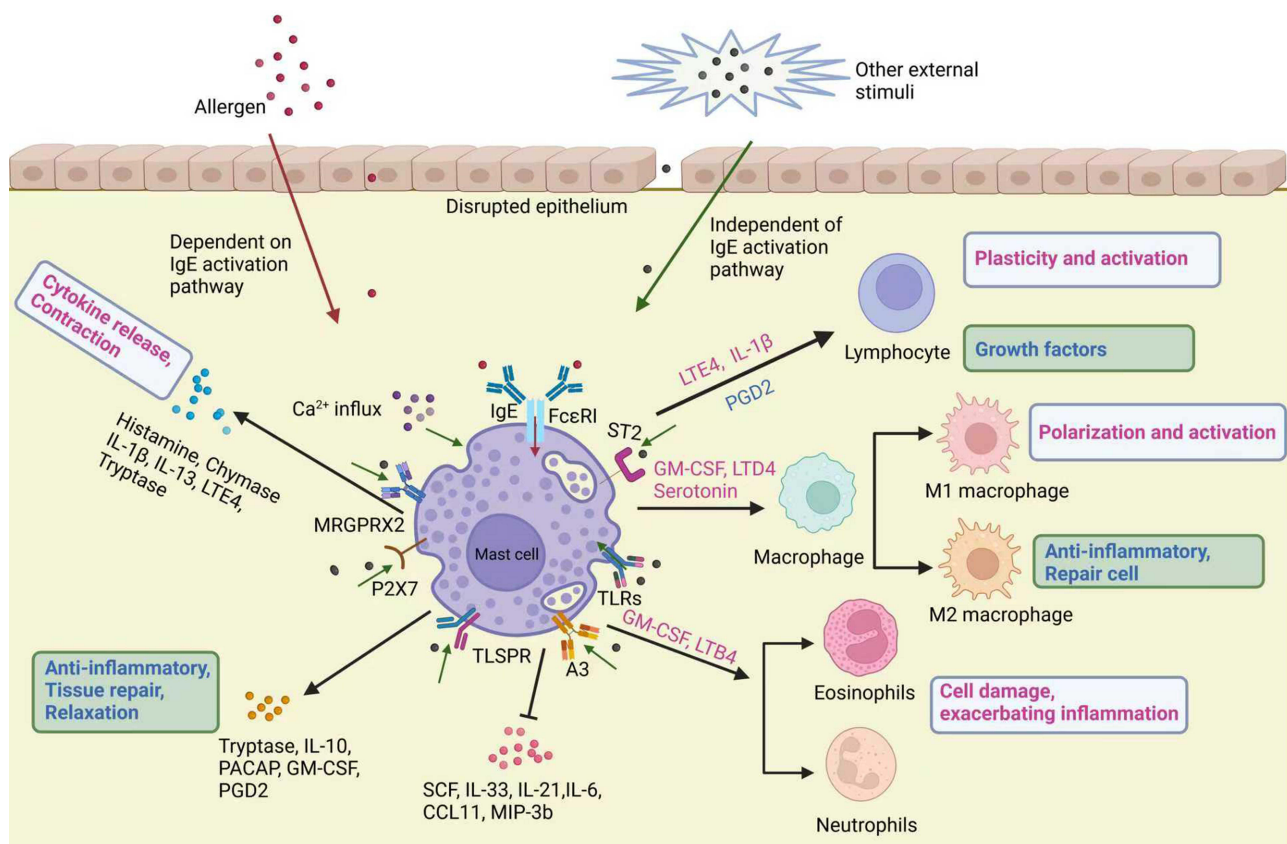
Mast cells are a critical type of immune cell, primarily originating from hematopoietic stem cells in the bone marrow.<sup>33</sup> They are generated by the yolk sac and embryonic liver during early embryonic development, subsequently replaced by bone marrow-derived progenitor cells.<sup>34</sup> Mast cells exhibit extensive distribution throughout the body, primarily localized in tissues such as the skin, respiratory tract, gastrointestinal tract, and perivascular areas.<sup>35</sup> Their tissue-specific localization is closely associated with their functions, particularly in orchestrating allergic reactions and immune responses. Studies indicate that the number and activity of mast cells in different tissues are influenced by multiple factors, including the local microenvironment, inflammatory status, and their interactions with other immune cells.<sup>25,36</sup>

Mast cells express FcεRI, C-KitR, toll-like receptors (TLRs), recombinant purinergic receptor P2X, ligand gated ion channel 7 (P2RX7), and other receptors on their surface. Mast cells exert their functions only after activation, which primarily occurs through two pathways: IgE-mediated and non-IgE-mediated.<sup>37</sup> IgE-mediated activation occurs when specific antigens bind to FcεRI on mast cell surfaces, leading to a rapid increase in intracellular calcium ion concentration and thereby triggering degranulation to release bioactive substances such as histamine and cytokines.<sup>37,38</sup> Non-IgE-mediated activation pathways include pathogen-associated molecular patterns (PAMPs) (eg, endotoxin) and products derived from the innate immune system (eg, complement components, cytokines, and endogenous peptides).<sup>39</sup> Studies have shown that calcium ionophores can promote the opening of calcium release-activated calcium (CRAC) channels, increasing intracellular Ca<sup>2+</sup> concentration to activate mast cells.<sup>40</sup> Additionally, TLR activation typically triggers mast cell activation, with some TLRs also inducing the release of lipid mediators. Similarly, activation of adenosine A3 receptors and ATP-gated P2X7 receptors on mast cells triggers the release of inflammatory mediators. Recent research has identified that Mas-related G protein-coupled receptor X2 (MRGPRX2) plays a critical role in non-IgE-mediated mast cell activation, providing new insights into understanding drug-induced pseudoallergic reactions.<sup>41,42</sup> Furthermore, both endogenous and exogenous stimuli can activate mast cells through different receptors, thereby regulating their functions and mediator release.<sup>42,43</sup>

Mast cells play a central role in allergic reactions. By releasing mediators such as histamine, leukotrienes, and prostaglandins, they rapidly induce local and systemic inflammatory responses, leading to the emergence of allergic symptoms like urticaria and asthma. Activation of mast cells triggers two critical events: first, phosphorylation of phospholipase C $\gamma$ 1 (PLC- $\gamma$ 1) mediates an increase in intracellular calcium levels, leading to the release of proteases, proteoglycans, and neuropeptides stored in mast cell granules;<sup>44</sup> second, activation of NF- $\kappa$ B mediates the secretion of lipid mediators and cytokines, which enhance the expression of numerous inflammation-related genes and influence endothelial, epithelial, and smooth muscle cells, thereby contributing to the pathogenesis of asthma.<sup>36,41,45</sup> Additionally, mast cells regulate the intensity and nature of immune responses through interactions with other immune cells, impacting the progression of allergic diseases. As illustrated in Figure 1, these findings provide potential targets and insights for developing novel allergic treatment strategies.

### Regulation of Acupuncture on Mast Cells

Acupuncture, a core therapeutic modality of traditional Chinese medicine and an internationally recognized form of complementary and alternative medicine, is widely used globally. Clinical studies have shown that key acupoints for treating allergic diseases include Danzhong (RN17), Zhongfu (LU1), Zusanli (ST36), Dingchuan (EX-B1), Dazhui (GV14), and Fengmen (BL12).<sup>46–48</sup> These acupoints are primarily distributed along the Lung Meridian (LU), Conception Vessel (CV), Stomach Meridian (ST), and Bladder Meridian (BL), which are highly consistent with data from TCM clinical meta-analyses and practical applications. In addition to these commonly used points, auxiliary



**Figure 1** The role of mast cells in allergic reactions. Mast cells have a bidirectional effect. On the one hand, mast cells release multiple mediators after activation, which exacerbate inflammation by activating other cells (pink). On the other hand, mast cells regulate their own activation and protease production, which can inactivate pro-inflammatory cytokines and control airway inflammation. They also participate in repairing the airway epithelial barrier by releasing growth factors and promoting anti-inflammatory M2 macrophage polarization (blue). The red dots represent allergens; The dark gray origin represents other external stimuli; The purple origin represents calcium ions; The yellow dots represent anti-inflammatory factors; Pink dots represent pro-inflammatory factors.

**Abbreviations:** GM-CSF, Granulocyte-Macrophage Colony Stimulating Factor; LTB4, Leukotriene B4; LTD4, Leukotriene D4; LTE4, Leukotriene E4; PGD2, Prostaglandin D2; CCL11, C-C Motif Chemokine Ligand 11; MIP-3b, Macrophage Inflammatory Protein 3 beta; PACAP, Pituitary Adenylate Cyclase-Activating Polypeptide; SCF, Stem Cell Factor.

acupoints such as Fuliu (KI7), Bishu (BL20), Yuji (LU10), Lieque (LU7), Fenglong (ST40), and Feishu (BL13)<sup>49–51</sup> also play important roles in relieving allergic symptoms, with their anatomical locations concentrated on the back and limbs ([Supplementary Figure 2](#)).

In recent years, the mechanism by which acupuncture exerts therapeutic effects through immune system regulation has become a research hotspot in this field. Studies have shown that acupuncture stimulation can significantly affect the activity of mast cells.<sup>52</sup> Mast cells are widely distributed throughout the body, particularly in tissues such as the skin and mucous membranes, where they play a critical role in immune and allergic responses. Acupuncture stimulation activates mechanosensitive channels in mast cells (eg, TRPV1, TRPV2, and TRPV4), promoting their degranulation and leading to the release of bioactive substances such as histamine and adenosine triphosphate (ATP). These substances exert important physiological functions in the local microenvironment.<sup>18,53</sup> Additionally, acupuncture stimulation can enhance the body's immune response and anti-inflammatory capacity by altering the microenvironment of local tissues, thereby promoting mast cell proliferation and activity.<sup>54</sup> These mechanisms provide a scientific basis for the application of acupuncture in pain management and anti-inflammatory therapy.

Acupuncture not only activates mast cells but also regulates the mediators they release. Studies have found that following acupuncture stimulation, the release of mediators such as histamine, serotonin, and adenosine from mast cells increases significantly, which play a key role in pain transmission and inflammatory responses.<sup>53,55</sup> For example, acupuncture induces the release of more serotonin from mast cells by stimulating specific acupoints. This substance not only participates in pain modulation but also enhances local blood flow and immune responses through interaction with neural receptors, thereby exerting analgesic effects.<sup>56</sup> Additionally, acupuncture can reduce the release of inflammatory mediators by regulating the degranulation process of mast cells, further alleviating pain and discomfort caused by chronic inflammation.<sup>18</sup>

Acupuncture influences mast cell function through multiple signaling pathways. Studies have shown that acupuncture stimulation can activate multiple intracellular signaling pathways in mast cells, including NF- $\kappa$ B, MAPK, and ERK, which play a central role in regulating mast cell activity and mediator release.<sup>10,11</sup> For example, acupuncture promotes mast cell degranulation and the release of growth factors by activating the MAPK signaling pathway, thereby enhancing local immune responses and anti-inflammatory capacity.<sup>18</sup> Additionally, acupuncture can modulate intracellular calcium ion concentration to affect mast cell signal transduction, thereby regulating their function and mediator release.<sup>11,53</sup> These mechanisms provide new perspectives and theoretical foundations for the application of acupuncture in treating allergic and inflammatory diseases.

## Clinical Application of Acupuncture in Allergic Diseases

### Analysis of Therapeutic Effect of Acupuncture on Asthma

Acupuncture has demonstrated promising therapeutic effects in asthma treatment, as shown in [Table 1](#). Recent studies on acupuncture mediated asthma management through immune system regulation emphasize that Th cell imbalance plays a key role in the development of asthma. Within the respiratory system, Th2 cells secrete cytokines including IL-3, IL-4, IL-5, and IL-6, which activate eosinophils to combat extracellular pathogens and stimulate B-cell proliferation for antibody production. However, inappropriate immune responses triggered by such pathways can lead to conditions like allergies and asthma.<sup>57</sup> Multiple studies have demonstrated that acupuncture can alleviate airway inflammation and improve symptoms in asthma patients by modulating immune responses. For instance, acupuncture effectively reduces airway hyperresponsiveness, decreases bronchial inflammation, and enhances pulmonary function indices such as forced expiratory volume in one second (FEV<sub>1</sub>) and peak expiratory flow (PEF).<sup>50</sup>

Additionally, acupuncture exerts anti-inflammatory effects by regulating the Th1/Th2 cell balance and inhibiting the release of allergic mediators.<sup>67</sup> Studies have shown that acupuncture stimulation of the GV14, BL12, and BL13 acupoints upregulates IL-2, IL-12, the Treg marker Foxp3, and IL-10, while downregulating IL-4, IL-5, IL-13 and IL-17A in lung tissues. This shifts the asthma model from a Th2/Th17-dominated phenotype to a Th1/Treg-dominated state. Additionally, Th1 cells further induce T-cell proliferation, and acupuncture mitigates airway inflammation in allergic asthma by stimulating this regulatory cascade. In murine asthma models, further upregulation of Treg cytokines and downregulation of Th17 cytokines have been confirmed to protect pulmonary function, reduce airway inflammation, and

**Table 1** Investigation of Acupuncture in the Treatment of Allergic Asthma

Reference	Model	Interventions	Acupoints	Acupuncture Parameters	Biochemical Measurements	Conclusion
Carneiro ER, 2010 <sup>58</sup>	Rats	EA	GV14, BL13, EX-B1, LUI, RN17, ST36, SP6	Every other day for 2 weeks	IL-1↑, IFN-γ↑, IL-4↑, NO↓, IL-10↓, LTB↓	The beneficial anti-inflammatory effect of EA on asthma is related to the balance of Th1/Th2 response and the reduction of LTB4 and NO.
Wei Y, 2015 <sup>59</sup>	Mice	MA	GV14, BL13, BL12	Every other day for 4 weeks	IL-17A↓, IL-17F↓, IL-22↓, IgE↓, IL-17R↓, RORγt↓, p65↓, IKKα↓	MA may treat asthma by regulating Th17, Treg activity and NF-κB pathway
Wei Y, 2017 <sup>60</sup>	Mice	MA	GV14, BL12, BL13	30min /every other day for 4 weeks	TNF-α↓, IL-1β↓, IL-5↓, eotaxin↓, Tol↓, Neu↓, Lym↓, Eos↓	Acupuncture can alleviate airway inflammation and regulate HPA axis and immune function in OVA induced mouse asthma model.
Dong M, 2018 <sup>61</sup>	Rats	MA	GV14, BL12, BL13	Manual manipulations every 10 min in 30 min	TNF-α↓, IL-1β↓, IL-33↓, sST2↑	MA can effectively protect lung function and reduce airway inflammation in OVA induced asthma mouse model.
Nurwati I, 2018 <sup>62</sup>	Rats	MA	BL13, ST36	15 min x3/ week, 6 weeks from 21st day after modeling	Neutrophil↓, Eosinophil↓	MA can reduce inflammatory reaction and prevent airway remodeling in chronic asthma mouse model.
Liu YL, 2018 <sup>63</sup>	Rats	MA	BL13	3 weeks	ChAT↓, AchE↑, mAChRs MI-M3↑	MA may treat allergic asthma by inhibiting the synthesis and release of Ach signal
Dong M, 2019 <sup>64</sup>	Rats	MA	GV14, BL12, BL13	30 min x3/week for 4 weeks.	IL-10↑, IL-5↓, IL-13↓, IL-17↓, p-p38↓, p-p44/42↓	MA can alleviate allergic airway inflammation by enhancing the activities of Th1 and Treg, thus regulating the balance of CD4+T cell subtypes in experimental asthma mice.
Cui J, 2021 <sup>65</sup>	Rats	MA	GV14, BL12, BL13	Twisted 360°, 60 times/min, 5 times, 20 min	IL-5↓, IL-9↓, IL-13↓, IL-25↓, IL-33↓, sST2↑	The inhibition of acupuncture on ILC2 may be related to the IL-33/ST2 signaling pathway and the level of IL-25, thus preventing asthma related airway inflammation.
Zhao H, 2021 <sup>66</sup>	Mouse	MA	GV14, BL13, ST36	Every other day for 13 days	ATG5↓, Beclin-1↓, p62↓, LC3B↓, p-PERK↓, p-IRE-1↓, Grp78↓, ATF6↓, IFN-γ↑, IL-4↓, IL-17↓, TGF-β↓	Regulating endoplasmic reticulum stress and CD4+T lymphocyte differentiation by inhibiting ATG5 mediated autophagy, thereby reducing airway inflammation and AHR in asthma.
Tang W, 2022 <sup>67</sup>	Rats	MA	GV14, BL12, BL13, GB30	Twisted 360°, 60 times/minx 4 times for 20 min	IL4↓, IL13↓, non-haem Fe <sup>2+</sup> level↓	MA can alleviate the deterioration related to iron death in airway inflammation.

(Continued)

**Table 1** (Continued).

Reference	Model	Interventions	Acupoints	Acupuncture Parameters	Biochemical Measurements	Conclusion
Yu Y, 2023 <sup>68</sup>	Rats	MA	GV14, BL12, BL13	Once every other day	p-p38MAPK↓	Inhibit the proliferation of ASMCs
Qiao Y, 2024 <sup>69</sup>	Rats	MA	BL13, EX-B1, LU6, LU10	30min x 7/ weeks for 2 weeks	TNF- $\alpha$ ↓, ET-1↓, cGMP↓, cAMP↑	Relieve airway smooth muscle spasms.
Miao XY, 2025 <sup>15</sup>	Rats	MA	GV14, GV12	20min x 7/ weeks for 20 days	IgE↓, IL-4↓, IL-5↓, PI3K/AKT↓	Inhibit airway remodeling and delay epithelial mesenchymal transition in allergic asthma rats.

**Notes:** ↑: Increased expression/level; ↓: Decreased expression/level.

**Abbreviations:** MA, Manual acupuncture; EA, Electroacupuncture; CV22, Tiantu; EX-HN9, Neiyangxiang; GV12, Shenzhu; GV14, Dazhui; BL12, Bilateral Fengmen; BL13, Feishu; BL20, Bishu; BL23, Shenshu; RN17, Danzhong; ST36, Zusanli; EX-B1, Dingchuan; LU1, Zhongfu; LU5, Chize; SP6, Sanyinjiao; GB30, Huantiao; ST40, Fenglong; Tol, Total leukocyte; Neu, neutrophil; Lym, lymphocyte; Eos, eosinophil; ChAT, Synthetase; Ach, Acetylcholine; AchE, Ach hydrolase; mAChRs, Muscarinic receptors; IKK $\alpha$ , NF- $\kappa$ B kinase- $\alpha$ ; ASMCs, Airway smooth muscle cells.

decrease mucus secretion.<sup>64</sup> The regulatory effects of acupuncture on Th cells can also be mediated through the IL-33/ST2 pathway. Studies have demonstrated that acupuncture stimulation of the GV14, BL12, and BL13 acupoints upregulates soluble ST2 (sST2), thereby inhibiting the binding of IL-33 to the ST2L receptor and downregulating the levels of TNF- $\alpha$ , IL-1 $\beta$ , and IL-33 in the respiratory tissues.<sup>61</sup> Notably, acupuncture also suppresses the expression of innate lymphoid cells type 2 (ILC2) by upregulating sST2, which subsequently downregulates IL-33 and IL-25 levels. This mechanism alleviates ovalbumin-induced epithelial damage in asthma models, significantly inhibiting airway inflammation and mucus secretion.<sup>65</sup>

As integrative research on acupuncture and medicine deepens, some researchers hypothesize that acupuncture may guide pharmacological agents to target specific organs for asthma treatment. However, due to the undefined underlying principles and mechanisms, the synergistic effects of acupuncture combined with drug therapy in asthma management require further validation.

### Analysis of Therapeutic Effect of Acupuncture on Allergic Rhinitis

Allergic rhinitis, a commonly encountered allergic disorder in clinical practice, has seen growing attention toward the therapeutic value of acupuncture in its management in recent years. Table 2 summarizes research findings from the past decade on acupuncture interventions for allergic rhinitis, with multiple clinical evidences indicating that acupuncture significantly improves nasal symptoms such as congestion, rhinorrhea, and sneezing. Systematic evaluations of clinical trials comparing auricular and body acupuncture have demonstrated that the acupuncture treatment group was significantly superior to the control group in both nasal symptom scoring and quality of life improvements.<sup>70</sup> From a mechanistic perspective, acupuncture may alleviate nasal allergic reactions by regulating immune system function, reducing serum IgE levels, and inhibiting inflammatory cell infiltration.<sup>71</sup> Multiple systematic reviews further indicate that acupuncture exhibits a certain level of superiority in efficacy compared to conventional Western medical therapies.<sup>72</sup>

Regarding acupoint selection, acupuncture treatment for allergic rhinitis primarily uses Yintang (GV29), Fengchi (GB20), Hegu (LI4), and Zusanli (ST36) as main acupoints, with additional syndrome differentiation-based point selection tailored to individual patient symptoms in clinical practice.<sup>81</sup> Gellrich et al demonstrated that acupuncture effectively inhibits the release of eosinophil chemokines and nonspecific pro-inflammatory cytokines such as IL-1 $\beta$ , IL-8, IP-10, MIP-1 $\beta$ , and MCP-1, thereby significantly reducing nasal symptom scores in patients.<sup>78</sup> Animal studies in murine models of allergic rhinitis have shown that acupuncture intervention significantly inhibits the expression of IgE and IL-4.<sup>85</sup> Notably, a meta-analysis involving 454 participants demonstrated that acupuncture not only significantly reduced symptom scores but also had a significantly lower incidence of adverse events compared to the conventional pharmacotherapy group.<sup>86</sup>

**Table 2** Investigation of Acupuncture in the Treatment of Allergic Rhinitis

Reference	Model	Interventions	Acupoints	Acupuncture Parameters	Biochemical Measurements	Conclusion
Chen Q, 2014 <sup>73</sup>	Human	MA	LI20, LI4, LI11, ST36, EX-NH3	30min x 3/week for 4 weeks	IgE↓, Mast cells↓	MA reduces mast cells in nasal mucosa glands.
McDonald JL, 2016 <sup>74</sup>	Human	MA	LI20, LI4, ST36, GV23	20min x 2/week for 8 weeks	IgE↓, SP↓	MA modulated mucosal immune response in the upper airway in adults with persistent allergic rhinitis.
Yang S, 2018 <sup>75</sup>	Rats	CIAA	LI20, ST36	14 consecutive days	IL-4↓, IgE↓, IFN-γ↑	CIAA can effectively alleviate allergic symptoms and inflammatory parameters in AR rat models.
Tu W, 2020 <sup>76</sup>	Rats	AAT	DUI4, BL12, BL13, BL20	28 days	NGF↓, IL-4↓, IL-5↓, IL-13↓, IgE↓, IFN-γ↑	AAT can alleviate allergic inflammation by inhibiting the expression of NGF and its downstream pathways.
Gong Z, 2021 <sup>77</sup>	Rabbits	INA	EX-HN9	20 min, once every other day for 7 days.	IL-4↓, IgE↓, IFN-γ↑	INA treatment can relieve symptoms of AR in AR rabbits.
Gellrich D, 2022 <sup>78</sup>	Human	MA	LI4, LI11, LI20, MH-N-3, GB20, SP6, ST36, BL13	2/week for 4 weeks	IL-1b↓, IL-8↓, IP-10↓, MIP-1b↓, MCP-1↓	MA reduces the intranasal unspecific inflammation.
Li Y, 2022 <sup>79</sup>	Human	MA, INA	EX-HN9, LI20, GV23, LI4, Biquiu	7/week for 2 weeks	IL-4↓, IL-6↓, IL-10↑	MA can effectively alleviate the symptoms of allergic rhinitis, and IA and moxibustion is more effective.
Wang Z, 2023 <sup>80</sup>	Human	MA	Xinwu, Xiaguan	2/week for 2 weeks	Histamine↓, IgE↓	MA at Xinwu acupoint combined with loratadine and fluticasone propionate can deliver a powerful efficacy on AR and alleviate the clinical symptoms, without increasing adverse reactions.
Liu LL, 2023 <sup>81</sup>	Human	MA	EX-HN9, Biquiu	20 min x 3/week for 2 weeks	NR	Intranasal acupuncture has good efficacy and safety in the treatment of PAR. Acupuncture has a good effect on improving nasal congestion, olfactory function and sleep.
Sun D, 2023 <sup>82</sup>	Human	WA	MH-N-3, LI20, GB20, LI4, Baihui, Taiyang, Shangyingxiang	20 min x 7/week	IgE↓, IL-6↓, IL-8↓, TNF-α↓	Warm needle therapy can effectively improve the clinical symptoms of AR patients with lung qi deficiency and cold type, reduce inflammation, and enhance immune function.
Tian MH, 2024 <sup>83</sup>	Rats	MA	BL13, BL23, DUI4	10 days	IgE↓, OVA-sIgE↓, IL-4↓, IL-17↓, GATA-3↓, TLR4↓, MyD88↓, NF-κB↓, IFN-γ↑, IL-10↑	Acupuncture can alleviate the symptoms of allergic rhinitis in rats and inhibit the inflammation of nasal mucosa, which may be related to the inhibition of TLR4/MyD88/NF-κB signal transduction and the balance of Th1/Th2 and Treg/Th17 cytokine levels as well as T-bet/GATA-3.
Dong BY, 2024 <sup>84</sup>	Human	MA	GV20, EX-HN1, PC7, HT7, GV24, LI20	20 min x 7/week for 2weeks	IgE↓, EOS↓, SP↓	MA can improve the nasal symptoms of AR patients by reducing EOS and IgE.

**Notes:** ↑: Increased expression/level; ↓: Decreased expression/level.

**Abbreviations:** MA, Manual acupuncture; WA, Warm Acupuncture; INA, intranasal acupuncture; AAT, Acupoint application therapy; NR, No report; CIAA, Catgut implantation at acupoint; LI11, Quchi; EX-HN9, Neiyangxiang; LI20, Yingxiang; PC7, Daling; HT7, Shenmen; MH-N-3, Yintang; GV23, Shangxing; GV24, shenting; GB20, Fengchi; LI4, Hegu; DUI4, Dazhui; BL12, Fengmen; BL13, Feishu; BL20, Pishu; BL23x, Shen shu; ST36, Zusanli; EX-B1, Dingchuan; SP6, Sanyinjiao; EX-HN1, Sishencong; EX-NH3, Yingtang; SP, Proinflammatory neuropeptide substance P; NGF, Nerve growth factor.

Collectively, evidence from multiple studies indicates that acupuncture, as a safe and effective intervention, offers multiple advantages in the clinical management of allergic rhinitis, including alleviating nasal symptoms, improving quality of life, reducing medication dependence, and enhancing patient satisfaction. Its efficacy and safety have been supported by evidence-based medicine.

### Application of Acupuncture in Skin Allergy

In the clinical management of skin allergies, acupuncture therapy has demonstrated significant potential for application. Clinical studies have confirmed that this therapy is effective in alleviating symptoms of common allergic skin diseases such as urticaria and atopic dermatitis. As shown in Table 3, traditional filiform needle acupuncture is the most commonly used intervention, followed by intradermal needle therapy and acupressure techniques. In contrast, electroacupuncture (EA), transcutaneous electrical acupoint stimulation (TEAS), and auricular acupuncture have been reported in only a few studies. Core acupoints selected in clinical practice include Quchi (LI11), Zusanli (ST36), Xuehai (SP10), and Shaohai (HT3). Acupoint stimulation effectively improves local blood circulation, enhances the skin's self-repair capacity, and exerts bidirectional regulation on immune responses.<sup>87</sup>

In the case of atopic dermatitis, clinical studies have demonstrated that patients receiving acupuncture treatment exhibit significant improvements in both symptom severity and quality of life scores.<sup>96</sup> Additionally, some scholars propose that the mechanism of acupuncture in treating allergic skin diseases may be associated with regulating the release of cytokines by immune cells, such as IL-4, IL-2, and IL-10. Elevated IL-4 signaling is closely linked to the development of pruritus in atopic dermatitis.<sup>97,98</sup> Through cytokine regulation, EA directly reduces the generation of itch signals and inhibits inflammatory responses in the skin in cutaneous pruritus. Recent findings indicate that acupuncture decreases the levels of IL-4 and IgE while increasing interferon- $\gamma$  (IFN- $\gamma$ ) in the blood of atopic dermatitis patients.<sup>94</sup> In humans, EA enhances serum levels of the anti-inflammatory cytokine IL-10 while inhibiting the pro-inflammatory cytokine TNF- $\alpha$ , thereby reducing skin inflammation.<sup>99</sup> Acupuncture is also thought to alleviate skin allergic reactions by inhibiting mast cell activation and the release of inflammatory mediators, providing a theoretical basis for its application in treating skin allergies.<sup>100</sup> Wang et al's research confirms that EA inhibits mast cell degranulation via cannabinoid CB2 receptors in a rat model of allergic contact dermatitis.<sup>7</sup> These examples demonstrate that acupuncture, as a non-invasive treatment method, can provide effective relief for patients with skin allergies.

### Potential Mechanism of Acupuncture Regulating Mast Cells

Acupuncture, as a traditional therapy, regulates the secretion of cytokines, thereby further influencing the function of mast cells and demonstrating favorable therapeutic effects in the treatment of allergic diseases (as shown in Figure 2). After acupuncture, macrophages changed from M1 pro-inflammatory type to M2 anti-inflammatory type, and PPAR  $\gamma$ , the negative regulator of TLR4, was activated, thus inhibiting the activation of NLRP3 inflammatory bodies, reducing the recruitment of ASC and caspase-1, downregulating pro-inflammatory factors (such as TNF- $\alpha$ , IL-1, IL-1  $\beta$  and IL-6), MCP-1, adhesion molecules ICAM-1 and VCAM-1) and INF- $\gamma$ , and promoting the release of anti-inflammatory cytokines (such as IL-10). In some cases of autoimmune diseases, acupuncture can down regulate Th1 cells and inhibit their secretion of proinflammatory cytokines, such as INF- $\gamma$ , IL-2 and TNF- $\alpha$ , while up cytokines, such as IL-4, IL-5, IL-10 and IL-13.

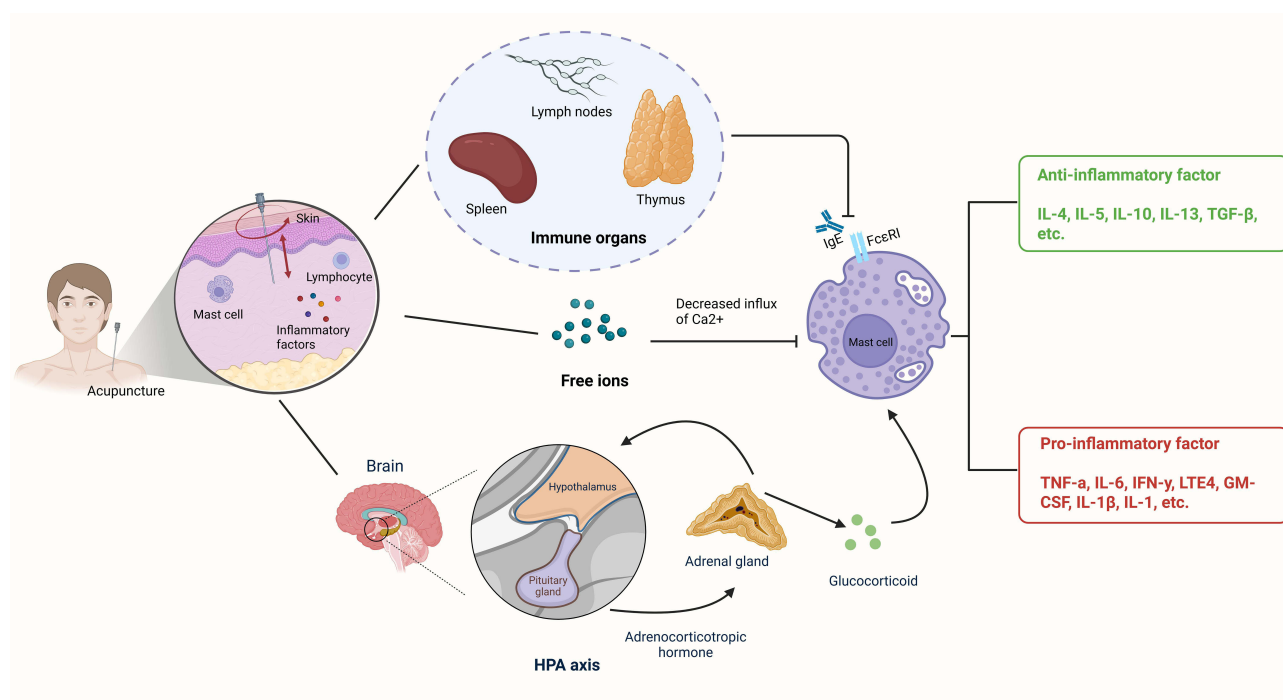
In addition, acupuncture also promotes the balance of the immune response by regulating the interactions between macrophages and other immune cells, thereby affecting the overall immune status.<sup>101</sup> Studies have shown that acupuncture can significantly reduce the levels of IgE in serum and the expression of various pro-inflammatory cytokines, such as tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) and interleukin-4 (IL-4), which play a crucial role in the activation and degranulation of mast cells.<sup>7</sup> In the Complete Freund's adjuvant (CFA) model, EA at ST36 can activate mast cells and promote mast cell degranulation by activating TRPV2 and inducing the release of histamine and adenosine, thus increasing the level of  $\beta$ -endorphin ( $\beta$ -END) in the cerebrospinal fluid and leading to analgesia.<sup>102</sup> Wang et al's study shows that EA at ST36 reduces the number of mast cells, down-regulates the release of TLR4, IL-1 $\beta$  and IL-8 by mast cells in the colon tissue, and improves the visceral hypersensitivity in the trinitrobenzene sulfonic acid (TNBS) - induced colitis model.<sup>103</sup> In addition, acupuncture also promotes the degranulation of mast cells and the structural remodeling of fibroblasts, inducing the release of substances such as adenosine triphosphate (ATP), substance P (SP), tryptase, histamine (HA), interleukins,

**Table 3** Investigation of Acupuncture in the Treatment of Allergic Skin Diseases

Reference	Model	Interventions	Acupoints	Acupuncture Parameters	Biochemical Measurements	Conclusion
Park JY, 2013 <sup>88</sup>	Mouse	MA	LII I	1/week	IgE↓, IL-4↓, IL-8↓, TNF-α↓, NF-κB↓, ERK1/2↓, JNK↓, p38↓	MA can effectively alleviate allergic contact dermatitis by reducing proinflammatory cytokines and proteins.
Wang Z, 2017 <sup>89</sup>	Rats	EA	ST36	1/week	IgE↓, p38 MAPK↓, IL-10↑	EA therapy may improve ACD related inflammation by triggering local IL-10 production and inhibiting p38 MAPK activation.
Zhang XH, 2020 <sup>90</sup>	Rats	EA	ST36, LIII, SPI0	20 min x7/week	NF-α↓, IL-6↓, p-ERK↓, JNK↓, p-JNK↓, p-P38MAPK↓	EA can reduce skin allergic reaction in rats with urticaria
Wang YM, 2020 <sup>7</sup>	Rats	MA	SPI0, LIII	30min 7/week for 2weeks	IgE↓, Histamine↓, Serotonin↓, p-Lyn↓, p-Syk↓	MA at LIII and SPI0 is applicable in the treatment of urticaria.
Park JG, 2021 <sup>91</sup>	Human	MA	LII I, ST36, PC6	15min x 2/week for 4 weeks	NR	MA treatment improved the symptoms of atopic dermatitis.
Zeng ZW, 2022 <sup>92</sup>	Mouse	A-AHT	ST36, LIII	Once every other day for 28 days	IL-4↓, IgE↓, IFN-γ↑, T-bet↑	A-AHT has shown significant effectiveness in AD model mice by regulating Th1/Th2 immune responses.
Liu SJ, 2023 <sup>93</sup>	Rats	EA	LII I, SPI0	20 min x 7/week	IgE↓, Histamine↓, IL-33↓, ST2↓	EA pretreatment can prevent urticaria in rats, which may be related to its function of reducing IgE levels by inhibiting IL-33 and ST2.
Shi Y, 2023 <sup>94</sup>	Human	MA	LII I, LI4, SPI0, ST36, SP6, Zhongwan, Tianshu, Guanyuan, Yinlingquan,	Twisted 360°, 60 times/min, once every other day for 12 days.	IL-4↓, IgE↓, IFN-γ↑	MA can significantly alleviate the symptoms and negative emotions of patients, and improve their quality of life, sleep quality and balance of Th1/Th2 cytokines.
Li JQ, 2024 <sup>95</sup>	Rats	EA	LII I, SPI0	20 min x 1/day for 10 days	IgE↓, 5-HT↓, NLRP3↓, IL-1β↓, IL-18↓, Caspase-1↓	EA pretreatment can prevent and treat UR by inhibiting inflammatory response, which is related to the regulation of pyroptosis.
Du Y, 2024 <sup>6</sup>	Rats	MA	GV20, CV12, LIII, SPI0, GV14, BL 27	15 min x 7/week for 2 weeks	IgE↓, TPS↓, IL-4↓, IL-5↓, TNF-α↓	MA effectively suppress mast cell degranulation in the sensitized skin tissue on the back of urticaria rats.

**Notes:** ↑: Increased expression/level; ↓: Decreased expression/level.

**Abbreviations:** MA, Manual acupuncture; A-AHT, Acupoint autohemotherapy; AAT, Acupoint application therapy; NR, No report; LIII, Quchi; LI4, Hegu; ST36, Zusanli; SP6, Sanyinjiao; SPI0, Xuehai; PC6, Neiguan; p-Lyn, phosphorylated tyrosine-protein kinase Lyn; p-Syk, phosphorylated tyrosine-protein kinase Syk.



**Figure 2** The mechanism of acupuncture regulating mast cells in the treatment of allergic diseases. Arrow represents the pathway of regulation and promotion; Flat arrow represents the inhibitory pathway; The red dots represent pro-inflammatory factors; The green dots represent anti-inflammatory factors; Green-upregulated by acupuncture; Red-downregulated by acupuncture.

**Abbreviations:** GM-CSF, Granulocyte-Macrophage Colony Stimulating Factor; LTE4, Leukotriene E4.

serotonin (5-HT), etc, which also mediate the effects of acupuncture.<sup>104</sup> These results indicate that acupuncture, by regulating the balance of cytokines, may play an important role in the immune response mediated by mast cells, thus providing new ideas for clinical treatment.

Acupuncture has increasingly gained attention for its role in regulating neuro-immune interactions. Recent studies indicate that the interaction between the hypothalamic-pituitary-adrenal (HPA) axis and the immune system plays a crucial role in maintaining tissue homeostasis and regulating immune responses.<sup>105</sup> The core components of the hypothalamic-pituitary-adrenal (HPA) axis include the paraventricular nucleus of the hypothalamus (PVN), adenohypophysis, and adrenal cortex, with PVN playing a key regulatory role in this neuroendocrine axis.<sup>106</sup> Cortisol, synthesized and released by this system, forms a complex with glucocorticoid receptors (GR), thereby exerting bidirectional regulation on the expression of genes related to pro-inflammatory and anti-inflammatory mediators: it inhibits the biosynthesis of multiple pro-inflammatory mediators on the one hand, and induces the production and release of anti-inflammatory mediators on the other.<sup>107</sup>

Acupuncture exerts anti-inflammatory effects by directly activating the endogenous HPA axis, thus avoiding side effects associated with excessive use of exogenous cortisol. In the pathological process of asthma, although persistent inflammation stimulates an increase in endogenous cortisol levels, activation of the negative feedback mechanism leads to reduced HPA axis reactivity.<sup>108,109</sup> Studies by Wei et al<sup>60</sup> have demonstrated that acupuncture effectively promotes the secretion of adrenocorticotropic hormone (ACTH) and cortisol, reversing the HPA axis from a hypo-reactive to a hyper-reactive state, thereby reducing the body's inflammatory burden. Specifically, this regulatory process decreases the infiltration of inflammatory cells in the airways (including leukocytes, neutrophils, lymphocytes, and eosinophils) and inhibits the biological activity of pro-inflammatory factors such as TNF-α, IL-1β, IL-5, and eosinophil chemokines.<sup>108,110</sup> Acupuncture stimulation can trigger the neuroimmune interaction pathway by activating the vagus nerve, thereby regulating the function of macrophages. Wang et al<sup>111</sup> proved that acupuncture activates the cholinergic anti-inflammatory pathway and induces macrophages to polarize into the anti-inflammatory phenotype (M2 type), which

significantly inhibits the local and systemic inflammatory response mediated by macrophages, and achieves two-way regulation of the inflammatory microenvironment.

The above research provides a theoretical basis for the application of acupuncture in the treatment of allergic diseases and inflammatory diseases, but the potential mechanism of HPA axis regulation mediated by acupuncture needs further research.

## Conclusion

In this article, we explored the potential of acupuncture in regulating mast cells and its prospects as an adjunctive therapy for allergic diseases. Mast cells play a central role in allergic reactions, with their activity influenced by multiple factors. By modulating interactions within the neuro-endocrine-immune system, acupuncture may exert positive effects on mast cell function and allergic responses. These findings offer a new perspective on acupuncture as an adjunctive approach for treating allergic conditions.

However, current research still harbors controversy regarding the specific mechanisms of acupuncture and the variability in its efficacy across different types of allergic diseases. While some studies demonstrate that acupuncture can effectively reduce allergic symptoms,<sup>112,113</sup> others fail to identify significant effects.<sup>114</sup> Such discrepancies may be attributed to differences in study design, acupuncture techniques employed, and individual patient variability. Therefore, designing more rigorous large-scale randomized controlled trials and standardizing acupuncture protocols and treatment courses will be essential steps in future research.

Future research should focus on the mechanisms by which acupuncture regulates mast cell function, with particular emphasis on its effects in different disease models. Through animal experiments and clinical trials, the impacts of acupuncture on mast cell activation, degranulation, and cytokine secretion should be evaluated to uncover therapeutic mechanisms. By integrating technologies such as gene editing and single-cell sequencing, studies can precisely analyze the effects of acupuncture on mast cells and their microenvironment, providing evidence for clinical applications in allergic diseases (eg, hay fever, asthma) and inflammatory disorders. Exploring the combined efficacy of acupuncture and conventional medications, while clarifying its specific mechanisms in various diseases, will offer comprehensive scientific support for clinical practice.

Overall, acupuncture holds significant research value and clinical prospects in regulating mast cells and their application in allergic diseases. Although current research findings remain inconsistent, further exploration and standardized studies may enable acupuncture to become an effective complementary approach in the treatment of allergic conditions.<sup>115</sup> To achieve this goal, it is essential to carefully balance the perspectives of different studies, promote the scientific development of acupuncture, and provide patients with more effective treatment options.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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