

# *Research progress of traditional Chinese medicine in regulating Th17 / Treg balance in asthma*

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**Keywords:** Traditional Chinese medicine, asthma, Th17 / Treg imbalance.

**Abstract:** In recent years, as people's research on the two newly discovered helper T cells-Th17 and Treg has become more and more in-depth, the imbalance between the two is generally believed to be involved in inflammatory diseases, especially in the onset of bronchial asthma. To a more to a more critical role, therefore, the regulation of its balance is considered to be a new target for the treatment of asthma. Due to the multi-target characteristics of traditional Chinese medicine, it has broad application prospects when targeting the complex Th17/Treg imbalance. Through a review of the literature over the past ten years, this article shows that traditional Chinese medicine can affect the differentiation of Th17 and Treg by Through a review of the literature over the past ten years, this article shows that traditional Chinese medicine can affect the differentiation of Th17 and Treg by regulating the expression of IL-6, *TGF-β*, FOXP3, and STAT3, thereby restoring the balance of Th17/Treg. Purpose, so as to achieve the purpose of alleviating airway reactions and treating asthma.

## 1. Introduction

Asthma, also known as bronchial asthma, is a common<sup>[2]</sup> chronic inflammatory heterogeneous respiratory disease of the airways characterised by airway hyperresponsiveness and reversible airflow limitation<sup>[1]</sup>, involving inflammatory cells such as eosinophils, mast cells, T lymphocytes and structural cells such as airway epithelial cells and their cellular components. The pathogenesis of asthma is still unclear<sup>[3]</sup>, although researchers have proposed hypotheses such as airway inflammation, genetic factors, and imbalance of second messenger (cAMP/cGMP) regulation. As research into the pathogenesis of asthma has progressed, researchers have suggested that dysregulation of the body's immune regulation, particularly T-lymphocyte dysfunction, is an important factor<sup>[4]</sup> in the development of asthma. The dysregulation of the Th1/Th2 balance leads to the secretion of large amounts of inflammatory cytokines and the proliferation of inflammatory cells, which in turn trigger inflammation and lead to the development<sup>[5]</sup> of asthma. For this reason, clinical attempts have been made in recent decades to treat asthma by regulating the Th1/Th2 balance, but the therapeutic effect has been minimal.

The discovery of Th17/Treg dysregulation in mice with asthma has led to the discovery of an important immunological basis for the pathogenesis of asthma, as well <sup>[6]</sup>as clinical evidence that

drugs such as montelukast sodium<sup>[7]</sup>, budesonide and salbutamol<sup>[8]</sup>, alone or in combination, can regulate Th17/Treg homeostasis in asthmatic patients. The discovery of Th17/Treg dysregulation has provided a new direction for the study of the pathogenesis and treatment of asthma.

Asthma belongs to the category of croup in Chinese medicine and refers to a group of diseases characterised by episodes of phlegm, shortness of breath, shortness of breath and croup in the throat. The knowledge of asthma in Chinese medicine has a long history. As early as The Essentials of the Golden Horoscope, the characteristics and treatment of croup were clearly pointed out, and pathologically, it was classified as a "voodoo drink" disease among phlegm-drinking diseases. Zhu Danxi coined the name "asthma" and proposed in his "Danxi Xinfu" the treatment principle of "to support Qi before an attack, and to attack evil Qi as a matter of urgency after an attack". With the application of research methods and techniques such as network pharmacology, researchers have gained a clearer understanding of the pharmacological effects of Chinese medicine, and in recent years, research on the mechanism of Th17/Treg homeostasis regulation by Chinese medicine has gradually become a hot spot in the study of Chinese medicine for asthma.

Since long-term use of modern medical drugs for bronchial asthma can lead to a decrease in the effectiveness of treatment and can cause some adverse reactions<sup>[1]</sup> in patients, while Chinese medicine has unique advantages<sup>[9]</sup> in terms of safety and efficacy in the treatment of asthma, so Chinese medicine has a broader application prospect for the treatment of asthma. In this paper, we review the basic and clinical related research literature in the past 10 years, and discuss the research on the mechanism of Th17/Treg balance in asthma regulation by Chinese medicine in recent years from three aspects: single herbal medicine, Chinese medicine monomer and Chinese medicine compound, respectively, in order to provide new ideas and references for the rational clinical use of Chinese medicine and the modernization of Chinese medicine and pharmacological research of Chinese medicine.

## 2. Relationship between Th17/Treg imbalance and the development of asthma

Th17 is a newly discovered helper T cell that specifically secretes cytokines such as IL-17A, activates and recruits neutrophils and promotes the secretion of inflammatory mediators by other structural cells<sup>[10]</sup>. Th17 and Treg are interrelated in their differentiation and function,<sup>[11]</sup> and under normal physiological conditions they are in a dynamic balance to maintain the stability of the immune system, therefore an imbalance between them will usually lead to an abnormal response of the immune system, which can lead to many diseases<sup>[12]</sup> including asthma. Th17/Treg imbalance has been shown to be associated<sup>[14]</sup> not only with allergic asthma, but also with the development of neutrophilic asthma<sup>[13]</sup> and moderate to severe asthma.

## 3. Factors regulating Th17/Treg balance

The regulation of Th17/Treg homeostasis is mainly related to IL-6 and <sup>[9]</sup>TGF- $\beta$ , a cytokine that can individually regulate Th17 and Treg differentiation, and when inflammation occurs in the body, IL-6 produced can act in conjunction with TGF- $\beta$  to regulate Th17 differentiation. In addition, the differentiation of Th17 and Treg is co-regulated by other cytokines and transcription factors.

### 3.1 Factors affecting Th17 differentiation

In 2005, researchers identified a subpopulation of helper T cells in mice with autoimmune encephalomyelitis with characteristics and functions different from those of Th1, Th2 and Treg, and named them Th17<sup>[15]</sup> because of their specific secretion of IL-17. The study of Th17 differentiation is currently the focus of attention, and the main factors of Th17 differentiation are environmental

factors and gene regulation<sup>[16]</sup>.

It was found that IL-6 and *TGF-β* are the most important cytokines targeting the regulation of Th17 cell differentiation. Removing or inhibiting the expression of both *TGF-β* gene and IL-6 gene can reduce<sup>[17]</sup> the differentiation of Th17 cells. Cytokines secreted by Th17 cells, such as *IFN-γ*, IL-27 and IL-2, also inhibit Th17 differentiation, while IL-21 promotes Th17 differentiation<sup>[18]</sup>. IL-2 has also been found to regulate Th17 cell differentiation<sup>[19]</sup> by inhibiting the STAT5 signalling pathway. The researchers<sup>[20]</sup> found that although IL-23R only appears at the initial stage of Th17 differentiation, it has an important role in the stability of the Th17 phenotype.

Th17 differentiation is influenced by STAT3, retinoic acid-related orphan receptor alpha (RORα) and retinoic acid-related orphan receptor gamma-t (RORγt) genes, and Laurence<sup>[22]</sup> et al<sup>[21]</sup>. showed that reduced Th17 differentiation was associated with reduced STAT3 expression. RORα is involved in regulating Th17 differentiation<sup>[23]</sup> and also synergizes with RORγt<sup>[24]</sup> to promote Th17 differentiation.

### 3.2 Factors influencing Treg differentiation

In 1995, Japanese scholars<sup>[11]</sup> first identified a type of helper T cell with a negative regulatory role, known as Treg, which plays a primarily immunosuppressive role in vivo and is involved in the induction of immune tolerance and tumourigenesis<sup>[25]</sup>. In recent years, there is increasing evidence that Treg cells play an important role<sup>[24]</sup> in the development and progression of allergic diseases, especially asthma.

The differentiation of Treg is regulated by a variety of transcription factors and cytokines. It has been shown that IL-2 and *TGF-β* promote the differentiation of adaptive regulatory T cells (iTreg) and that the differentiation of Treg cells is also dependent on Foxp3<sup>[24]</sup>, which functions not only to maintain Treg cell phenotype and function, but also has an important role<sup>[26]</sup> in the development of natural regulatory T cells (nTreg) cells.

## 4. Study on the regulation mechanism of Th17/Treg homeostasis by Chinese medicine

According to Chinese medicine, the pathogenesis of asthma is that phlegm lies in the lungs and is triggered by external evil, inappropriate diet, emotional stimulation, physical weakness and fatigue, resulting in phlegm congestion of the airways and malfunction of the lung qi in declaring and descending. Therefore, in terms of prescriptions, most of them are used to warm the lungs and dissolve the drinks and to promote the lungs and calm asthma during the exacerbation period, while those in remission are based on the principle<sup>[27]</sup> of helping the righteous or helping to dispel the evil. In recent years, research on the regulation of Th17/Treg in asthma patients by Chinese herbal medicine has made great progress with the application of new methods and techniques, especially in single herbal medicines and Chinese herbal compound prescriptions.

### 4.1 Effect of Chinese herbal medicine on Th17 differentiation

Most of the prescriptions that have an impact on Th17 differentiation are based on tonic prescriptions such as angelica, reflecting the pharmacological effects of tonic prescriptions that have immunomodulatory functions and are able to regulate the function of the human immune system at an overall macroscopic level through the neuroendocrine network.

Flavonoids, polysaccharides, coumarins, terpenoids and other herbal components also have an effect on the differentiation of Th17. Most of these herbal components also belong to the active ingredients of the tonic formula, which also proves in one way that the material basis of the immunomodulatory function of the tonic formula may be these active ingredients with

immunomodulatory function.

#### 4.1.1 Effect of single herbs on Th17 differentiation

It was shown that *Angelica sinensis* could alleviate asthma symptoms in mice due to its ability to significantly increase the expression of *TGF-β*<sup>[21]</sup> and inhibit the expression of *RORγt* in asthmatic mice<sup>[28]</sup>, affecting the differentiation of Th17 and thus regulating the balance of Th17/Treg. In addition, *Angelica sinensis* could synergize with dexamethasone to inhibit the expression<sup>[29]</sup> of *RORγt*. By using herbs that tonify the kidney and warm the yang to treat asthmatic mice, Li Xi et al<sup>[30]</sup> found that they could influence the differentiation of Th17 by increasing the expression level of *TGF-β1*, thereby alleviating the inflammation of asthma.

#### 4.1.2 Effect of herbal monomers on Th17 differentiation

Wei et<sup>[31]</sup> al. showed that *Epimedium* could down-regulate the expression of IL-6 and inhibit the differentiation of Th17, thus reducing airway hyperresponsiveness and chronic airway inflammation. Chen Na et al.<sup>[34]</sup> found that *TGF-β* levels in the blood of children given capsaicin were significantly increased compared to the control group. In vitro experiments showed that the expression of Th17 cells in the administered group was significantly lower compared to the control group, suggesting that capsaicin can significantly regulate the Th17/Treg balance, indicating that the drug can regulate the development of asthma through immunomodulatory effects.

#### 4.1.3 Effect of herbal polysaccharides and extracts on Th17 differentiation

Huang Jialin<sup>[33]</sup>'s study showed that *Astragalus* polysaccharide could effectively reduce the expression of IL-6, a cytokine that affects Th17 differentiation, in asthmatic mice. It was also<sup>[35]</sup> demonstrated that *Astragalus* polysaccharide may inhibit the differentiation of Th0 to Th17 by reducing the expression of IL-6, a cytokine upstream of Th17, thereby reducing the infiltration of inflammatory cells in the airways and decreasing the release of related inflammatory mediators and their cytokines, thus exerting an effect of controlling airway inflammation and achieving improvement in asthma attacks. The study by Xu et al. found that anthraquinone (AQ), an extract of cassia seeds, reduced inflammatory cell counts and increased *IFN-γ* levels in the BALF of asthmatic mice, thereby restoring Th17/Treg to a dynamic equilibrium.

#### 4.1.4 Effect of Chinese herbal compounding on Th17 differentiation

Some scholars found that Asthma Keji Injection, composed of *Epimedium* and *Bacopa monniera*, could inhibit the release of inflammatory factors such as IL-6 in asthmatic mice, thereby regulating the Th17/Treg balance<sup>[36]</sup>. Sui Bowen et al<sup>[37]</sup> concluded that *Shengan Ephedra Tang* could regulate the Th17/Treg balance by inhibiting the expression of *TGF-β1* in asthmatic mice, thereby suppressing the differentiation of Th17 cells, thus acting to delay airway remodelling.

### 4.2 Effect of Chinese herbal medicine on Treg differentiation

In addition to tonics, which are similar to those that regulate Th17 differentiation, there are also a large number of antiepidemic and antiresolving prescriptions. This suggests that the anti-inflammatory mechanism of action of the detoxifying and antiepidemic formulas may be related to their regulation of Th17/Treg homeostasis.

#### 4.2.1 Effect of single herbs on Treg differentiation

Zhang<sup>[38]</sup> Ya et al. showed that *Astragalus* can increase the expression of IL-2 in the bronchoalveolar lavage fluid of mice with asthma, suggesting that *Astragalus* may play a role in the treatment of asthma by promoting Treg differentiation. Wang Yongmei et al<sup>[39]</sup> gave high and low

dose groups of aqueous extracts of *Cicadellia* spp. to asthma model rats by gavage, and found that both high and low dose groups of *Cicadellia* spp. significantly reduced the IL-2 content in peripheral blood of rats, demonstrating that aqueous extracts of *Cicadellia* spp. could reduce the infiltration of inflammatory cells in lung tissues by inhibiting the differentiation of Treg, as well as promoting and maintaining the basic smoothness of bronchial and lung tissue walls, reducing intra-luminal exudates and reducing basement membrane hyperplasia.

#### 4.2.2 Effect of herbal monomers on Treg differentiation

Wei et al<sup>[31]</sup>. showed that Epimedium could down-regulate *TGF-β* and promote Treg differentiation to reduce asthma symptoms. The results showed that Epimedium could significantly increase the expression of Foxp3RNA and promote Treg differentiation, suggesting that restoring the balance of Th17/Treg function may be the main mechanism<sup>[34]</sup> of its anti-asthma effect. Chen Na et al<sup>[35]</sup>. found that with the significant increase of Foxp3 content in the blood of children in the Bianca Vine group, the number of Treg also increased significantly, indicating that Bianca Vine could restore the balance of Th17/Treg to a greater extent and regulate the development of asthma.

#### 4.2.3 Effect of herbal compounding on Treg differentiation

A study<sup>[40]</sup> by Xing Qiongqiong et al. showed that the mechanism of the treatment of asthma with Gouben Anti-croup Drink was related to its upregulation of IL-2 mRNA and protein expression levels to regulate the Th17/Treg balance. Ma Ting et al<sup>[41]</sup> al. showed that pacifying asthma combination could regulate the levels of IL-2 and other cytokines in the peripheral blood of children with asthma, which in turn regulated the differentiation of Terg, thus reducing the airway inflammation in asthma.

## 5. Conclusions and Discussion

With the continuous application of new research methods and techniques, we can see that Chinese herbal medicines, especially Chinese herbal compound, have a significant regulatory effect on the Th17/Treg imbalance in asthma patients, and this regulatory effect is multi-targeted and bidirectional. Chinese medicines can regulate the Th17/Treg balance both by means of regulating cytokine levels and by regulating the expression of related genes, and there are a number of Chinese medicines, such as Epimedium, that can restore the Th17/Treg balance by acting in both directions, that is, they can regulate both the differentiation of Th17 and Treg by regulating the differentiation of Treg come to put Th17/Treg in a dynamic balance.

Although, through the use of new methods and techniques represented by network pharmacology and other new technologies, there is more understanding of the mechanism of regulation of Treg/Th17 imbalance by Chinese medicine. However, the study of its specific mechanism of action, especially the target of action, is not yet specific, precise and thorough due to the limitation of technology. The types of active ingredients and their targets involved in the regulation of Th17/Treg homeostasis in Chinese medicine, especially in compound formulas, need to be specifically studied in depth. Adequate elucidation of the mechanisms of the regulatory effects of TCM on Th17/Treg imbalance will be of great guidance for pharmacological research and clinical TCM research.

## References

- [1] Boulet L P, J M FitzGerald, H K Reddel. *The revised 2014 GINA strategy report: opportunities for change [J]. Curr Opin Pulm Med, 2015, 21(01):1-7.*
- [2] Liu Guifu. *Clinical experience of bronchial asthma pharmacotherapy [J]. Chinese pharmacoeconomics, 2013, (1): 91-92.*
- [3] Peng P. *Research progress on the pathogenesis of bronchial asthma and the use of medication to treat the disease [J]. Contemporary Medicine Series, 2018, 16(10): 34-35.*

- [4] Chang X, Zhang T, Sui Yuyin, Zhang Qingxiang. Research on the pathological mechanism of bronchial asthma and the progress of clinical treatment in Chinese and Western medicine [J]. *Journal of Shandong University of Traditional Chinese Medicine*, 2018, 42(03): 272-275.
- [5] Gao Yang, Yang Fan. Expression levels of Th1, Th2 and Th17 cells in peripheral blood and clinical significance in patients with bronchial asthma [J]. *Journal of Liberation Army Medicine*, 2017, 29(01): 76-79.
- [6] Gong C, Deng J.M. The role of Th17/Treg in the pathogenesis of bronchial asthma and research progress [J]. *Chinese Journal of Asthma (electronic version)*, 2013, 7(03): 41-45.
- [7] Hao M, Song W, Lu L. Effects of montelukast sodium on Th17/Treg cell balance and lung function in children with bronchial asthma [J]. *Effects of montelukast sodium on Th17/Treg cell balance and lung function in children with bronchial asthma [J]. Contemporary Medicine*, 2017, 23(21): 11-14.
- [8] ZHANG Kunfeng, CHEN Hui, DING Jinsong. Effect of budesonide combined with salbutamol nebulized inhalation on Th17/Treg balance in bronchial asthma patients and correlation with airway remodeling [J]. *Journal of Hainan Medical College*, 2017, 23(11): 1474-1477.
- [9] Wan Q, Dai A.G, Jiang Y.L. Progress in the study of Th17/Treg and lung diseases [J]. *Journal of Clinical Pulmonology*, 2016, 21(05): 899-902.
- [10] Yoichiro Iwakura, Harumichi Ishigame, Shinobu Saijo, Susumu Nakae. Functional Specialization of Interleukin-17 Family Members [J]. *Immunity*, 2011, 34(2).
- [11] Sakaguchi Shimon, Sakaguchi Noriko, Asano Masanao, et al. Pillars article: immunologic self-tolerance maintained by activated T cells Pillars article: immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor  $\alpha$ -chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases. *J. Immunol.* 1995. [J]. *Journal of immunology (Baltimore, Md.: 1950)*, 2011, 186(7).
- [12] Gu N, Liu H B. Research progress of Th17/Treg immune imbalance in lung diseases [J]. *Tianjin Pharmacology*, 2019, 31(02): 58-62.
- [13] Raedler D, Ballenberger N, Klucker E, et al. Identification of novel immune phenotypes for allergic and nonallergic childhood asthma [J]. *J Allergy Clin Immunol*, 2015, 135(1): 81-91.
- [14] XLX, LIU J M, GUO J Y. Correlation of PD-1/PD-L1 Signaling Pathway with Treg /Th17 Imbalance from Asthmatic Children [J]. *Int Arch Allergy Immunol*, 2018(176): 255-267.
- [15] QIU Dan-Dan, SUN Jian-Yue, YANG Zi-Zhen, XIE Yu, CAI Hui-Soba. Research progress on the mechanism of the effect of Chinese medicine on Th17/Treg imbalance in asthma[J]. *Shanghai Journal of Traditional Chinese Medicine*, 2019, 53(08): 98-101.
- [16] Yutaka Komiyama, Susumu Nakae, Taizo Matsuki. IL-17 plays an important role in the development of experimental autoimmune encephalo- myelitis [J]. *The Journal of Immunology*, 2006, 177(1): 566-573
- [17] Zhao CHL, Yu HF, Lv X. The role of T lymphocytes in the pathogenesis of asthma [J]. *Chemistry of Life*, 2016, 36(06): 868-873.
- [18] Kimura A, Kishimoto T. IL-6: regulator of Treg /Th17 balance [J]. *Eur J Immunol*, 2010, 40(7): 1830-1835
- [19] Veronica Santarasci, Alessio Mazzoni, Manuela Capone, et al. Musculin inhibits human T helper 17 cell response to interleukin 2 by controlling STAT5B activity [J]. *European Journal of Immunology*, 2017, 47 (9): 1427-1442
- [20] Korn T, Bettelli E, Oukka M, et al. IL-17 and Th17 Cells. *Annu Rev Immunol*, 2009, 27: 485-517
- [21] Laurence A, Tato CM, Davidson TS, et al. Interleukin-2 signaling via STAT5 constrains T helper 17 cell generation. *Immunity*, 2007, 26(3): 371-381
- [22] Huang et al. Retinoid-related orphan receptor  $\gamma$ t is a potential therapeutic target for controlling inflammatory autoimmunity [J]. *Expert Opinion on Therapeutic Targets*, 2007, 11(6): 737-743.
- [23] Cheng H, Li Xue F, Zhao W P, Li S F. New progress in the study of ROR $\alpha$  and ROR $\gamma$ t properties and mediated Th17 cell differentiation [J]. *Chinese Journal of Clinical Physicians (Electronic Edition)*, 2015, 9(08): 1413-1417.
- [24] Zhang Xueya, Zhang Weixi, Li Chang Chong. Differentiation, function and role of Th17 cells/Treg cells in bronchial asthma [J]. *International Journal of Respiratory*, 2014, 34(05): 364-366.
- [25] Maryam Iman, Ramazan Rezaei, Sadegh azimzadeh-jamalkandi, et al. Th17/Treg immunoregulation and implications in treatment of sulfur mustard gas -induced lung diseases [J]. *Expert Rev Clin Immunol*, 2017, 13(12): 1173-1188
- [26] Chen Z, Lin F, Gao Y, et al. FOXP3 and ROR $\gamma$ t: transcriptional regulation of Treg and Th17. *Int Immunopharmacol*, 2011, 11(5): 536-542
- [27] Gao Xiaojie, Shang Lili. Overview of Chinese medicine treatment of bronchial asthma [J]. *Hunan Journal of Traditional Chinese Medicine*, 2015, 31(11): 175-177.
- [28] Ma Tingting, Feng Xingzhong, Wang Xueyan. Study on the effects and mechanisms of *Angelica sinensis* on Th1 /Th2 and Th17 /Treg in Balb /c mice with Yin deficiency asthma [J]. *Chinese Journal of Traditional Chinese Medicine*, 2017, 42 (4) : 758-762.
- [29] WANG Zhi-Wang, DU Hai-Yan, REN Yuan, CHENG Xiao-Li, LI Xue-Feng, LI Rong-Ke. Effects of *angelica* on Th17 dominant immune response in a mouse model of yin deficiency asthma [J]. *Journal of Immunology*, 2016, 32(01): 38-43.

- [30] Li X, Lin S Y. Induction of *Foxp3*<sup>+</sup> regulatory T cells in asthma immunotherapy by tonifying the kidney and warming the yang method [J]. *Modern distance education in Chinese traditional medicine*, 2015, 13(7): 142-144.
- [31] WEI Y, LIU B, SUN J, et al. Regulation of Th17 /Treg function contributes to the attenuation of chronic airway inflammation by icariin in ovalbumin- induced murine asthma model [J]. *Immunobiology*, 2015, 220(6): 789-797.
- [32] Huang Jialin. Effect of *Astragalus polysaccharide* on the expression of Th17-related cytokines in asthmatic mice[D]. Yunnan College of Traditional Chinese Medicine, 2012.
- [33] Xiong Youyi, Wei Jing, Yu Hao, et al. Anti-th17/Treg imbalance in a mouse model of asthma [J]. *China Modern Application*
- [34] Chen Na, Han Jie, Gao Chunyan. The effect and significance of biancetin on Th17 /Treg imbalance in children with bronchial asthma [J]. *Chinese Journal of Immunology*, 2017, 33(1): 58-61. *pharmacology*, 2015, 32(6): 671-676.
- [35] XU W, HU M, ZHANG Q, et al. Effects of anthraquinones from *Cassia occidentalis* L. on ovalbumin-induced airways inflammation in a mouse model of allergic asthma [J]. *J Ethnopharmacol*, 2018, 221(7): 1-9.
- [36] Sung YY, Kim SH, Yuk HJ, et al. *Siraitia grosvenorii* residual extract attenuates ovalbumin-induced lung inflammation by down-regulating IL-4, IL-5, IL-13, IL-17, and MUC5AC expression in mice. *Phytomedicine*. 2019 Aug; 61: 152835.
- [37] Yan ZP, Zhang XZ, Xu DN, et al. Exploring the mechanism of asthma treatment from regulatory T cells and Th17 cell changes in Anti-Allergies and Asthma Formula [J]. *Chinese herbal medicine*, 2014, 45(12): 1731-1735.
- [38] Sui BW, Wang D, Zhai PP, et al. Effects and mechanisms of Shegan Ephedra Tang on airway remodeling and Th17/CD4<sup>+</sup>CD25<sup>+</sup> Treg cells in asthmatic mice [J]. *Chinese Traditional Chinese Medicine Acute Care*, 2017, 26
- [39] ZHANG Ya, YANG Lin, JIANG Rong Yan, LI Ran Ran, LI Ping Ping, STATEMENT Ying. Effects of *Astragalus membranaceus* on IL-2 and IL-4 and their behavioral changes in bronchoalveolar lavage fluid of asthmatic mice [J]. *Journal of Taishan Medical College*, 2019, 40(12): 914-916.
- [40] Wang Yongmei, Xu Shunan, Hou Xianming, et al. Effects of *Cicadellia japonica* on bronchial and lung histomorphology and serum IL-2 and 5 in a rat model of asthma [J]. *Chinese Journal of Basic Chinese Medicine*, 2007, 13(12): 948-949.
- [41] Xing Xianghui. The effect of ping-asthma compound on IL-2 and IL-4 in plasma and BALF of asthmatic rats [J]. *Chinese Traditional Chinese Medicine Emergency*, 2004, 13(11): 758-759.
- [42] Ma Ting, Xing Xianghui. The effect of ping-asthma combination on the levels of IgE, IL-2, IL-4 and IFN-C in children with asthma and its mechanism [J]. *Journal of Guiyang College of Traditional Chinese Medicine*, 2011, 33(4): 73-74.