

# *Research Progress on Recognition and Treatment of RSV Infection in Traditional Chinese Medicine*

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**Abstract:** Respiratory syncytial virus (RSV) is the main cause of bronchiolitis and pneumonia in infants, the elderly and immunocompromised people worldwide. At present, there are no antiviral drugs and vaccines suitable for clinical use. In view of RSV infection, Chinese medicine has the advantages of less toxic and side effects and excellent therapeutic effect. Chinese scholars have carried out a lot of clinical observation and basic research, and found many single Chinese medicine and Chinese medicine compounds with remarkable curative effects. The results of clinical research show that Chinese medicine can relieve symptoms such as asthma, cough and sputum secretion. Basic research has found that the mechanism of anti-RSV infection of traditional Chinese medicine focuses on preventing virus replication and reducing the release of pro-inflammatory mediators. This paper reviews the related contents in order to provide theoretical basis for the study of traditional Chinese medicine against RSV infection.

## **1. Introduction**

Bronchiolitis is a common lower respiratory tract infection in infants and young children. It is common in infants under 2 years old. Respiratory syncytial virus (RSV) is the main cause of infant bronchiolitis and pneumonia. The main histopathological features of RSV infection are bronchial inflammation, mucosal and submucosal edema, and wheezing caused by sputum blocking the lumen; chemokines determine the degree of inflammation and the composition of the inflammatory infiltrate by recruiting specific leukocyte subsets, thus determining the severity of the disease. Modern medicine believes that the effectiveness of drugs in the treatment of viral respiratory tract infections depends on their ability to inhibit viral replication. Some research teams around the world are actively developing antiviral drugs against respiratory syncytial infection, but none are suitable for widespread clinical use. Traditional Chinese medicine has the advantages of strong pertinence, less toxic and side effects, and outstanding therapeutic effects. Scholars in my country have conducted many researches on traditional Chinese medicine for respiratory syncytial virus infection and obtained many excellent results.

## 2. Understanding of Bronchiolitis in Traditional Chinese Medicine

### 2.1 An overview of the etiology and pathogenesis of bronchiolitis in traditional Chinese medicine

There is no mention of the disease "bronchiolitis" in the classics of traditional Chinese medicine, because its main symptoms are "cough, wheezing, phlegm", which are similar to "wheezing syndrome", "asthma syndrome", "pneumonia wheezing" and other diseases, so it can be classified into the same category for reference. With years of research, motherland medicine has accumulated a lot of experience. "Internal Classics" says: "All qi stagnation belongs to the lungs; all fullness and wheezing also belong to the lungs." It shows that the disease is always caused by "disorders of lung qi ascending and descending". There are several exogenous pathogenic factors that can injure the lungs, including "wind-cold" and "wind-heat". Feeling the wind and cold, closing the fur outside, attacking the delicate viscera inside, and invading the lung inside; lung governing skin and hair, and its opening and closing coincides with the breathing of the lung. Wind-cold attacking lung, striae and interstitial space be blocked, lung's qi depression and reversed flow, trigger coughing and wheezing. The lung qi depression transforming into fire and let the lung fluid changes from clearing to turbidity, eventually become phlegm. Wind-heat invades lungs from the nose or mouth, consumes the clear qi in the lungs, turns stagnation into fire, reverses ups and downs, causing wheezing and coughing, and the evil fire frying and roasting Yin essence into phlegm.

"Yin and yang" of the three viscera of the lungs, spleen and kidney can be affected by internal injuries. As the seed of a tree, the kidney is the source of all qi in the human body. It cultivates the qi of the lung and spleen. If kidney qi is deficient, it fails to regulate respiring qi, which leads to coughing and asthma; spleen and lung select the best part of acquired essence, compound zong qi, if Zong Qi is deficient, breathing will be exhausted, and breathing will be blocked and wheezing and coughing will occur. Deficiencies in defensive qi will cause external pathogenic qi to enter the body, and it will damage the yin and hurt the qi, causing asthma and coughing. The lung, spleen and kidney's qi governing the regulation of water passages in sanjiao, and if they are damaged, the water essence will turn into phlegm. Spleen, lung, and kidney are considered mother-child organs in the theory of five elements. Among them, the yin essence is nourished sequentially. Dryness and fire will result from the loss of body fluids. If the fire burns the lung, the flow will be abnormal, cough, phlegm, and dyspnea will appear. The evil is more likely to attack the lungs when it is injured, and the internal and external evils combine, and the lung metal loses its order and is abolished.

In this disease, heat, phlegm, and blood stasis interact and change dynamically<sup>[1]</sup>, and the severity of the patient increases with the accumulation of pathological products. At the early stage of the disease, injury of metal due to exuberant heat only exists in the part of qi fen. Lung can't regulate the water passages anymore. The lung fluid is translated into phlegm-heat, and this makes lung injury more serious. Stagnant heat over time, from qi to blood, evil stagnation in lung collaterals, blood thickens into stasis, if not treated properly, phlegm heat and blood stasis intertwine, eroding flesh and blood and turning into pus. It refers to pulmonary carbuncle, which is mostly in the later stage of the disease, and the condition is severe.

### 2.2. A brief overview of TCM syndrome differentiation and treatment of bronchiolitis

According to traditional Chinese medicine, these diseases fall into deficiency and excess syndromes. Excessive syndromes are classified as wind-cold or wind-heat invading the lung, turbid phlegm or phlegm-heat obstructing the lung, and stagnation of lung-qi. The wind-cold hurts the person, causing stagnation of lung qi, which then reverses and rushes upwards, causing the patient

to wheeze or cough. To treat this with the method of dispersing the lungs and dispelling the cold, use Huagaisan decoction. Wind-heat attacks the lungs, causing the lungs to lose their function of respiration and detoxification, and stagnation of lung qi causes wheezing and coughing. When dispelling wind and clearing heat, Yinqiaosan is used for treatment. Due to emotion and other reasons, the lung qi is not running smoothly, and it is stagnant in the chest, and it is reversed and wheezing and coughing. It is treated with Wumoyinzi to disperse the stagnation. Irregular diet makes spleen qi transport unfavorable, and fluids become phlegm. More qi rise and less fall leads the shortness of breath, use Erchen Decoction combined with Sanzi Yangqin Decoction. Phlegm is turbid and stagnant, and over time it turns into fire, phlegm fire oppresses the lungs, qi reverses and wheezes and coughs, and Sangbaipi Decoction is used to clear it away.

A deficiency syndrome consists of deficiency of lung yin or lung yang, deficiency of lung qi, deficiency of kidney qi, kidney qi fail to control respiration, and collapse of the heart yang. Due to long-term illness, the lung function is abnormal, and the lung yin is damaged. With the yin injured, breathing becomes useless. It is nourished with Shashenmaidong decoction. Long-term illness due to exhaustion of lung qi, qi flow unfavorable and dyspnea, to supplement it with Shengmai decoction. Lung qi is deficient, and there is no way to nourish the child. Consequently, kidney qi is insufficient to control respiring qi, causing asthma. Take Jin Kui Shen Qi Wan for warming kidney qi. If the disease is left untreated, it will turn into a critical illnesses: the syndrome of sudden collapse of heart yang. After a long illness, the disease will reach the heart, and the vital qi will be exhausted, causing yang collapse, take Shenfu decoction as quickly as possible to save lives.

### **3. Traditional Chinese medicine's progress in preventing and treating RSV.**

Traditional Chinese medicine has the advantages of strong pertinence, less toxic and side effects, and outstanding therapeutic effects. Scholars in my country have conducted many researches on traditional Chinese medicine for RSV infection and obtained many excellent results.

#### **3.1 Traditional Chinese medicine prescriptions for preventing and treating RSV.**

According to traditional Chinese medicine, the disease belongs to the categories of "pneumonia and asthma", "asthma syndrome" and "asthma syndrome", through traditional treatment, it has a good curative effect.

Yinqiao San, published in "Detailed Analysis of Epidemic Warm Diseases", is an effective prescription for clearing away wind-heat due to exogenous pathogenic factors. It treats the stage of evil of epidemic febrile or wind-heat invading the weifen. The key points of syndrome differentiation focus on "aversion to cold and fever" and "sore throat". The exogenous disease due to evil of epidemic febrile first attacks the lung meridian, making the lung qi reversed and causing "wheezing", causing the lung yin be burned and causing "phlegm congestion". The cure method must strictly follow the three methods of "clearing", "nourishing" and "penetrating". The evil of epidemic febrile enter the body cause fire stagnation, and the treatment of "fire stagnation" is to clearing heat with bitter and cold medicine while penetrating stagnation with pungent and cool medicine, Fire stagnation will consume yin, so calm this problem by adding the medicine sweet and cool in nature and flavour, nourishing yin in efficacy. Shuanghua, Forsythia, and Peppermint, although these three flavors are cold in nature but frivolous in quality, they can relieve evil heat with the circulation of qi and blood, and the stagnation of qi and blood caused by fire can be relieved. Together with Platycodon, burdock is used to enter the lungs and dissipate heat, accumulate phlegm and cure sore throat, lighten heat in the chest, play the power of expel wind and heat. We need to reed roots nourish yin. Bamboo leaves clear the heat of heart and lungs through urination. Experiments have shown that Yinqiao powder can inhibit the release of a series of related

cytokines that trigger inflammation by reducing the production of NALP3, ASC and caspase-1<sup>[2]</sup>; it can also reduce the expression level of the upstream protein TLR4 of NF- $\kappa$ B to block signal, reduce the synthesis of pro-inflammatory interleukins<sup>[3]</sup>; it can also reduce the release of TNF- $\alpha$  to inhibit the inflammatory response, and increase the content of IFN- $\gamma$  to inhibit the replication of respiratory syncytial virus<sup>[4]</sup>.

Maxingshigan Decoction is specially used to treat pathogenic heat and block the lungs. Pediatric respiratory diseases such as pneumonia and bronchiolitis have been treated with it repeatedly. The shape of ephedra is as thin as hair, and the land where ephedra is planted will melt when the snow falls. It can be seen that its pungent, warm and clear qi is the most of all medicines, so its medicinal qi can penetrate upward and outward to suppress the stagnation of lung qi. Xingren can descending qi and slow down the stagnation of lung qi because its bitter flavour. It is compatible with ephedra, and the ascending and descending coincidence. They promote each other with their opposite and complementary forces, and amplify the power of flattening the lungs. Gypsum is white in color, cold in nature and pungent in flavour, enters the lungs to extinguish the smoldering flame, licorice nourishes the spleen and stomach to prevent powerful medicines from cutting down vital qi. After investigation, this formula can stop the phosphorylation of JAK on STAT, expand the inhibition of regulatory T cells on helper T cells 17, reducing the production of pro-inflammatory cytokine IL-17 and weakening the inflammatory response<sup>[5]</sup>; and it can reduce the expression level of TNF- $\alpha$  to reduce the stimulation of lung tissue, and regulate the erosion of the trachea by reducing the ECP secreted by eosinophils<sup>[6]</sup>; Another study found that Maxing Shigan Decoction can regulate TRPV1 to reduce the expression level of inflammatory proteins, antagonize the amount of PEG2, and down-regulate the activation degree of Th2<sup>[7]</sup>.

The asthma syndrome treated by Dingchuan Decoction has the etiology and pathogenesis of "lung-deficiency wind-cold bundled externally and internal fire-heat". Ephedra makes stagnant qi upward, and xingren guides stagnant qi downward; fearing xingren will not be able to descend, add perilla, ginkgo, and pinellia to restrain lung qi and reduce phlegm; cold and heat can damage lung yin, make it turn into phlegm, and the combination of phlegm and heat will aggravate the disease, so Huangqin and Sangbaipi are added to clear away heat and reduce phlegm; because of lung deficiency, add Kuandonghua to warm and benefit the lung, and Kuandonghua blooms in cold winter, the image of upward yang generation under the cold, and can be supplemented by ephedra to increase its propagating power; combined with the harmonizing power of licorice, it can make the lungs rectify evil and retreat. Several studies have shown that Dingchuan Decoction is capable of reducing the production and accumulation of inflammatory cells caused by RSV infection<sup>[8]</sup> and intestinal flora imbalance<sup>[9]</sup>. Additionally, it can correct imbalances in T cell differentiation, such as an abnormal conversion ratio between T helper 1 and 2 cells<sup>[10]</sup>. Both the decreased expression of TSLP and GATA 3 and the increased secretion of IFN- $\gamma$  can inhibit the production of cytokines IL-4, IL-10, IL-13, and IL-33, which represent the process of transforming T cells into Th2, and IFN- $\gamma$  can promote more differentiation of T cells to Th1, this prescription can increase the expression level of IFN- $\gamma$ , reduce the content of TSLP and GATA 3, thereby improving the imbalance of Th1 and Th2 caused by RSV infection, and restore immune function<sup>[11-12]</sup>.

### **3.2 Clinical research on prevention and treatment of RSV infection by modern Chinese medicine**

In recent years, with the continuous clinical application and innovation of traditional Chinese medicine, many effective single traditional Chinese medicines have been discovered, and many compound prescriptions with considerable curative effects have been created.

Wei Xiangyu et al<sup>[13]</sup> found that Houத்துynia cordata injection combined with montelukast

sodium treatment can effectively shorten the duration of fever and improve wheezing symptoms in children. Zhang Wenfeng et al<sup>[14]</sup> found that Qingfei Huatan Granules accelerated the reduction of symptoms such as fever, phlegm obstruction, cough, and pulmonary rales in children with RSV-infected pneumonia through comparison, and the treatment effect was more significant. Mo Yaoding et al<sup>[15]</sup> found that the self-made Qingfeijiedu decoction could cure cough and asthma and croup more quickly without many adverse reactions that occurred during the treatment of the western medicine group. Yuan Bin et al<sup>[16]</sup> found that the Qingfei Oral Liquid group had a higher degree of reduction in cough grade than the ribavirin group and a higher cure rate on the 3rd day and 10th day of treatment. Pan Yueting et al<sup>[17]</sup> found that chrysanthemum decoction can alleviate the lesions of airway epithelial cells in children with RSV-infected pneumonia. Reduced chemotaxis of RANTES and MCP-1 reduces the production of inflammatory cells, calms down the airway reaction, and reduces inflammation. Tong Dan et al<sup>[18-19]</sup> used respiratory rate and kilogram tidal volume as indicators for evaluating lung function and lung injury, and found that self-made Qingfei Pingchuan decoction combined with western medicine can improve the breathing of children with RSV-infected pneumonia better than western medicine alone. By down-regulating Eotaxin and IL-17, it reduces pathological damage, reduces sputum, and improves symptoms of asthma. Cheng Shen et al<sup>[20]</sup> used nebulized inhalation of Ventolin, Pulmicort Lingshu and Aiquanle as the treatment method of the control group, A traditional Chinese medicine compound called Maozhiyin was took to the treatment group. Within a year after recovery, digestive symptoms improved faster than the control group, with fewer adverse reactions and a lower asthma recurrence rate. Zhou Yongmao et al<sup>[21]</sup> found that oral Maxing Shigan Decoction was superior to oral budesonide combined with interferon nebulization therapy in improving airway response in patients, and there were fewer adverse reactions and a higher effective rate.

### **3.3 Basic research on the prevention and treatment of RSV with modern traditional Chinese medicine**

In basic experiments, individuals are not human, and symptoms and signs have a lower reference value than clinical observations. However, basic experiments can further explore the exact mechanism of traditional Chinese medicine to cure diseases.

#### **3.3.1 Single traditional Chinese medicine and its components**

He Yahui et al<sup>[22]</sup> took Shuanghuanglian as a control and found that Kudiezi had a higher lesion inhibition rate against RSV infection, but its internal antiviral mechanism is not clear, and has the potential for further research. Shi Chenxiao et al<sup>[23]</sup> found that Guijianyu can inhibit the biological effects of RSV-induced TLR3 and TLR4, thereby increasing the concentration of IL-4 and IFN- $\alpha$  in the body to prevent the replication of RSV and reduce the expression of TNF- $\alpha$  and TNF- $\beta$ . Guijianyu also can decrease the inflammatory response and minimize the damage to lung tissue caused by RSV infection. Wang Tianqing et al<sup>[24]</sup> used guinea pigs as experimental animals and found that Shegan can reduce the airway damage and coughing and other pathological reactions caused by RSV infection, Reducing the release of arachidonic acid and interfering with the information transmission of inflammatory reactions reduce symptoms. Wang Jifeng et al.<sup>[25]</sup> found through in vitro experiments that Xuejiancao could neither directly kill the virus nor prevent virus particles from adsorbing cells, but it could exert anti-RSV effects by interfering with a series of material synthesis processes after virus invasion; further in vivo experiments showed that Xuejiancao achieves this function by promoting the synthesis of IL-2 and IFN- $\gamma$  and reducing the expression of tumor necrosis TNF- $\alpha$ . Cui Zhenzhen et al.<sup>[26]</sup> found that Mufurongye had anti-RSV activity. Xu Jiaxin et al.<sup>[27]</sup> found that mint had a therapeutic effect on RSV infection. Yan Weiwei



et al.<sup>[28]</sup> found that Qicao and Baitouweng could inhibit the invasion of RSV into the body; these three drugs also achieve their effects through the regulation of related proteins, and the cytokines affected are the same as those of Xuejiancao. Qin Sheng et al.<sup>[29]</sup> found that baicalin can effectively inhibit the replication of RSV virus and increase the expression levels of IFN- $\alpha$  and IFN- $\beta$  through cell experiments and animal experiments, and proved that baicalin can interfere with the translation of M RNA and NS RNA by RT-qPCR. And the higher the concentration, the stronger the correlation effect. Shi Hengfei et al.<sup>[30]</sup> also found that baicalin can repair lung injury by reducing the inflammatory response caused by RSV infection. Hu Xiaoyuan et al.<sup>[31]</sup> screened out three substances with good anti-RSV effects from nine kinds of traditional Chinese medicine extracts, namely, Lubianqing water extract, From nine types of traditional Chinese medicine extracts, Luohuazizhu water extract and Jiaohuahutuizi water extract. However, its inner mechanism still needs to be further explored. Liu Chunyuan et al.<sup>[32]</sup> found through cell experiments that the apoptosis response triggered by RSV infection can be antagonized by *Sophora flavescens* alkaloids by regulating the NF- $\kappa$ B signaling pathway. Zhu Xiuzhen et al.<sup>[33]</sup> conducted experiments using Hep-2 cells as host cells, and found that isoorientin, the most significant anti-RSV component in the leaves of *Danzhu* leaves. Some interventions are performed on the process of RSV transcription and translation to inhibit the virus from adhering to cells, but not preventing the virus from entering the cells.

### 3.3.2 Traditional Chinese medicine compounds

As medical research progresses, traditional Chinese medicine is also constantly improving, and more and more traditional Chinese medicine compound prescriptions and Chinese patent medicines have been found to have good anti-RSV infection effects and have been widely used.

Bao Yanyan et al.<sup>[34]</sup> found through animal experiments that compound Qinlan oral liquid can reduce the degree of lesions, reduce the content of IP-10 and RANTES, reduce the lung index, and increase the inhibition rate, thereby preventing and treating RSV infection.

The flavonoids in Qingfei Oral Liquid can treat the damage caused by RSV infection through multiple mechanisms: It was found by Ling Xiaoying et al.<sup>[35]</sup> that the flavonoids in Qingfei Oral Liquid restored the disordered lipid metabolism caused by the virus, restored damaged mitochondria, and increased tight junction proteins to repair lung epithelial damage, and cure the wounds caused by the RSV virus to the body. Li Zhexiong et al.<sup>[36]</sup> found that the flavonoids in Qingfei Oral Liquid inhibited the phosphorylation of IKK $\alpha$  protein by reducing the expression of IKK $\alpha$  kinase complex, reducing the p65 released by IKK $\alpha$  protein, thereby reducing the occurrence of inflammatory reactions and relieving RSV infection Damage to lung tissue. Through the Akt signaling pathway, Li et al.<sup>[37]</sup> found that Qingfei Oral Liquid can alter the ratio of macrophages M1 and macrophages, reducing the number of M1 macrophages while increasing the number of M2 macrophages, thereby repairing the inflammatory response caused by RSV. Zhang Xin et al.<sup>[38]</sup> found through in vivo and in vitro experiments that Wuhu Decoction inhibited the upstream proteins related to PI3K/Akt/mTOR, aggravated the autophagy of dendritic cells, inhibited its function of activating T cells, by reducing inflammation, we relieved the damage caused by viral infection to the respiratory tract, reduced airway remodeling, and prevented abnormal secretions from aggregating, and acted as a therapeutic and recovery agent. Using dexamethasone, Wang Xianzheng et al.<sup>[39]</sup> reduced mice's immunity by increasing the number of myeloid suppressor cells. Jinping Decoction can reduce the number of myeloid suppressor cells to antagonize this effect, and can alleviate the pathological changes of lung tissue, which may be It is achieved by increasing the levels of IFN- $\beta$  and CD8+CD69+T cells. Ding Yuewen et al.<sup>[40]</sup> found that Lianhua Qingwen Capsules can play an anti-RSV infection role by regulating the secretion of IL-1 $\beta$  and IL-6 from immune cells. He Yumin et al.<sup>[41]</sup> found that Shaoyao Gancao Decoction can reduce the

inflammatory response of RSV infection by reducing the levels of various interleukins that promote inflammation; it can also reduce the expression area of B lymphocyte tumor-2 protein and increase the allosteric activation of apoptosis. The factor Bax is secreted, thereby promoting the apoptosis of eosinophils, and alleviating the asthmatic symptoms of RSV pneumonia. Li Junying et al<sup>[42]</sup> observed through in vitro experiments that Suhuang Zhike Capsules and San'ao Tablets could reduce the virus's invasion of A549 cells. Researchers Wang Jia et al. <sup>[43]</sup> conducted separate experiments on nourishing the kidneys and nourishing qi as well as clearing heat and activating blood, and found that these two prescriptions can promote the expression of T-bet mRNA of helper T cells 1, while inhibiting the expression of GATA3, STAT6 and ROR  $\gamma$  T mRNA of helper T cells type 2 and type 17, increasing the number of T-helper 1 cells and amplifying the inhibitory effect of T-helper 1 on the differentiation of helper T cells type 2 and helper T cells type 17, which alleviates various airway symptoms and damage.

Bian Wenqing et al<sup>[44]</sup> detected the content of various cytokines that can cause inflammation in the alveolar lavage fluid of RSV-infected guinea pigs, and found that Jinzhen Oral Liquid can reduce the damage of RSV infection to epithelial cells by alleviating the infiltration of inflammatory cells. Wang Min et al<sup>[45]</sup> found that Sangpi Zhike Formula can regulate the secretion of C-fos in the MAPK pathway from the genetic level, inhibit the differentiation of T cells into Th2 subgroups, thereby reducing the production of various interleukins that trigger inflammatory responses, thereby reducing asthma Airway responsiveness, antagonizing airway remodeling and pathological changes.

#### 4. Conclusion

Domestic scholars have made unremitting research on RSV infection and found several single prescriptions and a large number of compound prescriptions, which provide new ideas and directions for the treatment of RSV infection. At present, the clinical efficacy of traditional Chinese medicine in the prevention and treatment of RSV infection is mainly to improve pathological damage, reduce sputum secretion, and reduce the degree of cough and asthma; It works by inhibiting viral replication and relieving inflammation; most of the syndrome types are phlegm-heat closed lung syndrome. We still need to further search for other pathogenic mechanisms and TCM syndrome types in the treatment of RSV infection with traditional Chinese medicine.

#### References

- [1] Chen Wenxia, Yan Yongbin, Fan Shuhua. Analysis of syndrome differentiation and treatment of children with bronchiolitis obliterans [J]. *Traditional Chinese Medicinal Research*, 2016, 29(09): 7-9.
- [2] Qin Likui, Zhang Fengxue, Huang Xiaojuan, Song Hong, Gong Wenliang. Study on the Effect of Yinqiao Powder on the Respiratory System of Mice Infected with Respiratory Syncytial Virus [J]. *New Chinese Medicine*, 2018, 50(05): 24-30. DOI: 10.13457/j.cnki.jncm.2018.05.006.
- [3] Wang Xuefeng, Wang Siyuan, Yue Zhijun, et al. Study on the expression of inflammatory cytokines and the regulation of TLR-4/NF- $\kappa$ B signaling pathway in mice with RSV-induced pneumonia by three treatments[J]. *Liaoning Journal of Traditional Chinese Medicine*, 2014, 41(03): 385-387. DOI: 10.13192/j.issn.1000-1719.2014.03.001.
- [4] Zhu Wanqing. Experimental study on the effect of double table method on TNF- $\alpha$  and IFN- $\gamma$  in mouse pneumonia induced by RSV [D]. *Liaoning University of Traditional Chinese Medicine*, 2013.
- [5] Wang Siyuan, Bo Han, Nan Chunhong, et al. Effects of Moxing Shigan decoction on lung inflammatory response of asthmatic mice induced by RSV [J]. *Shandong Medical Journal*. 2020, 60(01):48-51.
- [6] Wang Weiqun, Shao Zhengyang, Xu Xianke, et al. Effects of Jia Wei Ma Xing Shi Gan Decoction on serum TNF- $\alpha$ , ECP and lung pathology in rats infected by respiratory syncytial virus. [J]. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine*, 2012, 22(06):420-423.
- [7] Li Mengwen. Study on mechanism of Ma Xing Shi Gan Decoction (MXSGD) in intervention of asthma airway inflammation and its compatibility [D]. *Nanjing University of Traditional Chinese Medicine*, 2021. DOI: 10.27253/d.cnki.gnjzu.2021.000057.
- [8] Cui Zhenze, Huang Yan, Xu Chao. Effect of Dingchuan decoction on the inflammatory cells in BALF of young rats

- infected with RSV [J]. *Chinese Pediatrics of Integrated Traditional and Western Medicine*, 2017, 9(05):369-371+461.
- [9] Ou Yangzhen, Chi Lei, Xu Chao, et al. Liquid chromatography-mass spectrometry-based metabolomics study of the efficacy of Chinese medicine asthma-relieving decoction on respiratory syncytial virus infection [J]. *Chinese Journal of Chromatography*, 2021, 39(03):281-290.
- [10] Huang Yan, Xu Chao, Cui Zhenze. Immunoregulatory effects of asthma - relieving decoction and its decomposed potion in rats with respiratory syncytial virus [J]. *Lishizhen Medicine and Materia Medica Research*, 2016, 27(09): 2078-2081.
- [11] Huang Yan, Xu Chao, Cui Zhenze, et al. Study on influence of Dingchuan Decoction on balance factors of immune network in respiratory syncytial virus (RSV) infected rats [J]. *Journal of Pediatrics of Traditional Chinese Medicine*, 2018, 14(02):10-15. DOI:10.16840/j.issn1673-4297.2018.02.03.
- [12] Cui Zhenze, Huang Yan, Liu mingtao, et al. Effects of Asthma-relieving Decoction on expression of TSLP and GATA3 in lung tissue of rats with respiratory syncytial virus infection [J]. *China Journal of Traditional Chinese Medicine and Pharmacy*, 2018, 33(12):5581-5583.
- [13] Wei Xiangyu. Clinical observation of Yuxingcao atomization combined with montelukast in treating respiratory syncytial virus pneumonia [D]. *Guangzhou University of Traditional Chinese Medicine*, 2017.
- [14] Zhang Wenfeng, Hu Fengren, Peng Kangda, et al. Clinical Analysis of Qingfei Jiedu Method in the Treatment of Children with Respiratory Syncytial Virus Pneumonia [J]. *Modern Diagnosis and Treatment*, 2017, 28(06):994-995.
- [15] Mo Yaoding. Efficacy of Traditional Chinese Medicine in Treating Children's Respiratory Syncytial Virus Pneumonia [J]. *Inner Mongolia Journal of Traditional Chinese Medicine*, 2019, 38(04): 27-28. DOI: 10.16040/j.cnki.cn15-1101.2019.04.020.
- [16] Yuan Bin, Sun Yiqiu, Ren Huijie, et al. Clinical Study on Qingfei Oral Liquid in Treating Children with RSV Pneumonia Syndrome of Phlegm-heat Closing the Lung [J]. *Jiangsu Journal of Traditional Chinese Medicine*, 2008, 40(12): 36-37.
- [17] Pan Yueting, Zhu Liang. Effects of traditional Chinese medicine chrysanthemum decoction on Pediatric RSV infection after A549 cell chemotactic factor [J]. *Chinese Journal of Biochemical and Pharmaceuticals*, 2015, 35(03): 82-84.
- [18] Tong Dan, Hong Yan, Chen Yuan, et al. Effects of Qingfei Pingchuan decoction on the tidal breathing lung function in children with respiratory syncytial virus pneumonia (phlegm-heat closing lung) [J]. *Chinese Pediatrics of Integrated Traditional and Western Medicine*, 2018, 10(05):413-417.
- [19] Tong Dan, Hong Yan, Zhan Ning, et al. Effect of Clearing Lung - Heat and Relieve Panting Decoction on Eotaxin and IL-17 in Children with Respiratory Syncytial Virus Pneumonia [J]. *Journal of Shaanxi University of Chinese Medicine*, 2019, 42(01):115-118. DOI:10.13424/j.cnki.jsctcm.2019.01.035.
- [20] Cheng Shen, Li Lan, Wang Liling, et al. Clinical Observation on Maozhi Decoction in the Treatment of Respiratory Syncytial Virus Infected Bronchiolitis in Children [J]. *Zhejiang Journal of Integrated Traditional Chinese and Western Medicine*, 2022, 32(07):637-639.
- [21] Zhou Yongmao, He Degen, Wang Xinfang. Curative effect observation of combination of TCM and western medicine in treating children with respiratory tract infection [J]. *Clinical Journal of Chinese Medicine*, 2016, 8(15): 92-93.
- [22] He Yahui, Jiang Chunying, Liu Xiaolin, et al. Observation on the Efficacy of Traditional Chinese Medicine Kudiezi against Respiratory Virus [J]. *Chinese Journal of Public Health*, 2006(08):980-981.
- [23] Shi Chenxiao. Study on Isolation and Purification of the Effective Anti-Respiratory Syncytial Virus from *Euonymus alatus* (Thunb.) Sieb and its Anti-viral Mechanism [D]. *Shandong University of Traditional Chinese Medicine*, 2020. DOI: 10.27282/d.cnki.gsdzu.2020.000478.
- [24] Wang Tianqing, Zhang Ying, Jiang Hong, et al. Effect of Belamcanda Chinensis on Airway Inflammation in Guinea Pig with Respiratory Syncytial Virus Infection [J]. *Chinese Archives of Traditional Chinese Medicine*, 2019, 37(09): 2128-2132+2313. DOI:10.13193/j.issn.1673-7717.2019.09.019.
- [25] Wang Jifeng. Extraction and Separation of Polysaccharides from Common Sage Herb and Study on Anti-Respiratory Syncytial Virus [D]. *Shandong University of Traditional Chinese Medicine*, 2019. DOI:10.27282/d.cnki.gsdzu.2019.000959.
- [26] Cui Zhenzhen. Study on Isolation and Purification of the Effective Anti Respiratory Syncytial Virus from *Hibiscus mutabilis* Leaf and its Anti-viral Mechanism [D]. *Shandong University of Traditional Chinese Medicine*, 2019. DOI: 10.27282/d.cnki.gsdzu.2019.000118.
- [27] Xu Jiixin. Study on the Effect Parts of *Methahaplocalyx* against Respiratory Syncytial Virus [D]. *Shandong University of Traditional Chinese Medicine*, 2019. DOI: 10.27282/d.cnki.gsdzu.2019.000955.
- [28] Yan Weiwei. Isolation of Active Fractions from *Holotrichiae Larva* and *Pulsatilla Chinensis* (Bge.) Regel and Study on Antiviral Mechanism of their Compatibility [D]. *Shandong University of Traditional Chinese Medicine*, 2019. DOI: 10.27282/d.cnki.gsdzu.2019.000970.
- [29] Qin Sheng. The Inhibitory Effect and Mechanism of Baicalin on Respiratory Syncytial Virus Infection [D].



- Southern Medical University, 2022. DOI:10. 27003/d. cnki. gojyu. 2022. 000200.
- [30] Shi Hengfei. *Baicalin is a naturally occurring flavone that efficiently inhibits RSV replication* [D]. Nanjing University, 2016.
- [31] Hu Xiaoyuan, Yin Feifei, Zhang Junqing, et al. *In Vitro Study on the Antiviral Activity of 9 Extracts of Traditional Chinese Herbal Medicine Against the Human Respiratory Syncytial Virus* [J]. *Journal of Hainan Medical University*, 2022, 28(21):1601-1607. DOI:10. 13210/j. cnki. jhmu. 20220705. 001.
- [32] Liu Chunyuan. *Study on the Inhibitory Effect and Mechanism of Five Sophora flavescens Alkaloids on Human Respiratory Syncytial Virus in Vitro* [D]. Guizhou Medical University, 2021. DOI: 10. 27045/d. cnki. ggyyc. 2021. 000027.
- [33] Zhu Xiuzhen, Shen Wenwei, Gong Cuiying, et al. *Antiviral Activity of Isoorientin against Respiratory Syncytial Virus in Vitro and in Vivo* [J]. *Journal of Sun Yat-sen University (Medical Sciences)*, 2015, 36(03):352-359. DOI: 10. 13471/j. cnki. j. sun. yat-sen. univ(med. sci). 2015. 0057.
- [34] Bao Yanyan, Gao Yingjie, Zhou Lili, et al. *The efficacy of compound Qinlan oral liquid on respiratory virus infection* [J]. *World Chinese Medicine*, 2021, 16(12):1809-1817.
- [35] Ling Xiaoying. *Mechanism of Qingfei Oral Liquid flavonoids in treating RSV pneumonia by regulating necroptosis* [D]. Nanjing University of Traditional Chinese Medicine, 2022. DOI:10. 27253/d. cnki. gnjzu. 2022. 000123.
- [36] Li Xixuan. *Study on the anti RSV mechanism of flavonoids in Qingfei oral liquid based on NF- $\kappa$ B signaling pathway* [D]. Nanjing University of Traditional Chinese Medicine, 2021. DOI:10. 27253/d. cnki. gnjzu. 2021. 000425.
- [37] An Li. *Professor Wang Shouchuan's Experience in Treating Pediatric Viral Pneumonia Based on Theories of 'Heat Depression with Phlegm and Stasis' and Research on the Metabolic and Immune Mechanism of Qingfei Oral Liquid* [D]. Nanjing University of Traditional Chinese Medicine, 2022. DOI:10. 27253/d. cnki. gnjzu. 2022. 000296.
- [38] Zhang Xin. *the effect of Wuhu Decoction through PI3K/Akt/mTOR signaling pathway to regulate DCs autophagy on the proliferation and activation of T cells and the secretion of inflammatory factors in RSV-induced asthmatic mice* [D]. Hunan University of Chinese Medicine, 2021. DOI:10. 27138/d. cnki. ghuzc. 2021. 000015.
- [39] Wang Xianzheng. *Professor Wang Shouchuan's experience and Mechanism of deficiency-excess differentiation in the treatment of infantile viral pneumonia* [D]. Nanjing University of Traditional Chinese Medicine, 2021. DOI: 10. 27253/d. cnki. gnjzu. 2021. 000885.
- [40] Ding Yüewen, Zeng Lijuan, Li Runfeng, et al. *Pharmacological Action of Lianhua Qingwen Granules on BALB/c Mice Infected with Respiratory Syncytial Virus* [J]. *Journal of Guangzhou University of Traditional Chinese Medicine*, 2016, 33(04):540-544. DOI:10. 13359/j. cnki. gzbtc. 2016. 04. 023.
- [41] He Yumin, Wang Jinyan, He Bingjie, et al. *Effects of Shaoyao Gancao Decoction on Expression of Inflammatory Factors, Bcl-2 and Bax and Immune Function in RSV-induced Asthma Mice* [J]. *Journal of Emergency in Traditional Chinese Medicine*, 2020, 29(06):1031-1034+1054.
- [42] Li Junying, Li Jiqiang. *Effects of Suhuang -zhike capsule on respiratory syncytial virus in vitro experimental study* [J]. *Hebei Journal of Traditional Chinese Medicine*, 2017, 39(04):575-578.
- [43] Wang Jia. *Anti-inflammatory effects of BuShen YiQi Formula in RSV-induced asthma exacerbation mice* [D]. Fudan University, 2014.
- [44] Bian Wenqing, Fu Yingxue, Xu Huiqin, et al. *Study on the Mechanism of JZKFY Treatment of Cough Induced by Respiratory Syncytial Virus Infection* [J]. *Journal of Nanjing University of Traditional Chinese Medicine*, 2018, 34(03): 277-281. DOI:10. 14148/j. issn. 1672-0482. 2018. 0277.
- [45] Wang Min, Bai Xiaohong, Liu Fang, et al. *Effect of Sangpi Zhike Recipe on RSV-induced post-infection coughing mice Effect of c-fos and related inflammatory factors expression* [J]. *China Journal of Traditional Chinese Medicine and Pharmacy*, 2020, 35(12):6038-6042.