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Review Article

Impact of Herbal Medicine and Probiotics in Pediatric Asthma

Yasamin Fatemeh Sadat Zojaji[1], Nafiseh Erfanian[2], Yazdan Ebrahimpour[3], Sahbasadat Khatami[4], Rana Tafrishi[5*], Hamid Ahanchian[6]

[1] *Department of Medical Sciences, Islamic Azad University of Medical Sciences, Mashhad, Iran*
[2] *Cellular and Molecular Research Center, Birjand University of Medical Sciences, Birjand, Iran*
[3] *Clinical Research Development Unit of Akbar Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
[4] *Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran*
[5] *Department of Allergy and Clinical Immunology, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran*
[6] *Allergy Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

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Abstract

Asthma, a prevalent chronic condition in children, poses significant challenges in management. While conventional treatments like inhaled corticosteroids and beta-agonists are standard, there is increasing interest in the role of herbal medicine and probiotics as complementary therapies. This paper reviews the impact of herbal remedies—such as Butterbur, Ginger, Turmeric, Boswellia, Licorice, and Ephedra—and probiotics on pediatric asthma. Evidence suggests these therapies may reduce inflammation and improve respiratory function, potentially benefiting asthma management. However, variability in product quality and study designs necessitates further research. Future studies should focus on validating these interventions through rigorous clinical trials to better integrate herbal medicine and probiotics into comprehensive asthma care for children.

Keywords: Herbal Medicine; Probiotics ; Asthma; Respiratory Disorder

***Corresponding Author:** Rana Tafrishi, MD
Department of Allergy and Clinical Immunology, Ghaem Hospital, Ahmad Abad Ave. Mashhad, Iran
E-mail: ranatafrishi96@gmail.com

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Introduction

Asthma is a chronic respiratory disorder characterized by airway inflammation and sensitivity to various triggers, resulting in symptoms such as wheezing, shortness of breath, chest tightness, coughing, and restricted airflow. This condition significantly impacts quality of life, productivity, and healthcare costs. Treatment typically involves a range of medications designed to reduce inflammation, relax airway muscles, and prevent attacks. These include inhaled corticosteroids, long-acting beta-agonists, combination inhalers, leukotriene modifiers, mast cell stabilizers, and theophylline, all of which contribute to improving respiratory performance and overall quality of life for asthma patients (1-4).

In children, asthma is the most common chronic condition, affecting up to 37% of children globally (5, 6). The management of asthma in pediatric patients often combines pharma-

cological and non-pharmacological approaches. Traditional medicine, defined by the World Health Organization as practices rooted in cultural beliefs and experiences, plays a significant role in this management (7). Complementary and Alternative Medicine (CAM), which includes various healthcare methods outside conventional medical frameworks, is commonly utilized by families seeking additional support(2, 8, 9). Factors such as age, gender, socio-cultural background, family social security, financial situation, and parental education level influence the use of CAM among children with asthma (10). Natural products are increasingly recognized for their role in asthma management. Research indicates that a diet rich in fruits and vegetables, along with reduced dairy and animal fats, can positively impact lung function in children with asthma (11). Herbal remedies and supplements, such as herbal teas, aloe plant juice, and herbal cough syrups, are noted for their potential benefits in managing asthma symptoms. These natural products are valued for their antiasthmatic properties and may offer a complementary approach to conventional treatments with potentially fewer side effects (12-14).

Recent advances in metagenomic sequencing and bioinformatics have enhanced understanding of the microbiota's role in immune development and asthma. Specific microbial compositions, rather than overall diversity, are linked to asthma risk. Early-life differences in home microbiota are associated with childhood asthma, while a farm-like indoor microbiota may protect against asthma development. These findings highlight the potential of indoor dust microbiota as both a predictor of asthma risk and a target for preventive strategies (15-19).

Herbal Medicine in Pediatric Asthma

Herbal medicine has shown promising results in the treatment of pediatric asthma, with studies indicating significant improvements in respiratory function. Research has highlighted the efficacy of herbal medicines, such as Butterbur, Ginger, turmeric, Boswellia, Licorice and Ephedra in enhancing lung function in children with respiratory diseases (20, 21). The use of herbal medicines in children has been deemed feasible, emphasizing the need for further high-quality clinical trials to support their efficacy and safety profile.

Butterbur

Butterbur (Petasites hybridus) is indeed a plant known for its medicinal properties, including potential benefits in treating children's asthma (22). The herb has been extensively studied and endorsed by reputable medical organizations for its effectiveness in migraine prophylaxis and other conditions like allergic rhinitis, asthma, and bladder spasms (22). While caution is advised due to its pyrrolizidine alkaloid content, which can cause liver issues, the essential oils from butterbur have shown promise in various therapeutic activities like anti-inflammatory effects, making them potentially safe for use without the alkaloids present (23). The plant's active compounds, such as sesquiterpene lactones like petasin and isopetasin found in the rhizomes, contribute to its antioxidant and anti-inflammatory properties, suggesting a potential role in managing conditions like asthma, including in children (23, 24). Research indicates that s-petasin not only reduces the accumulation of inflammatory cells in bronchoalveolar fluids but also inhibits mast cell degranulation and blocks phosphodiesterase (PDE) 3 and PDE4, with a preference for PDE4 (25, 26). This results in reduced airway hyperresponsiveness and inflammation. Furthermore, s-petasin modulates the immune response by decreasing specific immunoglobulin E (IgE) levels while increasing IgG2a levels, which suggests a shift towards a Th1 response. This balancing effect on the immune system, combined with its ability to alleviate asthma symptoms, highlights s-petasin's potential as a valuable therapeutic agent (27).

Ginger

Ginger (Zingiber officinale) has been historically recognized for its medicinal properties, including its potential in treating various conditions such as asthma (28), which renowned for its rich array of chemical constituents, including phenolic compounds, terpenes, polysaccharides, lipids, organic acids, and raw fibers. Additionally, ginger has been used traditionally to alleviate respiratory symptoms and could potentially aid in reducing asthma symptoms in children (29). The therapeutic properties of ginger are primarily attributed to its phenolic compounds, such as gingerols(GIN)

and shogaols (SHO) (30).

Compounds like SHO and GIN offer promising therapeutic options for airway diseases such as asthma, either alone or in combination with traditional treatments like β2-agonists. SHO and GIN are notably effective, inducing significant relaxation of airway smooth muscle and reducing airway hyperresponsiveness (31). Ginger extract, which contains these compounds, shows strong anti-inflammatory properties by inhibiting cyclooxygenase 2 (COX-2) and suppressing pro-inflammatory cytokines such as interleukin-1, interleukin-18, and TNF-α, thus mitigating airway inflammation (32). Additionally, ginger extract modulates immune responses by downregulating transcription factors associated with allergic reactions and altering Th1 and Th17 cell activity. This helps manage allergic asthma by reducing eosinophilia, mucus production, and Th2 cytokine levels. Moreover, SHO and GIN inhibit mast cell degranulation, decrease histamine release, and reduce oxidative stress, contributing to lower inflammation scores, reduced eosinophil recruitment, and diminished mucus production in asthma models (33).

Turmeric

Turmeric, specifically its active compound curcumin (Curcuma longa), shows promise in treating asthma, including in children (34-36). The chemical analysis of turmeric extract indicated several components including curcumin (polyphenol yellowish pigment of turmeric 2–5%), carbohydrates (40–70%), proteins (6–8%), oils (5–8%), and other elements (3–5%) (37). The mechanisms of action of curcumin include inhibition of inflammatory enzymes such as cyclooxygenase 2 (COX-2), lipoxygenase (LOS), and nitric oxide inducible synthase (iNOS), reduction in inflammatory cytokine levels (38, 39), inhibition of NF-κB activation (40) and Wnt/β-catenin signaling (41), activation of the nuclear factor-E2-related factor 2/haem oxygenase (HO)-1 signaling pathway (41), regulation of immune cells like CD4+CD25+ (42), and inhibition of the Notch1-GATA3 signaling pathway (43). In a randomized, double-blind, controlled trial conducted by G. Manarin et al. the administration of turmeric alongside standard treatment to children and adolescents with asthma resulted in several positive outcomes. After 3 and 6 months of treatment, participants experienced less frequent nighttime awakenings, reduced use of short-acting beta-agonist bronchodilators (SAβAA), and improved disease control (44).

Boswellia

Boswellia serrata, also known as Indian frankincense, has shown promising effects in the treatment of asthma, including in pediatric patients. Several studies have demonstrated that Boswellia serrata, specifically its active compound boswellic acid, can help attenuate airway inflammation and hyperresponsiveness in asthma (45-48). Boswellic acid targeting Th2 cytokines and associated transcription factors. Its mechanism involves inhibition of Th2 cytokines, particularly interleukin production such as IL-4, IL-5, and IL-13, which are pivotal in asthma pathogenesis. Additionally, it modulates transcription factors by downregulating GATA3 expression, a key transcription factor driving Th2 differentiation and cytokine production, and inhibiting pSTAT6 activation, critical for GATA3 induction. Boswellic acid administration also leads to a reduction in airway hyperresponsiveness, as evidenced by decreased airway resistance in mice (49-51).

Licorice

Licorice (Glycyrrhiza glabra) has been traditionally used to treat respiratory conditions such as bronchial asthma and children's asthma, thanks to its anti-inflammatory and expectorant properties. This plant contains various compounds, including glycyrrhizin, 18β-glycyrrhetinic acid, glabrin A and B, and isoflavones, all of which have demonstrated diverse pharmacological effects. Among these compounds, glycyrrhizin aids in expelling congestion from the upper respiratory tract and accelerates tracheal mucus clearance (52).

Licorice aids in asthma treatment through several mechanisms. It shifts the immune response by balancing TH1/TH2 cytokines, reducing allergic IgE levels, and modulating cytokine production to lessen asthma-related inflammation. Glycyrrhizin, a key component, inhibits the adhesion of inflammatory cells like eosinophils and neutrophils to endothelial cells, which helps reduce airway inflammation. Additionally, licorice reg-

ulates important chemokines and transcription factors, such as eotaxin-1 and nuclear factor-κB, which are involved in asthma pathology (53). It also suppresses Th2 cytokines (IL-4, IL-5, IL-13) while promoting Th1 cytokines (IFN-γ, IL-12), thus alleviating the Th2-dominated inflammatory response. Moreover, licorice treatment increases the population of regulatory T cells (Tregs) in the lungs and spleens, which helps suppress excessive immune responses and maintain immune balance, further reducing airway inflammation (54).

Ephedra

The Ephedra herb also known as Ma Huang, is a traditional medicinal herb, historically utilized to treat respiratory conditions like asthma, including children's asthma (55, 56). The active components of Ephedra herb are primarily ephedrine alkaloids, which are also utilized as pharmaceutical agents for treating bronchial asthma (57). Ma Huang inhibits the Toll-like receptor 9 (TLR9) signaling pathway, leading to downregulation of TLR9, TRAF6, TAB2, and other related proteins in lung tissues. Molecular docking analysis revealed that six compounds in MHT potentially interact with and modulate the TLR9 signaling pathway. MHT helps mitigate ovalbumin (OVA)-induced eosinophilic airway inflammation, pathological changes, and bronchial hyperresponsiveness in asthmatic mouse models (58).

Probiotics and their role in pediatric asthma

Probiotics are valuable in managing pediatric asthma by reducing lung inflammation, alleviating asthma symptoms, and decreasing the frequency of asthma attacks, although they do not significantly impact lung function (59-62). They work by rebalancing the immune response, repairing gut dysbiosis, and reducing airway inflammation, potentially preventing asthma relapses in children. Evidence on probiotics for treating atopic dermatitis (AD) is less conclusive, but some single-strain probiotics have shown positive effects (63). Many studies suggest that exposure to certain microorganisms like Bifidobacteria and Clostridium cluster I during childhood, can protect against allergic diseases by helping the immune system develop (64, 65). Bifidobacteria correlated with fewer respiratory infections and Clostridium cluster I was linked to atopy protection. These findings highlight the importance of early nutrition in shaping gut microbiota and improving outcomes for infants at risk of atopy and respiratory infections (66).

Another probiotic bacteria, such as Lactobacillus species, in pediatric asthma management has shown promising results in various studies. Research has demonstrated that probiotics like L. rhamnosus and B. subtilis can reduce airway resistance, suppress immune cell infiltration, and inhibit the production of allergy-related antibodies, including IgE and IgG1(67). Additionally, L. reuteri has been associated with significant improvements in lung function and asthma symptom control in newly diagnosed asthmatic children (68). Furthermore, a study on asthmatic patients revealed that probiotic supplementation led to reduced Th2 cells-associated IL-4 levels and improved pulmonary function tests, indicating the potential of probiotics as an adjunct to common asthma treatments (69). A meta-analysis also supported the use of probiotics in asthma patients, showing improvements in lung inflammation, asthma symptoms, and a reduction in the number of asthma attacks (60). These findings collectively suggest that probiotic strains that are readily available to consumers can reduce asthma exacerbations in children and provide a potential adjunctive therapy for primary care physicians(70).

Gut-lung axis and immune modulation

The gut-lung axis plays a crucial role in immune modulation, impacting lung health and the pathogenesis of various lung diseases. Studies highlight the communication between the gut microbiome and the lungs, influencing immune responses through metabolites like short-chain fatty acids (SCFAs) (71-73). Dysbiosis in the gut microbiota can lead to inflammation and altered immune responses in the lungs, affecting the severity of respiratory diseases (74). Furthermore, the gut microbiome's modulation through probiotics and fecal microbiota transplantation can alter lung homeostasis and immunity, offering potential therapeutic strategies for respiratory conditions (72). The gut-lung axis also impacts diseases like tuberculosis (TB) and pulmonary

arterial hypertension (PAH), where the gut microbiota composition and metabolites influence disease progression and immune responses (75, 76).

Early in human life, lower numbers of bacteria belonging to Ackermansia, Bifidobacteria, and Facalibacteria in the gastrointestinal tract are associated with a higher likelihood of asthma and atopy(77). In addition to allergic airway diseases, studies have also demonstrated the defense function of gut microbiota against several bacterial respiratory infections (78). Some pulmonary disorders such as asthma, COPD, and cystic fibrosis (CF) are associated with airway and gastrointestinal microbiota disturbances(79). The resulting change in the composition of intestinal microbiota through the enrichment of Enterobacteriaceae and the destruction of Lactococci and Lactobacillus populations causes inflammation and enteropathy. Therefore, an effective interaction between the gut and the lungs is crucial for maintaining homeostasis and host immune response(80). Understanding this intricate relationship provides insights into novel therapeutic approaches targeting the gut-lung interaction for improved lung health and disease management.

Synergistic Effects of Herbal Medicine and Probiotics

Recent research has highlighted the promising potential of combining herbal medicine with probiotics in managing pediatric asthma (59). Studies indicate that this combination may have synergistic effects, particularly through the gut-lung axis (81). One study focused on the gut-lung axis in asthmatic patients demonstrated significant improvements in both lung function and gut microbiome ecology with the use of a Lactobacillus probiotic and an herbal blend. This finding supports the potential safety and efficacy of this combination in addressing issues related to the gut-lung axis (82). Another investigation explored the effects of a probiotic-herbal mix named resB, which includes Lactobacillus strains along with extracts from turmeric, holy basil, and vasaka plants. This mix was found to be effective in reducing lung inflammation caused by gut microbiome dysbiosis. In vitro studies showed that resB inhibited the MMP-9 pathway and reduced neutrophil recruitment and inflammatory markers in mice exposed to pulmonary lipopolysaccharide (LPS). These results suggest that resB could serve as a potential therapeutic intervention for lung disorders linked to gut-lung axis dysfunction and inflammation induced by proteobacteria (83).

Moreover, the combination of herbal extracts and probiotics holds promise as a potential replacement for antibiotic growth promoters (AGPs). Probiotic strains such as Lactobacillus acidophilus and Lactobacillus brevis exhibit strong adhesion to intestinal cells, which may protect against pathogens. This protection is likely enhanced by the production of lactic acid, which reduces intestinal acidity and impedes pathogen adhesion. Thus, the synergy between herbal extracts and probiotics not only combats pathogens effectively but also supports the development of natural supplements for gut health (82).

Challenges and Future Directions

Traditional herbal medicines have been used for centuries, particularly in developing countries. Regulatory bodies work to ensure their safety and efficacy through stringent registration and manufacturing standards. However, the complex nature and variable quality of herbal ingredients make standardization challenging, often requiring producers to develop their assessment methods (84). The probiotics industry is rapidly expanding, with ongoing research to identify strains with proven health benefits. Despite this, approved health claims for probiotics are limited due to variability in gut flora among individuals and strains. Progress in translating laboratory findings into clinical applications will depend on understanding biological mechanisms and conducting further bio-guided research and clinical trials (85).

Research on combining herbal medicine and probiotics for pediatric asthma faces challenges like inconsistent study designs and product quality. To address these issues, consistent evaluation methods and rigorous trials are necessary. Future studies should explore the synergistic effects of herbal medicine and probiotics, focusing on the gut-lung axis and immune modulation. An evidence-based approach is essential for integrating these treatments into asthma management to enhance outcomes and clinical practices.

Table 1. Summary of Herbal Medicines in Pediatric Asthma

Herbal Medicine	Active Compounds	Mechanism of Action	Key Findings	Reference
Butterbur	Petasin, Isopetasin	Inhibits mast cell degranulation, PDE3/4 inhibition, reduces airway hyperresponsiveness	Improved lung function and reduced airway inflammation in children	(20)
Ginger	Gingerols, Shogaols	Anti-inflammatory (COX-2 inhibition), immune modulation, mast cell stabilization	Anti-inflammatory effects and airway relaxation demonstrated	(28)
Turmeric	Curcuminoids (Curcumin)	Inhibits NF-κB, COX-2, and inflammatory cytokines; antioxidant properties	Reduced asthma symptoms and improved disease control	(34)
Boswellia	Boswellic Acids	Modulates Th2 cytokines reduces airway inflammation and hyperresponsiveness	Attenuated airway inflammation and improved respiratory parameters	(48)
Licorice	Glycyrrhizin, Glabridin	Balances TH1/TH2 response inhibits inflammation and allergic responses	Modulation of immune response and reduction in inflammatory markers	(51)
Ephedra	Ephedrine Alkaloids	Inhibits TLR9 signaling, reduces eosinophilic inflammation, bronchial hyperresponsiveness	Suppression of bronchial hyperresponsiveness and eosinophilic inflammation	(53)

Conclusion

In conclusion, while faced with hurdles such as study design variability and product standardization issues, research on herbal medicine and probiotics for pediatric asthma offers prospects. Standardized assessment techniques and rigorous clinical trials are critical for overcoming these barriers. Future research should focus on the synergistic mechanisms of herbal medicine and probiotics, notably the gut-lung axis and immune regulation pathways. Healthcare professionals can include these medicines into asthma management techniques, focusing on evidence-based approaches to significantly enhance pediatric asthma outcomes and clinical care practices.

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