Treating Asthma with Herbs and their Constituents - Is Greater Use Warranted?

Asthma is a major public health problem worldwide, and the morbidity and mortality of asthma has increased in the past two decades (Li et al., 2000). Asthma is a chronic disease, characterized by airway inflammation, airflow limitation, hyper-reactivity and airway remodeling. It is believed that asthma is caused by the interaction between genetic and environmental factors (Tanaka & Takahashi, 2013). Asthma is a delayed hypersensitivity and a chronic inflammatory mucosal disease that is associated with excess production of IgE, eosinophilia, T helper 2 (Th2) cytokines, and bronchial hyper-responsiveness (Chen et al., 2010). Instead of histamine, the chemicals mediating these reactions are cytokines released by the activated T cells.

Antihistamines do not help with delayed hypersensitivities. Rather, corticosteroid drugs are used to provide relief (Chan et al., 2016). Allergic asthma is associated with Th2-mediated inflammation (Yang et al., 2013). Regulatory T cells (Treg) are critical regulators of asthma (Ding, Su, Zhang & Ma, 2015). Blocking Th2 cytokine production is proven to have a potent therapeutic effect against asthmatic inflammation (Chen et al., 2013). In addition to the morbidity and mortality, Asthma causes high economic burden (Li, Zhang & Li, 2015).

Additionally, asthma is considered one of the diseases of oxidative failure (Kolarzyk, Pietrzycka, Kaczynsk-Ratka & Skop-Lewandowska, 2016). Dietary change is thought to be one of the environmental factors affecting asthma (Tanaka & Takahashi, 2013). Pietrzycka et al 2015 noted that primary and secondary prevention of diseases resulted from antioxidant failure and changes towards oxidation processes (autoimmunological/allergic diseases, especially asthma) with intake of exogenic antioxidants from food is crucial. As a result, enrichment in natural antioxidant diets of asthmatic individuals should become an important element of primary and secondary prophylaxis in bronchial asthma (Kolarzyk et al., 2016).

Written by Njeri Kai Jarvis MS/RD/LDN for www.BearNutritionandHerbs.com 202-390-4938 NKJarvis@BNHwellness.com

Treating Asthma with Herbs and their Constituents - Is Greater Use Warranted?

Despite evidence pointing to Tcells and oxidative stress as causal, current treatment of Asthma is with inhaled corticosteroids (ICS), leukotriene modifiers and long-acting beta agonists (LABAs) (Marieb, 2015). Inhaled Corticosteroids effectively reduce the risk of exacerbations, hospitalizations, and asthma-related death and improve asthma symptoms, quality of life, lung function, and airway responsiveness. ICSs also reduce airway inflammation and remodeling. However, this improvement comes at a cost. This could be a problem, long term for children, as these medications can slow growth in children (Genetech USA and Novartis Pharmaceuticals Corporation, 2017). Further, Main et al. (2008) noted that there is very limited evidence available for the efficacy and safety of ICS and LABAs in children. They also indicated there is a need for the long-term adverse events associated with ICS use to be assessed systematically.

In contrast to ICSs and LABAs, the reputed efficacy, low cost, and relative absence of side effects of traditional Chinese medicines (TCMs) have led to increasing interest in the use of TCMs for the treatment of asthma in Western countries (Li et al., 2000). Consider that Current therapies for asthma are aimed at controlling disease symptoms and for the majority of asthmatics inhaled corticosteroid anti-inflammatory therapy is effective. However, this approach requires life-time therapy while a subset of patients remains symptomatic despite optimal treatment creating a clear unmet medical need.

Biopharmaceutical approaches may identify new therapies that target key cells and mediators that drive the inflammatory responses in the asthmatic lung. Such an approach may provide disease-modifying treatments. They are developing drugs that target IgE, IL-4 and IL-5, asthma relevant cytokines or chemokines. Another approach is to target asthma relevant mediators or the pathways controlling pro-inflammatory leukocyte accumulation within the

asthmatic lung (Walsh, 2008). Many Herbal Medicines and their constituents target these very mediators.

Traditional Chinese medicine (TCM) has a long-lasting history of using herbal medicine in the treatment of various respiratory diseases including asthma. In the last several decades, an increasing number of herbs have been shown to be effective in the treatment of asthma in clinical trials or asthmatic inflammation in animal models. Accumulating evidence suggests that TCM can directly inhibit the activation and migration of inflammatory cells, regulate the balance of Th1/Th2 responses, and suppress allergic hyperreactivity through inducing regulatory T cells or attenuating the function of dendritic cells (DCs). These studies provided useful information to facilitate the use of TCM to treat asthma (Li, Zhang & Li, 2015).

Li XM et al. (2000) in investigating the effects of the Chinese herbal medicine formula MSSM-002 derived from TCMs looked at allergic asthma's effects on mice. Lung histologic features showed that MSSM-002 reduced inflammation and mucus production. These effects were equivalent to the effects of dexamethasone, but in contrast to the overall immunosuppressive effects of dexamethasone MSSM-002 treatment decreased antigen-specific IgE, IL-4, IL-5, and IL-13 levels without suppressing IgG2a and IFN-gamma synthesis (all mediators of inflammation and immunity). MSSM-002 exhibited anti-airway hyper-responsiveness, anti-airway inflammation, and immunoregulatory effects on T(H)1/T(H)2 responses (Li et al., 2000). This is key to consider as the pharmaceutical industry is currently working on developing medications that have these exact actions.

Jayaprakasam et al. (2013) investigated a combination of three traditional Chinese medicinal herbs developed in their laboratory. These herbs demonstrated efficacy in both mouse models of allergic asthma, and a double-blind placebo-controlled clinical trial in patients

Treating Asthma with Herbs and their Constituents - Is Greater Use Warranted?

with asthma. They found that constituents in ASHMI(TM) synergistically inhibited eotaxin-1 production as well as Th2 cytokine production. Traditional Chinese medicine aYPFS as an add-on to montelukast improved symptoms of asthma control. Further studies with larger sample size are needed to evaluate its efficacy and safety in childhood asthma (Covar, 2016). Single studies of Boswellia, Mai-Men-Dong-Tang, Pycnogenol, Jia-Wei-Si-Jun-Zi-Tang and Tylophora indica showed potential to improve lung function, and a study of 1.8-Cineol (eucalyptol) showed reduced daily oral steroid dosage (Clark, Arnold, Lasserson, & Wu, 2010).

Astragalus membranaceus (AM), is a major medicinal herb commonly used in many herbal formulations in the practice of traditional Chinese medicine (TCM) to treat a wide variety of diseases and body disorders noted Auyeung, Han and Ko (2016) and has been widely used for centuries to treat asthma in China. Previous studies demonstrated that AM had inhibitory effects on airway hyperresponsiveness, inflammation and airway remodeling in murine models of asthma. Notably, AM significantly increased population of CD4(+)CD25(+)Foxp3(+) Treg cells and promoted Foxp3(+) mRNA expression in a rat model of asthma. Together, these results suggest that the anti-asthmatic effects of AM are at least partially associated with CD4(+)CD25(+)Foxp3(+) Tregs (Jin et al., 2013).

Astragalus membranaceus may be good fit for inflammatory disease due to its chemical constituents. Its major components are polysaccharides, flavonoids, and saponins. Contemporary use of Astragalus membranaceus mainly focuses on its immunomodulating, anti-oxidant, and anti-inflammatory abilities. Astragalus saponins extract called AST interacts

with specific transcription molecules providing protection against gastrointestinal inflammation (Auyeung, Han, & Ko, 2016). The number of eosinophils decreased and infiltration of inflammatory cells and collagen deposition declined in lung sections after Astragalus membranaceus administration. Additional results indicated that Astragalus membranaceus had an inhibitory effect on airway inflammation in a murine model of asthma through modulating the imbalanced relationship between Th1 and Th2 cytokines (Chen et al., 2014). Astragaloside IV (AST) the main active constituent of Radix Astragali (Dried Astragalus root), after AST treatment, the airway hyperresponsiveness was sharply relieved, accompanied by the reduction of collagen deposition and mucus production, meanwhile the inflammatory cells were decreased but the IFN-gamma level increased in BALF (Yuan, Sun, Wang & Sun, 2011).

Echinacea purpurea is another herb used in traditional medicine for the treatment of respiratory diseases. Modern interest in Echinacea is directed to its immunomodulatory activity. Recent studies have shown that secretion of asthma-related cytokines in the bronchial epithelial cells can be reversed by Echinacea preparations. Pharmacodynamic studies have confirmed significant bronchodilatory and anti-inflammatory effects of Echinacea complex that was similar to effects of classic synthetic drugs. Sutosvska et al. (2015) noted that these results provide a scientific basis for the application of this herb in traditional medicine as a supplementary treatment of allergic disorders of the airways, particularly noting in the use of asthma.

Bu-Shen-Yi-Qi formulae (BSYQF) is frequently used in the treatment of chronic inflammatory diseases of the respiratory system in traditional Chinese medicine (TCM). Results

demonstrated that BSYQF could suppress chronic airway inflammation and regulate Th17/Treg imbalance by inhibition of Th17 and enhancement of Treg function in the murine OVA asthma model, which Wei et al. (2015) believes may help to elucidate the underlying regulatory mode of BSYQF on asthma treatment.

Further, Crocetin is isolated from the Chinese herb saffron and is a natural carotenoid dicarboxylic acid with anti-inflammatory potential. Crocetin may activate Foxp3 through TIPE2 in asthma-associated Treg cells to mitigate the severity of asthma (Ding et al., 2015).

Consider the results of a 2012 study conducted in China on the therapeutic effects of an herbal patch for asthma. In this randomized study, the herbal medicine patch group surpassed the other 2 groups in controlling the number of attacks and increasing the asymptomatic days. The level of IgE and IL-4 of all the 3 groups studies decreased sharply after treatment. The authors concluded that the new percutaneous absorption herbal patch had exact effect on asthma, noting that the treatment may reverse the imbalance condition of Th1 and Th2 through regulation on cell factor and its specific transcription factors (Li, Liu & Li, 2012).

Bavachinin, a single compound isolated from a Chinese herb, significantly inhibited Th2 cytokine production, including IL-4, IL-5 and IL-13. Notably, this compound almost completely blocked inflammation in the ovalbumin (OVA)-sensitized animal asthma model. Blocking Th2 cytokine production is proven to have a potent therapeutic effect against asthmatic inflammation (Chen et al., 2013).

Several flavonoids were isolated from Glycyrrhiza uralensis, one of the herbs in an anti-asthma herbal medicine intervention. An investigation by Yang et al. (2013) determined that Glycyrrhiza uralensis flavonoids have inhibitory effects on memory Th2 responses in vitro and antigen-induced Th2 inflammation in vivo but that chronic treatment with 7, 4'-DHF in a

murine model of allergic asthma not only significantly reduced eosinophilic pulmonary inflammation, serum IgE levels, IL-4 and IL-13 levels, but also increased IFN- γ production in lung cell cultures in response to antigen stimulation (Yang et al., 2013).

Flavonoids, which are polyphenolic plant secondary metabolites ubiquitously present in vegetables, fruits and beverages, possess antioxidant and anti-allergic traits, as well as immune-modulating activities. Flavonoids are powerful antioxidants and anti-allergic nutrients that inhibit the release of chemical mediators, synthesis of Th2 type cytokines, such as interleukin (IL)-4 and IL-13, and CD40 ligand expression by high-affinity immunoglobulin E (IgE) receptor-expressing cells, such as mast cells and basophils. They also inhibit IL-4-induced signal transduction and affect the differentiation of naïve CD4+ T cells into effector T-cells through their inhibitory effect on the activation of the aryl hydrocarbon receptor. Various studies of flavonoids in asthmatic animal models have demonstrated their beneficial effects. The results of several epidemiological studies suggest that an increase in flavonoid intake is beneficial for asthma. Moreover, clinical trials of flavonoids have shown their ameliorative effects on symptoms related to asthma. Human studies are currently limited (Tanaka & Takahashi, 2013).

Tanaka and Takahashi (2013) indicate that even with the current research, herbal medicines may not be used more for asthma because many human studies in this area are currently limited. Also, herbs are not well regulated. Their quality can vary from source to source. Prevalence and concentration of some toxic (Pb, Cd, and As) and essential metals (Zn, Cu, Cr, Ni, and Co) were determined in the blood samples collected from asthmatic patients in Karachi, Pakistan using atomic absorption spectrophotometer. All selected patients were habitually taking crude drugs and home remedies as self-medication to treat and

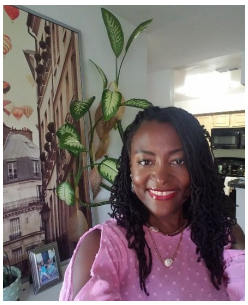
prevent asthma. Having reliable, quality traditional medicines free from heavy metal contamination is essential especially in cases of bronco asthmatic conditions (Hina, Rizwani & Zahid, 2011).

Sarma, Deka, Deka and Saikia (2011) conducted an extensive review of the literature and discovered that a maximum permissible level (MPL) of Pb (Lead) is exceeded in 21 plant medicine species, Cd (cadmium) in 44 species, and Hg (Mercury) in 10 species. Vetiveria zizanioides a potential candidate species for the treatment of cardiovascular diseases absorbs a wide range of heavy metals from metal-contaminated soils. They believe that this species is the single most impressive example of a potentially hazardous medicinal plant. Based on their review, Sarma et al. (2011) endorsed the hypothesis that heavy metal accumulation by medicinal plants is mainly caused by extraction of soluble metals from contaminated soil, sediments and air. As a result, those in the field of herbal medicine need to determine ways to ensure that herbs used are sourced from quality, reliable, trusted places.

Finally, the biggest draw back from greater use of herbs in asthma therapy is that, there are few well-controlled scientific studies on the efficacy, safety, and mechanisms of action of TCMs used to treat asthma (Li et al., 2000). Though the body of literature is small, it is convincing and may in fact be the future of asthma therapy, as it is effective with limited side effects, particularly when herbs are sourced from quality suppliers.

Treating Asthma with Herbs and their Constituents - Is Greater Use Warranted?

ABOUT THE AUTHOR



Njeri Kai Jarvis MS/RD/LDN owns **Bear Nutrition and Herbs**, an integrative nutrition and wellness practice located in Washington, DC. Her nutrition practice covers a wide range of health issues from body composition, cardiac, endocrine and kidney imbalances to cancer and autoimmunity. She also specializes in food-sensitivity issues as they relate to ADHD, autism, mood regulation, and chronic health conditions.

Ms. Jarvis uses a variety of functional testing methods to look for wellness potential as well as underlying imbalances upon which to target diet and nutritional programs. She uses this testing along with an extensive health assessment to develop individualized nutrition and lifestyle programs. Her desire is that her clients realize their health potential as they create lives devoted to healthy eating and healthy living.

Njeri has a Masters in Herbal Medicine and is a board-certified, licensed dietician with over 19 years clinical practice experience with additional study and specialization for ADHD / Autism Spectrum Disorders and Functional Nutrition. She utilizes best practices for digestion, absorption, food sensitivities, inflammation and immunity support. Njeri also works to improve outcomes in this area by working with people on improving sleep hygiene through lifestyle and nutritional support. Contact her to find out how she can support you in your journey to better health !

References

Abou-Arab AA, Abou Donia MA. (2000). Heavy metals in Egyptian spices and medicinal plants and the effect of processing on their levels. *Journal of Agricultural and Food Chemistry*. Jun;48(6):2300-4.

Akinci AC, Zengin N, Yildiz H, Sener E, Gunaydin B. (2011). The complementary and alternative medicine use among asthma and chronic obstructive pulmonary disease patients in the southern region of Turkey. *International Journal of Nursing Practice*. Dec;17(6):571-82. doi: 10.1111/j.1440-172X.2011.01976.x.

Auyeung KK, Han QB, Ko JK. (2016). Astragalus membranaceus: A Review of its Protection Against Inflammation and Gastrointestinal Cancers. *American Journal of Chinese Medicine* ;44(1):1-22. doi:10.1142/S0192415X16500014.

Treating Asthma with Herbs and their Constituents - Is Greater Use Warranted?

Brocklebank D, Ram F, Wright J, Barry P, Cates C, Davies L, Douglas G, Muers M, Smith D, White J.
(2001). Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature. *Health Technology Assessment*. 5(26):1-149.

Chan PH, To CY, Chan EY, Li H, Zhang X, Chow PY, Liu PL, Leung SY, Chan CH, Chan KY, Chan JY, Ng JP, Ng DK. (2016).
A randomized placebo-controlled trial of traditional Chinese medicine as an add-on therapy to oral montelukast in the treatment of mild persistent asthma in children. *Complementary Therapies in Medicine*. Dec;29:219-228. doi: 10.1016/j.ctim.2016.10.010. Epub 2016 Oct 1

Chen SM, Tsai YS, Lee SW, Liu YH, Liao SK, Chang WW, Tsai PJ. (2014). Astragalus membranaceus
modulates Th1/2 immune balance and activates PPAR γ in a murine asthma model. *Biochemistry and Cell Biology*. Oct;92(5):397-405. doi: 10.1139/bcb-2014-0008. Epub 2014 Sep 2.

Chen X[1], Wen T, Wei J, Wu Z, Wang P, Hong Z, Zhao L, Wang B, Flavell R, Gao S, Wang M, Yin Z. (2013).
Treatment of allergic inflammation and hyperresponsiveness by a simple compound, Bavachinin, isolated from Chinese herbs. *Cellular and Molecular Immunology.* Nov;10(6):497-505. doi: 10.1038/cmi.2013.27. Epub 2013 Sep 9.

Chipps BE, Lanier B, Milgrom H, Deschildre A, Hedlin G, Szefler SJ, Kattan M, Kianifard F, Ortiz B, Haselkorn T, Iqbal A, Rosén K, Trzaskoma B, Busse WW. (2017). Omalizumab in children with uncontrolled allergic asthma: Review of clinical trial and real-world experience. *Journal of Allergy and Clinical Immunology*. May;139(5):1431-1444. doi: 10.1016/j.jaci.2017.03.002.

Clark CE, Arnold E, Lasserson TJ, Wu T. (2010). Herbal interventions for chronic asthma in adults and
children: a systematic review and meta-analysis. *Primary Care Respiratory Journal.* Dec;19(4):307-14. doi: 0.4104/pcrj.2010.00041.

Covar RA. (2016). Pivotal efficacy trials of inhaled corticosteroids in asthma. *Annals of Allergy Asthma & Immunology.*

Dec;117(6):582-588. doi: 10.1016/j.anai.2016.07.035. 1 National Jewish Health, Denver, Colorado. Electronic address: CovarR@njhealth.org.

Ding J, Su J, Zhang L, Ma J. (2015). Crocetin Activates Foxp3 Through TIPE2 in Asthma-Associated Treg CellsCell. Cellular *Physiology and Biochemisty International Journal of Experimental Cellular Physiology, Biochemisty, and Pharmacoloy*. 37(6):2425-33. doi: 10.1159/000438595. Epub 2015 Dec 9.

El-Qutob D, Raducan I. (2016). Recent Patents for the Treatment of Asthma. *Recent Patents on Inflammation and Allergy Drug Discovery.* 10(1):13-20.

Hina B, Rizwani GH, Zahid H. (2014). Hematological screening of heavy metals among patients of asthma using medicinal herbs in Karachi, Pakistan. *Pakistan Journal of Pharmaceutical Science.* Nov;27(6):1899-904.

Jayaprakasam B, Yang N, Wen MC, Wang R, Goldfarb J, Sampson H, Li XM. (2013). Constituents of the anti-asthma herbal formula ASHMI(TM) synergistically inhibit IL-4 and IL-5 secretion by murine Th2 memory cells, and eotaxin by human lung fibroblasts in vitro. *Journal of Integrative Medicine*. 2013 May;11(3):195-205. doi: 10.3736/jintegrmed2013029

Jin H, Luo Q, Zheng Y, Nurahmat M, Wu J, Li B, Lv Y, Wang G, Duan X, Dong J. (2013). CD4+CD25+Foxp3+ T cells contribute to the antiasthmatic effects of Astragalus membranaceus extract in a rat model of asthma. *International Immunopharmacology.* Jan;15(1):42-9. doi: 10.1016/j.intimp.2012.11.009. Epub 2012 Nov 24.

Kolarzyk E, Pietrzycka A, Kaczyńska-Ratka A, Skop-Lewandowska A. (2016). Diet with high antioxidant capacity as important factor in primary and secondary prevention of asthma. Przeglad Lekarski. 72(12):743-6.

Li XM, Huang CK, Zhang TF, Teper AA, Srivastava K, Schofield BH, Sampson HA. (2000). The Chinese herbal medicine formula MSSM-002 suppresses allergic airway hyperreactivity and modulates TH1/TH2 responses in a murine model of allergic asthma. The *Journal of Allergy Clinical Immunology*. Oct;106(4):660-8.

Li J, Zhang F, Li J. (2015). The Immunoregulatory Effects of Traditional Chinese Medicine on Treatment

of Asthma or Asthmatic Inflammation. The *American Journal of Chinese Medicine.* 43(6):1059-81. doi: 10.1142/S0192415X15500615. Epub 2015 Sep 14.

Li YM, Liu Q, Li XY. (2012). New percutaneous absorption herbal patch for asthma of paracmasis and its
effect on the relative transcription factors of patients. *Zhongguo Zhen Jiu / Chinese Medicine and Moxibustion.* May;32(5):459-63. [Article in Chinese]

Main C, Shepherd J, Anderson R, Rogers G, Thompson-Coon J, Liu Z, Hartwell D, Loveman E, Green C, Pitt M, Stein K, Harris P, Frampton GK, Smith M, Takeda A, Price A, Welch K, Somerville M. (2008).
Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting beta2 agonists for the treatment of chronic asthma in children under the age of 12 years. *Health Technology Assessment*. May;12(20):1-174, iii-iv.

Marieb, Elaine. (2015). *Essentials of Human Anatomy and Physiology*, (Chapter 12 – The Lymphatic
System and Body Defenses). 11th Edition. Pearson. Boston, Massachusetts.

Sarma H, Deka S, Deka H, Saikia RR. (2011). Accumulation of heavy metals in selected medicinal plants.
Reviews of Environmental Contamination and Toxicology. 214:63-86. doi: 10.1007/978-1-4614-0668-6_4

Šutovská M, Capek P, Kazimierová I, Pappová L, Jošková M, Matulová M, Fraňová S, Pawlaczyk I, Gancarz R. (2015).
Echinacea complex--chemical view and anti-asthmatic profile. *Journal of Ethnopharmacology.* Dec 4;175:163-71. doi: 10.1016/j.jep.2015.09.007. Epub 2015 Sep 11.

Tanaka T, Takahashi R. (2013). Flavonoids and asthma. *Nutrients*. Jun 10;5(6):2128-43. doi: 10.3390/nu5062128.

Walsh GM. (2008). Emerging drugs for asthma. *Expert Opinion Emerging Drugs*. Dec;13(4):643-53. doi:
10.1517/14728210802591378 .

Wei Y, Luo QL, Sun J, Chen MX, Liu F, Dong JC. (2015). Bu-Shen-Yi-Qi formulae suppress chronic airway
inflammation and regulate Th17/Treg imbalance in the murine ovalbumin asthma model. *Journal of Ethnopharmacology.* 2015 Apr 22;164:368-77. doi: 10.1016/j.jep.2015.01.016. Epub 2015 Jan 24.

Xolair. (Accessed October 2017)
http://www.xolair.com/allergic-asthma/how-xolair-works.html

Yang N, Patil S, Zhuge J, Wen MC, Bolleddula J, Doddaga S, Goldfarb J, Sampson HA, Li XM. (2013).
Glycyrrhiza uralensis flavonoids present in anti-asthma formula, ASHMI™, inhibit memory Th2 responses in vitro and in vivo. *Phytotherapy Research - PTR.* Sep;27(9):1381-91. doi: 10.1002/ptr.4862. Epub 2012 Nov 19.

Yuan X, Sun S, Wang S, Sun Y. (2011). Effects of astragaloside IV on IFN-gamma level and prolonged
airway dysfunction in a murine model of chronic asthma. *Planta Medica*. 2011 Mar;77(4):328-33. doi: 10.1055/s-0030-1250408. Epub Oct 13.