HIGH SCHOOL EDITION
Journal of Student Research
Volume 12 Issue 1 (2023)

A Review on the Natural Treatments of Allergic Rhinitis

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ABSTRACT

Allergic rhinitis affects millions of people and can significantly lower an individual's quality of life. The most common treatment for allergic rhinitis lies in over-the-counter medications. However, most over-the-counter antihistamines are either sedating, interfere with an individual's life, and make them more prone to accidents or are non-sedating, but less researched. An increasing distrust of pharmaceuticals alongside the development of tolerance and even eventual withdrawal to treatment has made it necessary to evaluate other avenues of allergy treatment, including herbal medications. An analysis of 9 clinical trials on three herbs, butterbur, astragalus membranaceus, and tinospora cordifolia, determined that the butterbur's efficacy is the most well-established. Meanwhile, astragalus membranaceus features the most potential for success in treating allergies, but confidence within its clinical trials is also the lowest. These herbs are generally more cost effective and incur fewer side effects than current antihistamines, but more research is necessary to ensure the safety of their consumption.

Introduction

Allergic rhinitis (AR) is a disorder in which the nasal mucosa becomes inflamed upon exposure to the allergen.[1] AR affects around 60 million people in the United States or 10-30% of adults and 40% of children.[2] The four most common symptoms of AR include sneezing, nasal itching, rhinorrhea (clear nasal leakage), and nasal congestion. In severe cases, symptoms of allergic rhinitis can disrupt performance at work or in school, hurting one's quality of life.[2]

The most common allergens that trigger allergic rhinitis are airborne particles including dust mite and pollen.[3] When the individual is exposed to the allergen, the response is classified into an early and late phase reaction. During the early phase, the antibody ImmunoglobulinE (IgE) found on mast cell surfaces binds to the allergen and releases the mediator, histamine. Histamine then causes sneezing and rhinorrhea through stimulation of the mucosal glands.[3] Blood vessels also constrict causing nasal congestion as a result of the immune mediators leukotrienes and prostaglandins.[3] During the late phase, cytokines then further activate the immune system, causing white blood cells such as eosinophils and T-lymphocytes to produce nasal swelling and congestion.[3] Aside from the common symptoms, the eosinophilic infiltration during the late phase of allergic rhinitis can also cause a hyper response to stimuli such as cold air.[1]

Treatment of AR starts with limiting exposure to the allergen, including wearing a mask in areas with high concentrations of the airborne particles and washing clothes to remove any allergens still present.[1] Immunotherapy is also utilized in certain patients, where patients are given controlled exposure to the allergen in increasing doses. This is done in order to cause the immune system to become less sensitive to the allergen.[1] The most common form of treatment still lies in oral decongestants and antihistamines that can alleviate symptoms and block the early phase reaction in the allergic response.[4]

Current antihistamines that treat AR can typically be separated into sedating and non-sedating antihistamines. The issue with sedating antihistamines is that they have been shown to interfere with rapid eye movement sleep, harm the quality of life of patients, and increase the likelihood of transportation-related accidents.[5] Meanwhile, the relatively

newer, non-sedating antihistamines are less researched, making sedating antihistamines potentially safer to use during pregnancy.[6] These uncertainties associated with antihistamines foster a distrust of pharmaceuticals that can disincentivize individuals to pursue typical treatments. Furthermore, consistently utilizing one antihistamine can lead to the development of tolerance to the treatment and even withdrawal upon stopping.[7]

As such, this paper will focus on three alternatives to current over-the-counter (OTC) pharmacotherapy, butterbur, astragalus membranaceus, and tinospora cordifolia, to determine the potential of herbal treatments of allergic rhinitis, especially since they are often less expensive and incur fewer side effects. A review of various studies and trials will be conducted to determine the efficacy of the herbs and to analyze whether or not it is advantageous to OTC medications.

Butterbur

Butterbur is an herbaceous plant native to Europe, northern Africa, and southwest Asia.[8] The leaves and roots of butterbur contain petasin, a naturally occurring chemical compound which has properties that allow it to serve as both an antihistamine and form of treatment for late phase allergic reactions in AR.[9]

This holds true in various trials, where butterbur has been demonstrated to be an effective form of natural treatment for allergic rhinitis. Schapowal et al., performed a double-blind study of 186 patients exhibiting symptoms of AR and treated them with varying doses of Ze339 butterbur extract.[10] They showed that both doses of butterbur were significantly superior in alleviating the symptoms of allergic rhinitis compared to the placebo, and a high dose of butterbur was significantly superior to the low dose.[10] In another trial, Shimoda et al. performed a study where they found that Japanese butterbur could suppress anaphylaxis reactions in rats.[11]

In Shimoda et al.'s research, butterbur was found to inhibit B-hexosaminidase and leukotriene release.[10] As B-hexosaminidase is present in mast cells and released alongside histamines during degranulation, decreased B-hexosaminidase release serves as an indicator of lower histamine release levels.[12] Leukotrienes, a lipid mediator present during the early phase reaction of allergies, regulate the immune system and cause the tightening of airway muscles upon contact with the allergen, leading to congestion.[13] Thus, lower levels of leukotrienes would also alleviate symptoms of AR. Additionally, butterbur has the potential to treat IgE-independent allergic reactions as it was also found to lower TNF-alpha production.[10] Tumor necrosis factor (TNF)-alpha is an inflammatory cytokine released by mast cells and eosinophils during acute inflammation, indicating that the inhibition of its production would also alleviate symptoms of allergies.[14]

Both the findings of Schapowal et al. and Shimoda et al. are consistent with a study conducted on the efficacy of the active component in butterbur, petasin. In a study by Shih et al., petasin was able to significantly suppress inflammatory cells including eosinophils, cytokines, and TNF-alpha.[15] This additionally solidifies butterbur's efficacy as a form of drug for treating symptoms associated with AR.

Butterbur is advantageous compared to common OTC antihistamines such as Zyrtec as it is capable of treating late phase allergic reactions and does not cause central nervous system suppression or drowsiness.

However, in a cost comparison, 50 mg of butterbur extract is priced at around $10 and is slightly more expensive than 50 mg of Zyrtec, costing around $7.50. Butterbur is also a plant within the daisy family. If an individual is allergic to plants within this family, allergy testing should be performed prior to taking butterbur. This can avoid an allergic reaction to the herb and prevent the potential of entering anaphylactic shock upon ingestion. Furthermore, butterbur can contain chemicals known as pyrrolizidine that are potentially carcinogenic and can damage circulation.[8] Thus, it is essential to purchase only PA-free butterbur products.

Astragalus Membranaceus

Astragalus membranaceus (AM), also known as milk vetch, belongs to the legume family and contains the active component, astragalus polysaccharide (APS), a water-soluble heteropolysaccharide with the potential of regulating the immune response and reducing immune hypersensitivity.[16,17] Astragalus is present in a little over ¾ of Chinese herbal medications, making it one of the most commonly utilized herbs in treating allergic rhinitis.[18]

Astragalus has been demonstrated to be effective within a few clinical trials. Matkovic et al. conducted a double-blind study on 48 patients with moderate to severe symptoms of seasonal AR and treated them with 80 mg of astragalus membranaceus.[19] It was found that the group that received treatment did show a statistically significant improvement in symptoms of rhinorrhea, but there was no significant difference in IgE and eosinophil levels.[19] Furthermore, Makino et al. investigated the effects of astragalus membranaceus used in conjunction with Atractylodes ovata and Saposhnikovia divaricata to treat AR induced by cedar pollen in guinea pigs.[20] The guinea pigs ingested the herbs prior to pollen exposure, and they found that the group treated with the combination of herbs showed significantly less sneezing than the control group upon inhaling pollen.[20] Additionally, the herbs seemed to remain effective even when treatment was paused.[20]

Within Matkovic et al.'s research, it was analyzed that AM could alleviate allergic reactions because it regulates Th1 and Th2 cytokine secretion patterns.[19] Th1 produces IFN-gamma while Th2 secretes interleukins including IL-4, IL-5, and IL-6.[21] Matkovic et al. found that AM could prevent a decrease in IFN-gamma which is often associated with severe asthma and allergic reactions, and decreased the production of interleukins that synthesize IgE and lead to eosinophil recruitment.[22,23] Meanwhile, Makino et al.'s research hypothesizes that AM is also an immunostimulator, allowing it to strengthen the nasal mucosa's ability to protect the body from pollen antigens.[20]

The effectiveness of AM found in Matkovic et al. and Makino et al.'s studies remains consistent with a clinical trial performed on AM's most significant active component, APS. He et al. found that AP treatment downregulated IgE, IgG, TNF-alpha, and IL-6 in guinea pigs with AR.[24]

Astragalus is considered safe and without major adverse effects. Similar to most herbal medications, it is advantageous to common OTC antihistamines as it does not cause central nervous system suppression or drowsiness.[19] In a cost comparison, 470 mg of astragalus is around $5, making it cheaper than most OTC antihistamines. Astragalus also seems to be effective for longer periods of time after treatment has stopped, whereas stopping the usage of OTC medications can lead to a rebound in symptoms and withdrawal reactions such as severe itching.[7]

Astragalus also has disadvantages, particularly as it has not been extensively studied within human clinical trials. Matkovic et al. discussed that astragalus is effective because it lowers IgE and eosinophil levels.[19] This is inconsistent with their own clinical trial where IgE and eosinophil levels did not demonstrate a significant difference upon AM treatment, though they did hypothesize that it could be due to how short the trial was. Furthermore, since astragalus is amphoteric, more research is necessary to determine the correct forms of administration to ensure that its immunostimulatory effects do not strengthen the allergic reaction.

Tinospora Cordifolia

Tinospora cordifolia (TC), more commonly known as Guduchi, belongs to the Menispermaceae family and contains multiple active ingredients including alkaloids, steroids, and diterpenoid lactones (DL).[25] In particular, the natural compound DL may have anti-inflammatory effects that can alleviate AR symptoms.[26]

TC was shown to benefit those suffering from AR in clinical trials. Badar et al. conducted a double blind trial on 75 patients and administered 300 mg of TC obtained from the stem to the treatment group.[27] They found that there was significant improvement in AR symptoms such as sneezing, nasal blockage, and nasal discharge.[27] Moreover, Geeta et al. administered 250 mg of TC to 25 patients and observed that it was effective in relieving clinical symptoms of AR.[28]

In Badar et al.'s research, it was determined that TC was effective because it decreases goblet cells and eosinophils.[27] Goblet cells secrete mucin to create a mucus layer in allergic reactions, so a decrease in goblet cell presence may indicate lighter symptoms of AR, such as nasal congestion and leakage.[29] Additionally, Geeta et al. explained that the observed relief in clinical symptoms was potentially connected with the lower neutrophil and eosinophil counts recorded upon TC administration.[28] Neutrophils are associated with AR severity and inflammation, potentially due to its production of leukotrienes and cytokines that further stimulate allergic reactions.[30] Thus, TC's ability to inhibit neutrophil recruitment is indicative of its ability to treat AR and even prevent the development of allergic sensitization.

The findings of Badar et al. and Geeta et al. remain consistent with a study on Andrographis paniculata (AP) containing the same active ingredient, DL. In Gan et al.'s study, 17 DLs were isolated from AP and evaluated. It was found that most of the 17 DL compounds could significantly reduce the release of inflammatory cytokines IL-6 and TNF-alpha.[26]

Aside from previously mentioned benefits of herbal treatments, TC does not demonstrate other significant advantages to OTC medications. However, it does provide an alternative to utilize if other medications have proven to be ineffective or to prevent tolerance from building up due to the continued usage of one drug.

No severe adverse reactions were recorded in the clinical trials in which TC was administered, but in Badar et al.'s trial, two patients did report nasal pain and one had a headache that responded well to analgesics.[27] More studies are also necessary in order to ensure the safety of TC usage both long-term and during pregnancy or lactation.

Table 1: Summary of Main Referenced Clinical Trials

	Butterbur Active Ingredient: **Petasin**	**Astragalus Membranaceus (AM)** Active Ingredient: **Astragalus Polysaccharide (AP)**	**Tinospora Cordifolia (TC)** Active Ingredient: **Diterpenoid Lactones (DL)**
Study #1	Schapowal et al. - High doses are significantly superior to low doses; low doses are significantly superior to the placebo.	Matkovic et al. - Caused significant improvement in rhinorrhea - No significant difference in IgE and eosinophil levels - Regulated Th1/Th2 levels	Badar et al. - Significant improvement in symptoms ex. sneezing/nasal blockage - Decreased goblet cells and eosinophils
Study #2	Shimoda et al. - Suppressed anaphylaxis in rats - Significantly lowered leukotriene, histamine, and TNF-alpha release levels	Makino et al. - Ingestion led to significantly less sneezing upon allergen exposure in guinea pigs - Stimulates immune system and strengthens body's ability to protect from antigens	Geeta et al. - Significantly lowered neutrophil and eosinophil counts
Active Ingredient Study	Shih et al. - Petasin suppressed eosinophils, cytokines, and TNF-alpha	He et al. - AP downregulated IgE, IgG, TNF-alpha, and IL-6	Gan et al. - DL compounds significantly reduced IL-6 and TNF-alpha release

Discussion

From Table 1, it can be seen that all three herbs demonstrated the ability to treat both early and late-phase allergic reactions in AR since they all lowered the levels of antibodies (ex. IgE) and inflammatory cytokines (ex. IL-6). However, AM is unique as it also regulates Th1 and Th2 levels and remains effective after treatment has stopped. These abilities indicate that it may be the best herb for treating symptoms associated with the IgE-independent phase of AR. One study also found that AM's ability to alleviate allergic reactions stems from the fact that it strengthens the body's ability to fight against antigens, increasing the rate at which allergic reactions can be resolved. It seems that AM is capable of striking a delicate balance between reducing inflammatory responses and boosting the immune system, something the other two herbs have not been observed to do.

Compared to most OTC medications, all three herbal treatments are advantageous as they do not cause drowsiness and can treat the late-phase reactions of AR. AM and TC are also more cost-effective than OTC medications. At the same time, the lack of research on the herbs means that it can not be guaranteed with certainty that they are safe to consume long-term or while breastfeeding or pregnant. TC may have also triggered mild side effects such as headaches in patients, and butterbur is more expensive than current OTC treatments.

Analyzing the quality of the research on the herbs, confidence in butterbur's efficacy seems to be the greatest. The findings of all three butterbur studies tested butterbur specifically and were consistent. On the other hand, while AM's capabilities are the most broad and long-lasting, its efficacy based on its trials seems to be the most uncertain. AM's amphoteric abilities are not well-known, and the fact that immunoglobulin levels were not significantly lowered in one of its clinical trials is odd. Not only this, Makino et al.'s study on AM consisted of treating patients with a combination of three herbs. Though AM made up a significant portion of the combination, the risk that the treatment was only effective because of the other herbs remains. Finally, TC's efficacy certainly falls between that of butterbur and AM. This is because Gan et al.'s study on TC's active component, DL, isolated 17 different compounds of DL from a different herb. Though the active ingredient is the same, compounds of DL have not been isolated in TC. Therefore, it cannot be determined whether or not the same compounds that reduced inflammatory cytokine release in Gan et al.'s study is also present in TC.

Conclusion

Upon a review of 9 studies on three different herbal treatments of AR, confidence in butterbur's efficacy is the highest. Nevertheless, more research is necessary in order to ensure the safety of all three herbs for patients. Further investigation into AM's amphoteric properties and TC's various DL compounds can also strengthen confidence in AM and TC's efficacies. It is found that herbal treatments undoubtedly have potential in alleviating symptoms of AR, and continuing to study them can lead to the development of safer, varied, affordable, and effective allergy medications.

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