LAMIAECEAE, MEDICINAL POTENTIAL & ANTI-ALLERGENIC DEVELOPMENTS

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ARTICLE INFO

National recipient for the NSTA Angela STEM award
Sanika high-school sophomore from Inglemoor High School in Kirkland, Washington has been working with a Senior PhD Candidate through a program called Polygence
Accepted by Ariaian Young Innovative Minds Institute (AYIMI)

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ABSTRACT

Recently, allergic disorders have become a prevalent global epidemic affecting millions of people who experience asthma, allergies, and medication hypersensitivities. Medicinal plants such as Lamiaceae, commonly known as mint, are proving to be much more effective in treating the problem as they contain natural anti-allergenic compounds that act as anti-inflammatory agents to reduce and prevent cascading allergic reactions. This research paper will demonstrate how this plant’s properties work, medicinal uses, and provide up-to-date research about the phytoconstituents from the Lamiaceae family and anti-allergenic activity.

Key Words: Lamiaceae, Allergic reaction, IgE, anti-histamines, anti-allergenic compound

1. Introduction

Allergies are the immune system's reaction to foreign substances in the body. These reactions can have a wide range of severity, from a runny nose and coughing, to anaphylaxis, a life-threatening reaction. The typically harmless foreign substances that cause these reactions are called allergens and can be found in dust, pets, pollen, food, and some medicines. Allergies can affect anyone and are generally more common in children. People whose family had allergies have a genetic tendency to develop allergies, and this is known as atopy [1]. When atopic people are exposed to the allergen, the immune system has a reaction, it over reacts by producing antibodies that attack the allergen, and this can cause allergic inflammation.

2. Significance of Allergies

The prevalence of allergies are increasing worldwide, and becoming more severe and complex. Allergies are the 6th leading cause of chronic illness in the U.S., costing an excess of $18 billion annually. More than 50 million people in the U.S. alone experience various types of allergies each year. In the U.S. asthma affects more than 24 million people, food allergies affect about 32 million people, and seasonal allergic rhinitis, or hay fever, affects about 24 million people [1]. In addition, data published from the 2014 National Health Interview Survey shows that 8.4% of US children under age 18 suffered from hay fever, 10% from respiratory allergies, 5.4% from food allergies, and 11.6% from skin allergies [2].

A major cause of allergies, other than genetics, is environmental conditions. Climate change and pollution contribute to people's health declining and increasing allergies. Health care costs are also high in many places, making it hard for people to get tested and the right medicines they need, making it harder to solve this worldwide issue. Allergies have many effects on individual people, including economic troubles, interruptions in quality of life, and possibly death. Allergies can prevent people from partaking in certain activities and can increase risks for other medical health problems.

3. Immunological Response

Common allergic reactions are linked to an antibody the body produces, called immunoglobulin E (IgE) [3]. The purpose of antibodies in our immune system is to help remove any foreign substances that invade our body. Everyone produces IgE antibodies but allergic people produce much larger quantities of it. Each IgE is very specific, which is the reason people can be allergic to one substance, yet not another. A person becomes sensitized when exposed to an allergen, causing B cells, a specific type of white blood cell, to produce IgE antibodies and release them in the blood. Some of the IgE attach themselves, using the high-affinity IgE receptor, FceRI, to the surface of allergy-specific cells called mast cells and basophils, which are filled with grains containing allergic mediators [3]. All of these cells cause allergic symptoms by releasing the mediators stored in them. Repeated exposure to the allergen leads to an immediate reaction, triggered by cross-linking of the IgE, which is the binding to allergens, also called Activation, and results in rapid release of the allergic mediators, and this process is called degranulation [4]. Other white blood cells called T-cells drive a delayed and prolonged inflammatory reaction that can be seen hours later with itching, swelling, and other visible symptoms. These phases in the allergic reaction can be classified as immediate and late. The immediate responses are triggered by fast mast cell degranulation, and the late responses are caused by other inflammatory cells like eosinophils (also used in the immediate responses), neutrophils, and lymphocytes being attracted to the site because of chemotactic factors released by the mast cells, and producing more mediators [3].

4. Current Treatments, Downsides & Limitations

There are three main treatment options once it is known that a person has an allergy: avoiding the allergen, going through immunotherapy, or most commonly, taking medicine. Lastly, epinephrine is used during a severe reaction called anaphylactic shock and stimulates the adrenal glands and increases the rate and force of the heartbeat. [5] Despite all of the benefits that the three main treatment options provide, there are arguably many more downsides and limitations to them as well. In order to avoid the allergen, the allergy triggers need to be identified so they can be avoided. This is often not a viable option if the allergen is present in many places and in large amounts. It's...
also unwise to avoid medications in the hopes that the allergen won’t be encountered, which could cause a serious reaction.

Another treatment option is immunotherapy. The two types are allergy shots and sublingual immunotherapy (SLIT) [6]. Allergy shots are a series of injections of purified allergen extracts increasing in dose over time (usually a few years). The person gradually becomes less sensitive to that allergen because by gradually increasing the doses, the immune system is able to build up a tolerance to that allergen. Allergy shots slow down and reduce the production of the IgE antibody. Sublingual immunotherapy can be used for pollen allergies, and involves small doses of an allergen, in the form of a tablet, placed under the tongue, improving tolerance to the substance and reducing symptoms without using injections. This occurs because the allergen from the tablet crosses the mucous membranes in a matter of minutes and are captured by tolerogenic dendritic cells and are processed as small peptides. Through the lymphatic system, an immune response occurs and results in an early decrease in mast cell and basophil degranulation.

These immunotherapy methods can also have limitations. Allergy shots are generally limited to working for pollen, pets, dust, bees, and asthma allergies, but don't work well for allergies to food, medicines, feathers, or for hives or eczema. These shots can also cause redness, swelling, or irritation at the injection site, and there is also potential for a severe allergic reaction. Sublingual immunotherapy's most common side effects include itching and mild swelling inside the mouth, which can last up to an hour, and is experienced by one-quarter of people in SLIT therapy. Medications are used in allergy treatments are in table (1).

### Table 1: Medications currently used in allergy treatments & limitations

<table>
<thead>
<tr>
<th>Type of allergy that</th>
<th>Medication example (oral, nasal, or intramuscular)</th>
<th>Mechanisms of Action</th>
<th>Use</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergies of asthma</td>
<td>Reslund (inhaled steroids)</td>
<td>Decrease the effects of bronchoconstrictors, reduce swelling, and block mast cell degranulation</td>
<td>To prevent asthma attacks</td>
<td>Can cause dry cough, mouth ulcers, and taste changes</td>
</tr>
<tr>
<td>Allergies of asthma</td>
<td>Leukotriene inhibitors</td>
<td>Block leukotrienes, prevent bronchoconstriction, and reduce inflammation</td>
<td>To prevent asthma attacks</td>
<td>Can cause dizziness, headache, and gastrointestinal problems</td>
</tr>
<tr>
<td>Allergies of asthma</td>
<td>Antihistamines</td>
<td>Block H1 receptors, prevent histamine-induced symptoms</td>
<td>To control symptoms</td>
<td>Can cause sedation, dry mouth, and blurred vision</td>
</tr>
<tr>
<td>Allergies of asthma</td>
<td>Corticosteroids</td>
<td>Reduce inflammation, block cytokine production, and inhibit cell proliferation</td>
<td>To control symptoms</td>
<td>Can cause weight gain, osteoporosis, and cataracts</td>
</tr>
</tbody>
</table>

### Medications are used as a treatment to help reduce immune system reaction and alleviate symptoms. This can include prescriptions as well as over-the-counter medicines. Some of the most widely used medicines include antihistamines, mast-cell stabilizers, corticosteroids, and leukotriene inhibitors [3]. Currently, allergy medicines are generally helpful for allergic reactions, however, they only help with short-term symptoms, and don't usually provide long-term effects or help cure the allergy. Due to this, an alternative should be explored for these medications. In addition, some medicines' effects only come into play days later, which can cause allergic discomfort until that time. Many medications are required to be taken multiple times a day and long-term use can cause many adverse effects, and may even worsen the condition. Most medications, if not all, have some sort of side effects and can be expressed differently in different people. As seen in Figure 1, the mechanism of action in current allergy medications create unnatural imbalances and lead to side effects in patients (Fig. 1).

**Fig.1: Current Limitations and Downsides of Allergy Treatments**

Medicinal plants are being considered as a positive replacement to general medicines as it provides similar effects and benefits, but is often safer and healthier since it's natural. As many as 80% of people globally rely on herbal medicinal products for healthcare needs [10]. Herbal medicines include plant products that can be ingested as well as topical products that come from plants. Also, new drug discoveries and developments are being made as interest in herbal medicine increases. In fact, many drugs used nowadays include ingredients derived from medicinal plants. This is because plant-based chemicals are being seen as safe and more effective than synthesized chemicals. The versatility and effectiveness of natural treatments are causing herbal medications to become increasingly used worldwide, and one plant family that has been shown to have these potential benefits is Lamiaceae.

The plant family Lamiaceae has 236 genera and over 7,000 species, the largest family of the order, Lamiales [3]. Lamiaceae can be found nearly worldwide, and is known for its species’ fragrant leaves and attractive flowers. Lamiaceae is usually found in dry, rock, woodland, or grassland habitats along forest margins and in fynbos. Some popular plants in this family include lavender, basil, mint, rosemary, sage, oregano, catnip, and thyme. Humans use these herb plants for flavor, fragrance, or its wide range of medicinal properties.

### 5. Uses of Lamiaceae

Lamiaceae has been known to be effective in alleviating conditions like exhaustion, weakness, depression, memory enhancement, circulation improvement, strengthening of fragile blood vessels, skin allergies, and asthma. Certain plants like Lamiaceae possess phytochemicals with anti-allergenic properties. These phytochemicals include flavonoids, terpenoids, and additional essential oils. The flavonoids within Lamiaceae plants are known for their antioxidant and anti-inflammatory properties, and have been shown to play a role in the treatment of various health conditions, including allergies and asthma. Terpenoids are responsible for the characteristic aromas of many plants in the Lamiaceae family. They also have anti-inflammatory and anti-allergic properties, and they have been found to be effective in the treatment of various skin conditions. The other essential oils in the Lamiaceae plants have...
phytochemicals that obtain similar properties to flavonoids and terpenoids.

These bioactive compounds have various mechanisms of action to combat the mediators or immune system involved in the inflammatory cascades or allergic reaction pathways, and these can be used as medicine for allergic symptoms [3]. For example, flavonoids have been shown to inhibit the release of histamine, a key mediator involved in the development of allergic symptoms. They also have been found to modulate the immune system and reduce the production of pro-inflammatory cytokines, which play a role in the development of allergies and other inflammatory conditions. Additionally, the essential oils present in Lamiaceae plants have been found to have a relaxing effect on the airways, which can help to relieve symptoms of asthma and other respiratory conditions.

6. Lamiaceae Studies

Prior research has been conducted to look into the potential benefits of Lamiaceae in allergic responses. These studies encompass the different mechanisms of actions that alter the immune response. Some of these studies have investigated the mechanisms of action of Lamiaceae species in modulating immune responses, particularly in suppressing IgE levels and IgE-mast cell cross-linking. The in-vivo studies highlighted in table 2 elucidate the therapeutic effect of Lamiaceae species in treating allergies by reducing passive cutaneous anaphylaxis and decreasing mortality due to anaphylactic shock-induced bronchospasm. In these studies, different Lamiaceae species, including Mentha arvensis, Mosla dianthera, and Perilla frutescens, have been shown to have a suppressive effect on IgE levels and the reaction to allergens. The usage of Lamiaceae plant is in table (2).

<table>
<thead>
<tr>
<th>Specie(s)</th>
<th>Extract</th>
<th>Application &amp; Concentration</th>
<th>Observation &amp; Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ova 10% Alum</td>
<td>N/A</td>
<td>N/A</td>
<td>Essential oil of Mentha arvensis significantly decreased the serum IgE level. Isolation of bioactive compounds in the essential oil of Mentha arvensis, with particular high percentage of menthol.</td>
</tr>
<tr>
<td><em>Mice sensitised with compound 40% OVA and anti-DNP IgE</em> [2]</td>
<td>Aqueous extract of <em>Mosla diana</em></td>
<td>Intraperitoneal pretreatment of ≤1,000 mg/kg</td>
<td>Reduction in passive cutaneous anaphylaxis (PCA) reaction.</td>
</tr>
<tr>
<td><em>Mice treated with anti-allergen serum</em> [3]</td>
<td>Isoflavone extract from <em>Perilla frutescens</em></td>
<td>N/A</td>
<td>Perilla extract significantly suppressed the PCA reaction, which was brought about by rye grass pollin, anti-allergic reaction induced by rye grass pollin. The anti-allergic activity of the extract was more pronounced at a lower dose of extract.</td>
</tr>
<tr>
<td><em>BALS mice sensitised intranasally with OVA</em> [4]</td>
<td>Water &amp; ethanol extracts of <em>Perilla frutescens</em></td>
<td>Each group of mice was given intranasally saline (control), 80 and 160ug (PNL), or 320ug (PNL), or 80ug (PNP) at 0 and 2 weeks</td>
<td>OVA-specific IL-4 and IL-5 secretion from OVA-sensitized splenocytes were significantly suppressed in the ethanol extract groups and PNL. Serum level of anti-OVA IgE was lower in the PNL group.</td>
</tr>
</tbody>
</table>

These studies show the progress the scientific community has made towards research towards Lamiaceae, but there are next steps needed to be taken and future directions that can be explored. In studies where multiple compounds were shown to cause anti-allergic activity, it’s important to isolate the primary compound that contributed to this, and perform experiments that show its potential as herbal medicine. Some experimental studies could also focus on the prospective of including compounds from multiple plant species in a medication. It is also essential to obtain research related to toxicology studies for Lamiaceae. Lamiaceae used as a medication would clearly be plant-based, therefore providing a more sustainable option.

7. Additional Benefits of Manufactured Lamiaceae

Currently, large-scale drug production is known to have negative impacts on the environment due to the large number of medications being produced. A research project by Laksmi Narayan, Duse, Wattal et al published in The Lancet in November 2013 shows that “contamination of water sources with antimicrobial drugs (combined with mass misuse of antibiotics and poor sanitation) has had grave consequences in India, where an estimated 58,000 new-borns die from multidrug-resistant infections every year”. Pharma pollution affects people and animals who live near production plants because water and food sources can be contaminated with waste products from the pharma.

[15] Plant-based medications could reduce environmental effects such as pollution and would be more sustainable for the environment in the long-term. Further analysis will be needed to determine positive outcomes of plant-based manufacturing.

Specifically, green manufacturing with Lamiaceae is a much more ethical and sustainable option for mass producing allergy medication, and would be a better alternative for the wellbeing of the planet as well as the benefits it offers to individual people, as an allergy medication. The use of plant-based products can be more beneficial because they have fewer toxic byproducts that often find themselves polluting streams, rivers, and communities nearby during the drug's manufacturing. Plant-based drug manufacturing has been shown to produce much lower levels of greenhouse gas emissions as demonstrated in US biotech Amgen's biomanufacturing plant where 69% less carbon emissions are produced compared to a traditional manufacturing facility. [16] As described in this paper, current allergy medications have many limitations as well as downsides related to their sustainability. Lamiaceae is an important alternative to consider and further research will be able to prove its effectiveness.

8. Conclusion

In conclusion, allergic disorders have become a major global health concern, with millions of people suffering from asthma, food allergies, allergic rhinitis, and medication hypersensitivities. While traditional medicines may not be as effective, natural products derived from medicinal plants, such as the Lamiaceae family, have been found to contain anti-allergic compounds. The research provided in this paper has shown that Lamiaceae plants have been proven to target IgE responses in the allergy cascade, and act as anti-inflammatory agents, reducing allergic reactions. This paper has highlighted the properties, medicinal uses, and up-to-date research on the phytoconstituents and anti-allergic activity of the Lamiaceae family, and their potential use as a natural alternative in the treatment of allergies. However, additional research needs to be done in a clinical setting in order to explore Lamiaceae's use as a viable option to replace current allergy medications.

References

1] “Facts and Stats - 50 Million Americans Have Allergies:
Acaai Patient.” ACAAI Public Website, American College of Allergy, Asthma & Immunology, 16 Sept. 2022.


