The Potential Usefulness of Several Insects and Fatty Acids in Allergic Disorders

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Abstract
Insects are the largest and widely distributed group of animals and contain high quality essential fatty acids, proteins and minerals. Insects, which relieves pain, can play a key role in anti-inflammatory responses by inhibiting inflammatory mediators and are used as a medicine for the treatment of inflammatory diseases. We hypothesized that potential insects and their main ingredients regulates airway inflammation and asthma and can be developed as therapeutic drugs for the treatment of asthma. In our review we try to show the potential usefulness of insects and fatty acids in searching for new therapeutic solutions for allergic diseases. We summaries the knowledge about properties of insect fatty acids to indicate usefulness of knowledge about insect fatty acids in drug design. The field of possible using of insect and their fatty acids delivered to therapy of various human allergic diseases is still not sufficiently investigated. Undoubtedly, more attention should be paid to insects and their fatty acids due to searching new therapeutic agents in allergic disorders.

Keywords: Insect; Fatty Acids; Allergic Diseases

Introduction
Insect medicine is an old ancient medicinal concept that is still used in Asia. It can be understood as the traditional animal species medicines, including the dried animal bodies, secretions and processing natural products of medicinal insects. Entomotherapy is the use of insects as medicines and is an important complementary and alternative to modern therapy in many parts of the world [1]. One of the most considerable differences in the drug materials in East Asian traditional and modern scientific medicines is the use of insects [2,3]. Nutritionally, insects are high in protein and fat compared with typical dietary items like fruit and vegetation. In small quantities, they may serve to provide important fatty acids. It is well known that insects are not only selected based on their environmental availability, but also their nutrient composition. Insects can play a key role (in anti-inflammatory responses by inhibiting secretory) inflammatory mediators) in the diet of many nations. Their high nutritive value is mainly determined by a high content of protein, essential fatty acids, vitamins, minerals and other bioactive substances [4].

Potential Usefulness of Fatty Acids
As shown Table 1 [5-14], the major components of medicinal insects were myristic acid, oleic acid, palmitic acid and palmitoleic acid. There are many kinds of necessary amino acids and inorganic elements for mankind in insects. As shown Table 2 [15-33], oleic acid reduces IgE binding to allergens and decreases the production of inflammatory mediators by inhibition the endothelial expression of VCAM-1, E-selectin and ICAM-1. Linoleic acid reduces broncho-alveolar inflammatory cell count and lung IL-5 levels in an animal model. Also, it reduces proinflammatory cytokines production by eosinophils and bronchial epithelial cells. Palmitoleic acid promotes anti-inflammatory effects in macrophages exposed to LPS. However, palmitic acid sensitzes dendritic cells resulting in augmented secretion of Th1/Th17 cytokines upon proinflammatory stimulation. n-3 PUFA may directly regulate the function of the effector cells that mediate the allergic inflammatory response. Increased n-3 PUFA preferentially modulate the Th2-cell response, there was a marked down-regulation of IL-5, IL-9, IL-13 and RANTES n-3 PUFA suppress FcεRI-mediated activation of mast cells.
Table 1: Summary of major compounds (fatty acids) identified from several kinds of medicinal insects and their biological activities.

| Herbs (Latin Names) | Major chemical Compounds | Molecular Formula | Pharmacological Activities | References |
|---------------------|---------------------------|-------------------|---------------------------|------------|
| Locusta Migratoria (Grasshopper) | Myristic acid | C_{14}H_{28}O_{2} | Anti-inflammation and analgesic effect | Clarkson C et al. [5] |
| | Palmitic acid | C_{16}H_{32}O_{2} | - Anticonvulsant action | Zhonghua Bencao et al. [6] |
| | Palmitoleic acid | C_{16}H_{30}O_{2} | - Sedative action | Gao X et al. [7] |
| | Stearic acid | C_{18}H_{36}O_{2} | - Analgesic action | | |
| | Oleic acid | C_{18}H_{34}O_{2} | - Antipyretic action | | |
| | Linoleic acid | C_{18}H_{32}O_{2} | - Anti-allergic effects | | |
| | α-Linolenic acid | C_{18}H_{30}O_{2} | - Decrease symptoms of Allergic Contact Dermatitis | | |
| | | | - Acne-remedy effects, antimicrobial activity | | |
| | | | - Improved the pathological changes in rat kidney, reduce cholesterol and proteinuria symptoms on MsPGN rats, and its mechanism may be related to inhibition of the over-expression of TGFβ1 | | |
| | | | - Treatment of nonspecific anaphylactic reactions. | Shin TY et al. [11] |
| Periostracum Cicadae (the cast off skin of Periostracum Cicadae) | Alanine | C_{3}H_{7}NO | | |
| | Proline | C_{5}H_{9}NO_{2} | - Anti-allergic effects | Kim BNR et al. [8] |
| | Aspartic Acid | C_{4}H_{7}NO_{4} | - Sedative action | Lin JP et al. [9] |
| | Serine | C_{3}H_{7}NO_{3} | - Analgesic action | Wang Hh et al. [10] |
| | Threonine | C_{3}H_{7}NO_{3} | - Antipyretic action | | |
| Bombyx mori L. (Original Silk Moth) | Proline | C_{5}H_{9}NO_{2} | - DNA synthesis inhibiting action | Zhonghua Bencao, et al [6] |
| | Ornithine | C_{4}H_{12}N_{2}O_{2} | - Immunofacilitation | | |
| | Cystine | C_{6}H_{12}N_{2}O_{4}S | | | |
| | Niacin | C_{6}NH_{5}O_{2} | | | |
| | Oleic acid | C_{18}H_{34}O_{2} | | | |
| | Palmitic acid | C_{16}H_{32}O_{2} | | | |
| | Palmitoleic acid | C_{16}H_{30}O_{2} | | | |
| | Stearic acid | C_{18}H_{36}O_{2} | | | |
| | Glutamic acid | C_{5}H_{9}NO_{4} | | | |
| | Aspartic acid | C_{5}H_{9}NO_{4} | | | |
| | Holotrichia diomphalia (Grub) | Oleic acid | C_{18}H_{34}O_{2} | - Anti-inflammation and analgesic effect | Pei K et al. [12] |
| | Palmitic acid | C_{16}H_{32}O_{2} | - Antibacterial effect | | |
| | Palmitoleic acid | C_{16}H_{30}O_{2} | Immunomodulating effect on macrophage secretory and cellular activities | Kang NS et al. [14] |
### Table 2: Summary of major fatty acids and their biological activities in the development of lung diseases like asthma or COPD.

| Fatty Acids & Mixture of Fatty Acids | Molecular Formula | Pharmacological Activities & Key Findings                                                                                     | References |
|-------------------------------------|-------------------|-------------------------------------------------------------------------------------------------------------------------------|------------|
| Oleic acid                          | \( C_{18}H_{34}O_2 \) | Reduces IgE binding to allergens<br>Anti-inflammatory effect<br>10-nitro-oleic acid blocked phosphorylation and degradation of IkB and enhanced inhibitory binding of PPARγ to NF-kB<br>Oral administration of oleic acid decreases the production of inflammatory mediators (IL-1β, IL-6) by Rat macrophages<br>Inhibits the endothelial expression of VCAM-1, E-selectin and ICAM-1 | Chung SY et al. [15]  <br> Carrillo C et al. [16]  <br> Reddy AT et al. [17]  <br> Magdalón J et al. [18]  <br> Carluccio MA et al. [19] |
| Linoleic acid                       | \( C_{18}H_{32}O_2 \) | Reduce broncho-alveolar inflammatory cell count and lung IL-5 levels in an animal model of allergic asthma through a PPARγ-dependent mechanism<br>Reduce pro-inflammatory cytokines production by eosinophils and bronchial epithelial cells<br>Decrease ex vivo IL-4 production in splenocytes<br>Reduce allergen-induced IgE levels<br>Conjugated linoleic and vaccenic acids suppress inflammation and changes to the airways in an animal model of allergic airway disease<br>Anti-inflammatory effects in allergic subjects with birch pollen allergy | Jaudszus A et al. [20]  <br> Jaudszus A et al. [21]  <br> Kelley DS et al. [22]  <br> Yamasaki M et al. [23]  <br> Kanwar RK et al. [24]  <br> Turpeinen AM et al. [25] |
| Palmitoleic acid                    | \( C_{16}H_{30}O_2 \) | Promotes anti-inflammatory effects in macrophages exposed to LPS through inhibition of inflammasome pathway<br>Negatively associated with percentage predicted FEV1 and FVC | Souza CO, et al. [26]  <br> Kompauer I, et al. [27] |
| Palmitic acid                       | \( C_{16}H_{32}O_2 \) | Palmitic acid sensitizes DCs resulting in augmented secretion of TH1/TH17-instructive cytokines upon pro-inflammatory stimulation<br>Induced MCP-1 and augmented LPS-primed production of IL-1β and TNF-α in macrophages<br>& Increased the number of lung macrophages and augmented high fat diet-induced neutrophilic airway inflammation in a high fat diet mouse model | Stelzner K, et al. [28]  <br> Tashiro H, et al. [29] |
| Docosahexaenoic acid (DHA)          | \( C_{22}H_{32}O_2 \) | Positively associated with FEV1 (% predicted) and FVC (% predicted) | Kompauer I, et al. [27] |
| Eicosapentaenoic acid (EPA)         | \( C_{20}H_{32}O_2 \) | Dietary intake of EPA (and DHA) was even positively associated with asthma in a case-control study<br>Eicosanoids derived from the n-3 fatty acid EPA down-regulate the production of PGE2 | Broadfield EC, et al. [30]  <br> Kankaanpää P, et al. [31] |
Mixture of fatty acids (1)  

| n-3 PUFA | C_{n}H_{2n}O_{2} (EPA) | C_{n}H_{2n}O_{3} (DHA) |
|----------|----------------------|----------------------|

n-3 PUFA may directly regulate the function of the effector cells that mediate the allergic inflammatory response. Increased n-3 PUFA preferentially modulate the Th2-cell response, there was a marked down-regulation of IL-5, IL-9, IL-13 and RANTES. n-3 PUFA suppress FceRI-mediated activation of mast cells.

Bilal S, et al. [32]  

Wang X, et al. [33]

Conclusion

Therefore, above results provide evidence about the potential usefulness of the mixture of fatty acids from medicinal insects in allergic disorders. Overall, fatty acids have various roles in the way they affect the immune system and allergic responses and no single dietary fatty acid is suitable for treating allergic disorders. It is necessary to conduct more large scale studies with relevant animal models to arrive at meaningful recommendations for various fatty acid interventions for clinical usefulness. Further scientific research will be accomplished. This issue is and will be subject of work of many researchers from different areas.

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