Allergy to Propolis in Beekeepers—A Literature Review

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Abstract
Propolis is a bee product which has shown antimicrobial, anti-inflammatory and immunomodulatory activity. It also stimulates wound-healing. Propolis has a lot of components, but also some allergens were identified. Propolis may induce allergy, mainly allergic contact dermatitis after topical application. It has been recognized as an occupational contact allergen, mainly in beekeepers but also in musicians and people who make stringed musical instruments. Beekeepers are exposed to allergens from propolis more often than general population. Propolis allergy in beekeepers occur 0.76%-4.04%. There are some factors which may influence on the occurrence of propolis allergy in beekeepers, which were presented in this review.

Keywords: Propolis; Beekeepers; Allergic contact dermatitis; Occupational allergen

Introduction
Propolis is a substance collected by worker bees from the resin of trees, mostly from the buds of poplar and conifers. It is used by bees as a multifunctional material to build and repair the hive as well as the protection against micro-organisms. Propolis has a long history of use. The Ancient Romans and Greeks used propolis for many purposes. The most important and the most well-known properties of propolis is its antibacterial, antiviral and antifungal activity, but also anti-inflammatory and regenerative properties. It is now used as the active substance of some medicinal products for external use in the treatment of wounds, burns and frostbite, but also as an ingredient in dietary supplements and cosmetics [1-4].

Composition
The chemical composition of propolis is variable and depends on the vegetation of the geographical area, the time of year and bees species. Currently, the researchers extracted over 300 substances from propolis. Generally, the composition of propolis comprises: resin (50-80%), beeswax (8-30%), plant wax (6%), essential oils (10-14%), pollen (5%), tannin (10 %), mechanical impurities (5%), lipid-protein substances, macronutrients such as calcium, magnesium, zinc, tin, copper, silicon, iron, aluminum, silver, sodium, potassium, chromium, strontium and vitamins: provitamin A, vitamin B1, B2, B5, B6, C, D, E [5, 6]. Among the aromatic acids the following may occur: cinnamon, coffee, ferulic, benzoic, salicylic and 2-amino-3-methoxybenzoic acid. The most important aromatic esters include ethyl esters of cinnamic and caffeic acid, phenylethyl esters of benzoic acid. Frequently detected in propolis are flavonoids, such as chrysin, tectochrysin, pinostrobin, caffeic acid, phenylethyl esters of benzoic acid. The fourth major contact allergen is benzyl cinnamate showing weak after applying some cosmetics which contain benzyl salicylate [12].

Allergens
Propolis has a rich composition, but also it includes allergens. Scientists have identified 26 allergens so far. Major allergens are caffeic acid esters (such as 1,1-dimethylyl ester of caffeic acid, benzyl caffeate, geranyl caffeate) and cinnamic acid esters (for example cinnamyl cinnamate, benzyl cinnamate, cinnamyl alcohol). In the Central Europe caffeic acid esters found in poplar buds may be responsible for the induction of contact allergy. These substances may be present in other products of plant origin. The topical application of propolis may occur in cross-allergy with other products containing these components. In the literature the cross-reactivity between propolis and Peru balsam, rosin, turpentine, essential oils, fragrances is described. According to the literature the incidence of hypersensitivity reactions to propolis is two to three times less common than the hypersensitivity reactions to Peru balsam [8-10].

The most important contact allergen identified in propolis is a compound LB-1 (consisting mainly of three pentenyl esters of caffeic acid) derived from the buds of poplar [11]. The GC/MS analysis determined the exact composition of LB-1. It consists of 3-methyl-2-buthyl-caffeate (54.2%), 3-methyl-3-buthyl-caffeate (28.3%), 2-methyl-2-buthyl-caffeate (4.3%), phenethyl caffeate (7.9%), caffeic acid (1.3%), benzyl caffeate (1.0%) [12]. Another important contact allergens in propolis is caffeic acid phenethyl ester (phenethyl caffeate (CAPE)) which is presented in smaller quantities than LB-1. After administration of the same low concentrations (0.1%) of these two allergens similar response is showed [12].

The third major contact allergen is benzyl salicylate. This compound is an allergen of medium strength, which, however, may lead to the occurrence of cross-reactivity in patients allergic to propolis after applying some cosmetics which contain benzyl salicylate [12]. The fourth major contact allergen is benzyl cinnamate showing weak allergenic properties [12].

Allergy to Propolis
Data from the literature indicate that allergy to propolis is not often
Allergy to Propolis in Beekeepers

Initial reports of allergic reactions to propolis were reported from beekeepers, as well as musicians and artists that modulate figures with wax [15,16]. The first case of allergic contact dermatitis after propolis was published in 1915 and described a beekeeper who had skin lesions on his hands. Since then, propolis is recognized as an occupational contact allergen mostly in beekeepers as they are an occupational group, the most exposed to allergens from propolis. Review of the world literature indicates that ¼ people allergic to propolis are beekeepers.

A study conducted by Münstedt [17] on the German population of beekeepers indicates that 3.6% of respondents are allergic to propolis (37 of 1051 beekeepers). More than 72% of them are allergic to other substances (21 of 37 beekeepers who are allergic to propolis). Reactions to propolis appear after 5 to 48 hours (mean time 11 hours). Side effects lasted from 5 hours to 20 days (mean 5 days). The study confirmed that propolis may cause not only a type IV hypersensitivity reaction, but also systemic reactions associated with immediate-type hypersensitivity. The most common skin reactions after propolis is itching, burning, urticaria, local rash [17,18]. An interesting thesis has been presented in this study that the use of solvents (mainly ethanol) may have influence on the development of allergy to propolis. The authors suggest that this hypothesis can explain the transport of antigen into the deeper layers of the skin, which can lead to hypersensitivity. This hypothesis should be confirmed in future studies [9,17,18]. Authors point out some factors correlated with the occurrence of propolis allergy. Contact allergy to propolis was significantly associated with lung diseases and other allergies. This hypothesis can explain the transport of antigen into the deeper layers of the skin or mucous membranes than after oral administration [9,13].

Allergic reactions to propolis usually occur as contact dermatitis after topical administration, although there are some reports of propolis allergy manifested as rhinitis, conjunctivitis, inflammation of the mucous membranes of the mouth and ulcers, bronchospasm with shortness of breath and wheezing, associated with fever, urticaria, headache, nausea [13]. In 2004 the case of laryngeal edema and anaphylactic shock after topical application of propolis in acute inflammation of nasopharyngeal cavity was also described [14]. To World Health Organization database of monitoring side-effects only 29 adverse events after propolis were reported for the period 1986-2006.

<table>
<thead>
<tr>
<th>Population</th>
<th>Number of respondents</th>
<th>% Allergic to propolis</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beekeepers (German)</td>
<td>1051</td>
<td>3.80%</td>
<td>[18]</td>
</tr>
<tr>
<td>Beekeepers (Poland)</td>
<td>297</td>
<td>4.04%</td>
<td>[19]</td>
</tr>
<tr>
<td>Farmers (Poland)</td>
<td>132</td>
<td>0.76%</td>
<td>[20]</td>
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<tr>
<td>Farmers (Poland)</td>
<td>101</td>
<td>2%</td>
<td>[21]</td>
</tr>
<tr>
<td>Beekeepers (Poland)</td>
<td>558</td>
<td>3.05%</td>
<td>[22]</td>
</tr>
</tbody>
</table>

Table 1: The prevalence of propolis allergy in beekeepers and farmers according to the available data.

Conclusion

Data from literature indicate the possibility of an allergic reaction while using propolis, but much more frequently reported are cases of hypersensitivity to propolis and its preparations used externally. Propolis given per os is considered as a non-toxic product to humans, although in the literature some cases of hypersensitivity after oral administration are described.

Allergy to propolis is not a common phenomenon, but there are groups of greater risk of sensitization like beekeepers and their family members who are the most exposed to contact to propolis and its allergens. Sensitization in this group ranges from 0.76 to 4.04%. Beekeepers are more affected with propolis allergy than healthy population (0.64%-1.3%), but are not more affected with propolis allergy than dermatological patients cured earlier because of allergic dermatoses (1.2%-6.7%) [22].

References

15. Ilg and Sanokowska stated that the percentage of beekeepers allergic to propolis in Malopolska region in The South of Poland is 4.04% [19].
16. In another study on Polish farmers was shown that allergy to propolis was the reason of allergic contact dermatitis in 1 case (0.76%-1/132 farmers). Peru balsam was the reason of allergic contact dermatitis in 10 cases (7.6%=10/132 farmers) [20].
17. Spiewak reported that propolis was the reason of occupational dermatoses in Polish farmers in 2 out of 101 farmers (2%) [21].
18. A study conducted by Basista and Filipek on Polish population of beekeepers indicates that 17 out of 558 (3.05%) beekeepers were allergic to propolis. There was no report on concomitant allergy to propolis and other bee products. Only 14 of 2205 (0.63%) family members, using propolis as therapeutic agent, reported propolis allergy. Factors, which can have an influence on the occurrence of allergy, are allergic diseases (for example atopic allergic dermatitis) or other allergies for different