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DERLEME /REVIEW

# A LITTLE KNOWN BEE PRODUCT WITH THE POTENTIAL TO BECOME A FUNCTIONAL FOOD AND NUTRITIONAL SUPPLEMENT: APILARNIL

## Fonksiyonel Bir Gıda ve Besin Takviyesi Olma Potansiyeline Sahip Az Bilinen Bir Arı Ürünü: Apilarnil

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**ABSTRACT**

**Beekeeping plays a crucial role in supporting agricultural sustainability and the economy through pollination and the production of honey and other bee products. Among these products is apilarnil, a less known substance derived from drone larvae that provides health benefits. Apilarnil is rich in essential nutrients and has been reported to have favorable effects on the reproductive system, autonomic nervous system and cardiovascular health. In addition to its natural medicinal properties, its nutritional and pharmaceutical potential is increasingly recognized, leading to the commercial production of apilarnil. This bee product is very important for health as it contains amino acids, fatty acids, vitamins, minerals, hormones and antioxidants. Apilarnil is recognized as a complete food and is included in various food products. Research emphasizes the androgenic, estrogenic, antioxidant and immune system boosting effects of apilarnil. Animal studies indicate its potential to improve reproductive health, reduce stress and promote growth and development. It also shows promise in protecting against oxidative stress and improving general health. In this review, information on apilarnil and its uses is compiled.**

**Keywords: Honeybee Products, Drone Brood Homogenate, Apitherapy, Edible Insects, Nutritional Supplement**

**ÖZ**

**Arıcılık, tozlaşmanın yanında bal ve diğer arı ürünlerinin üretimi yoluyla tarımsal sürdürülebilirliğin ve ekonominin desteklenmesinde çok önemli bir rol oynamaktadır. Bu ürünler arasında, erkek arı larvalarından elde edilen ve sağlık açısından fayda sağlayan, az bilinen bir madde olan apilarnil de yer almaktadır. Apilarnil temel besinler açısından oldukça zengindir ve üreme sistemi, otonom sinir sistemi ve kardiyovasküler sağlık üzerinde olumlu etkileri olduğu bildirilmiştir. Doğal tıbbi özellikleri yanında, besleyici ve farmasötik potansiyeli giderek daha fazla kabul görmekte ve apilarnilin ticari üretimine yol açmaktadır. Bu arı ürünü amino asitler, yağ asitleri, vitaminler, mineraller, hormonlar ve antioksidanlar içerdiğinden sağlık için oldukça önemlidir. Apilarnil tam bir gıda olarak kabul edilmekte ve çeşitli gıda ürünlerine dahil edilmektedir. Araştırmalar apilarnilin androjenik, östrojenik, antioksidan ve bağışıklık sistemini güçlendirici etkilerini vurgulamaktadır. Hayvanlar üzerinde yapılan çalışmalar, üreme sağlığını iyileştirme, stresi azaltma ve büyüme ve gelişmeyi destekleme potansiyeline işaret etmektedir. Ayrıca oksidatif strese karşı koruma ve genel sağlığı iyileştirme konusunda da umut vaat etmektedir. Bu derlemede apilarnil ve kullanım alanlarına ilişkin bilgiler derlenmiştir.**

**Anahtar Kelimeler: Balarısı Ürünleri, Erkek Arı Larva Homojenatı, Apiterapi, Yenilebilir Böcekler, Besin Takviyesi**

## GENİŞLETİLMİŞ ÖZET

**Amaç:** Bitkilerin tozlaşmasına katkı sağlayan arılar, tarımın verimliliğinin artmasına destek olmaktadır. Bu nedenle arıcılık, tarımsal sürdürülebilirlik için son derece önemli bir sektördür ve küresel ölçekte kırsal ekonomiye katkı sağlamaktadır. Arıcılık faaliyetleri sırasında arıcılar bal ve balmumunun yanı sıra polen, arı ekmeği, arı zehri, propolis ve apilarnil gibi farklı ürünler de üretmektedir. Bu ara ürünler, arıcılık sektörüne ürün portföyünü çeşitlendirme ve gelirini artırma fırsatı sunmanın yanı sıra sürdürülebilirlik konusunda da etkin bir katkı sağlamaktadır. Bal ve diğer tüm arı ürünleri, günümüzde apiterapi olarak isimlendirilen geleneksel ve tamamlayıcı tıpta yaygın olarak kullanılmaktadır. Doğal gıda takviyelerine ve tamamlayıcı tedavilere artan ilgiyle birlikte bu ürünlere olan talep de giderek artmaktadır. Bu ürünler arasında erkek arı larvalarından elde edilen apilarnil, zengin amino asit, vitamin, yağ asidi, antioksidan ve mineral içeriği ile öne çıkan değerli bir üründür. Bu derlemede, apilarnilin üretimi ve kullanım alanlarına ilişkin bilgiler sunulmaktadır.

**Tartışma:** Tam bir gıda olarak kabul edilen apilarnilin bağışıklık sistemini desteklediği, antioksidan etkilere sahip olduğu, üreme sistemi, otonom sinir sistemi ve kardiyovasküler sağlık üzerinde olumlu etkiler gösterdiği çeşitli çalışmalarda rapor edilmiştir. Hayvanlar üzerinde yapılan çalışmalarda da üreme sağlığını iyileştirme, büyüme ve gelişmeyi destekleme ve stresi azaltma potansiyeline sahip olduğu gösterilmiştir. Çalışmalar, apilarnilin oksidatif strese karşı koruma sağladığını ve genel sağlığın iyileştirilmesine katkıda bulunabileceğini göstermektedir. Apilarnil içeren gıda takviyeleri ve tamamlayıcı tedavi amaçlı üretilen ürünler çeşitli ülkelerde farklı isim ve markalar altında uzun zamandır üretilmektedir. Bu tür ürünlere artan ilgi sebebiyle Avrupa Birliği tüketici güvenliğini sağlamak amacıyla ara arı ürünlerine üretim standartlarını da içeren sıkı yasal düzenlemeler getirmiştir.

**Sonuç:** Arı ürünlerinin alerjik reaksiyon oluşturma riski daima göz önünde bulundurulması gereken önemli bir husustur. Bu nedenle arı ürünleri üzerindeki etiketler mutlaka tüketiciyi yeterince bilgilendirecek gerekli tüm uyarıları içermelidir. Yasal düzenlemelerde bu etiketleme uygulamasını zorunlu kılmaktadır. Ayrıca apilarnil yüksek su içeriği ve hassas besinsel öğeleri sebebi ile son derece kolay bozulabilen bir ürün olduğu için üretiminde hijyen ve güvenlik standartlarına uyulması büyük önem taşımaktadır. Son olarak, apilarnil ve diğer ara arı ürünlerinin hak ettikleri değeri bulmaları için alternatif gıda veya besin takviyesi olarak tamamlayıcı tıpta kullanımları üzerine daha fazla bilimsel çalışma yapılması gerekmektedir.


## INTRODUCTION

Beekeeping is an important agricultural production sector that not only ensures the vegetative continuity of nature and the sustainability of agricultural production, but also makes a significant economic contribution to local economies. Many agricultural products are pollinated by bees and increase their productivity. On a global scale, 35% of agricultural products are pollinated with the help of bees and other pollinators, and the economic value of this service is estimated at approximately 235-577 billion dollars per year (IPBES 2016). Annual honey production worldwide is around 1.8 million tons, and the commercial value of this production is quite high (FAO 2024). For this reason, important beekeeping activities are carried out in different regions of the world under various climatic conditions. In addition to honey, beekeepers produce a wide variety of bee products such as beeswax, pollen, bee bread, royal jelly, bee venom, propolis and apilarnil (Bogdanov 2012; 2017; Silici 2023). All these honeybee products were used by many ancient civilizations in traditional medicine to treat diseases and injuries. Today, these bee products are continuing to be used in complementary medicine called apitherapy in different doses and compositions and provide important health benefits (Olas 2022). With the increasing interest in natural remedies and food supplements in recent years, the demand for bee products has also begun to increase (Akcicek and Yucel 2015). This situation has lead beekeepers who want to increase production efficiency and their income to start producing variety of bee products and to increase production diversity in recent years (Akcicek and Yucel 2015).

One of the lesser known and invaluable honeybee products is drone bee larvae or drone brood homogenate called apilarnil (Bogdanov 2012; 2017). This bee product produced from 7 days old drone larvae was first patented in Romania and named by apitherapist Nicolae V. Iliesiu, using the Latin abbreviations "Api" for bees, "lar" for larvae, and "nil", the first letters of his own name (Ilesiu 1991). Apilarnil is known for its positive effects on the male and female reproductive glands, the autonomic

nervous system and the cardiovascular system of the elderly and is used in many countries as a natural nutritional supplement containing drone milk or a mixture of drone milk and propolis. In addition, with the increasing trend towards natural products and traditional treatment methods such as apitherapy, apilarnil also began to be used in the pharmaceutical and cosmetic industry. As a result of these developments, the number of studies on its large scale production and biological effects has increased in recent years. So, this review was prepared to evaluate apilarnil production and the experimental animal studies on its biological effects in order to draw a projection for its increasing use.

**Apilarnil Production**

Male bees, which constitute approximately 5-10% of the populations, are produced from spring to autumn, mostly between April and June, for fertilization of the queen bee. The surplus males that do not have pollen collecting combs, stingers or wax glands and die after mating are usually destroyed by beekeepers as soon as possible in order to prevent worker bees from spending unnecessary energy to feed them and to protect hives from the *Varroa* parasite (Jensen et al. 2019, Sawczuk et al. 2019, Ulmer et al. 2020). This practice turns this bee product, which has high nutritional value and various pharmaceutical effects, into waste. However, in recent years, with the increasing interest in natural products with pharmaceutical properties, the number of research on the commercial production of apilarnil has begun to increase. In a study conducted in Denmark (Lecocq et al. 2018), it was shown that drone combs, which are used effectively in the biological control of *Varroa* mite, can be used to produce high amounts of apilarnil. As a result of the study, it was determined that the average total biomass of drone larvae extracted from each colony during a production season can reach over 1,000 kg per colony. The researchers suggested that drone larvae, which has a national production potential of 80 tons/year, could be used as a raw food material (Lecocq et al. 2018) and thus promote sustainable beekeeping (Ulmer et al. 2020). In another study, it was shown that production can be stimulated by removing combs carrying drone larvae from the hive every 7-11 days (Jensen et al. 2019).

**Physical Properties and Chemical Composition of Apilarnil**

Apilarnil is produced from 3–11 day old male bee larvae before pupation. It can be yellow, cream or gray in color, has a thick viscous liquid structure, a characteristic egg odor, slightly acidic taste and low solubility in water and alcohol (Barnutiu et al. 2013, Sidor and Dzugan 2020). It has a high water content, which makes it susceptible to rapid deterioration (Jensen et al. 2019). To preserve it without losing its quality and biological activity, different storage methods such as mixing with honey, freezing or absorbing lactose are recommended (Bogdanov 2012, 2017). If the cold chain rules are strictly followed, the product has been shown to be stored at -15°C for 1 year without much deterioration in its quality (Topal et al. 2018). For longer-term storage, it needs to be subjected to processes such as grinding, homogenization, filtration, and lyophilization (Topal et al. 2018). Lyophilization has been proven the most effective technique in preserving the active ingredients of apilarnil. In this technique, larvae dried by sublimation can be stored for a long time without changing the active ingredient content (Sidor et al. 2021a).

The nutritional components of fresh apilarnil, which may contain some honey, propolis and royal jelly, may vary depending on the region, season or larval age, as in all other bee products. Together with this, studies show that it contains all essential amino acids necessary for human and animal health, is a rich source of palmitic, stearic, and oleic acids as well as polyunsaturated fatty acids, and is a good source of B complex vitamins ve vitamin C and E, choline, and coenzyme Q10 as well as minerals such as phosphorus, potassium and magnesium (Table 1). In addition, it contains hormones such as testosterone, estradiol, progesterone and prolactin, phenolic (such as ferulic and ellagic acid) and flavonoid compounds that have antioxidant effects (Table 1). Studies have shown that drone larvae can be considered as a potential health enhancing agent due to their levels of amino acids, fatty acids, vitamins, minerals, antioxidant substances and hormones (Silici 2023).

**Table 1.** Physical properties and chemical composition of fresh and lyophilized apilarnil

| | Fresh | Lyophilized | References |
|---|---|---|---|
| **Sensory characteristics** | Yellow colored thick viscous liquid | Yellow or beige colored amorphous powder | |
| **Solubility** | Low in water and alcohol | | Balkanska et al. 2014, Sidor and Dzugan 2020, Kosum et al. 2022, Moraru et al. 2024 |
| **pH** | 5.5-7.5 | 4.5-6.8 | |
| **Acidity (ml 0.1 N NaOH/g)** | 0.7-2.6 | - | |
| **Conductivity (µS/cm)** | 144-178 | - | |
| **Proximate composition** | | | Lazaryan 2002, Finke 2005, Lipinski et al. 2008, Barnitiu et al. 2013, Balkanska et al. 2014, Isidorov et al. 2016, Margaoan et al. 2017, Shoinbayeva et al. 2017, Silici 2019, Sidor et al. 2021a, Borkovcova et al. 2022, Kosum et al. 2022 |
| Total energy (kcal/100 g) | 111.9-120.3 | 472-501.4 | |
| % Moisture | 68.5-78.5 | 3.5-6.0 | |
| % Ash | 0.7-3.0 | 2.7-4.1 | |
| % Protein | 7.2-15.4 | 32.0-52.4 | |
| % Carbohydrate | 6.9-12.2 | 17.8-38.9 | |
| % Lipid | 3.1-8.4 | 20-24.2 | |
| **Amino acids (%)** | | | Lazaryan 2002, Finke 2005, Isodorov et al. 2016, Margaoan et al. 2017, Silici 2019, Gosh et al. 2020, 2021, Sidor et al. 2021a |
| Alanine | 0.17-2.4 | 1.83-2.36 | |
| Arginine | 0.11-2.1 | 2.18-3.00 | |
| Asparagine | 0.77 | 2.4 | |
| Aspartic acid | 0.08-3.6 | 3.23-3.57 | |
| Phenylalanine | 0.63-1.8 | 1.84-2.08 | |
| Glutamic acid | 2.13-6.9 | 5.63-7.94 | |
| Glycine | 1.15-1.8 | 1.5-2.29 | |
| Glycine-Proline | 0.012 | - | |
| Histidine | 0.41-1.1 | 0.99-1.21 | |
| Methionine | 0.38-0.8 | 0.50-1.15 | |
| İsoleucine | 0.5 -1.9 | 2.02-2.43 | |
| Lysine | 1.21-3.2 | 3.52-7.20 | |
| Leucine | 1.07-4.0 | 3.26-3.96 | |
| Proline | 2.78-3.6 | 1.58-3.92 | |
| Serine | 0.09-0.87 | 1.4-2.03 | |
| Cysteine | 0.016-1.8 | 0.25-1.61 | |
| Threonine | 1.23-1.7 | 1.30-1.86 | |
| Tryptophan | 0.32-0.5 | - | |
| Tyrosine | 0.77-2.4 | 2.02-2.55 | |
| Valine | 0.81-2.6 | 2.27-2.87 | |
| Phosphoserine | 0.11-0.12 | - | |
| % Essential amino acids | 0.071 | - | |
| % Free amino acids | 0.022 | - | |
| **Fatty acids (%)** | | | Finke 2005, Yucel et al. 2019, Gosh et al. 2020, Erdem and Inci 2022 |
| 10-Heptadecenoic acid | 1.41 | - | |
| Lauric acid | 0.2 | 0.03 | |
| Myristic acid | 1.2 | 0.36-2.61 | |
| Palmitic acid | 14.7 | 4.81-42.6 | |
| Palmitoleic acid | 0.2 | 0.06-0.59 | |
| Stearic acid | 4.3 | 1.11-10.42 | |
| Oleic acid | 18.2 | 4.72-42.69 | |
| Alpha-Linoleic acid | 0.4 | 1.06 | |
| Gamma-Linoleic | 0.3 | 2.54 | |
| Linolenic acid | 0.4 | ND | |
| Arachidic acid | 0.2 | ND | |
| Eicosenoic acid | 0.1 | 1.11 | |
| Behenic acid | 0.1 | 0.97 | |
| % Saturated fatty acids | 51.75 | 63.06 | |
| % Mono saturated fatty acids | 46.25 | 47.77 | |
| % Poly saturated fatty acids | 2.0 | 0.11 | |
| | | | |

| | | | |
|---|---|---|---|
| **Minerals (µg/g)** | | | |
| Calcium | 138 | 194.2-1336 | Finke 2005, Gosh et al. 2020, Sidor et al. 2021a, Borkovcova et al. 2022 |
| Phosphorus | 1790 | 3021.7-6868.8 | |
| Magnesium | 211 | 382.6-680.6 | |
| Sodium | 128 | 80.4-300.8 | |
| Potassium | 2690 | 2887.7-8910.8 | |
| Chlorine | 870 | - | |
| Iron | 12.9 | 11.8-60.87 | |
| Zinc | 16.0 | 14.4-257 | |
| Manganese | 0.6 | 2.4-8.7 | |
| Copper | 4.0 | 1.1-54.8 | |
| Selenium | 0.06 | - | |
| Sulphure | - | 941.8 | |
| **Carbohydrates (%)** | | | |
| Fructose | 0.3-8.4 | 0.38 | Lipinski et al. 2008, Barnitiu et al. 2013, Balkanska et al. 2014, Isidorov et al. 2016, Margaoan et al. 2017, Sidor and Dzugan 2020 |
| Glucose | 3.61-72.7 | 3.55 | |
| Sucrose | 0.05-1.5 | - | |
| Turanose | 0.05-2.4 | - | |
| Maltose | 0.33-5.3 | 0.9 | |
| Trehalose | 0.44-6.6 | 0.25 | |
| Isomaltose | 0.11-4.2 | - | |
| % Total sugar | 6.2-8.2 | - | |
| % Glycogen | 9.2-11.7 | - | |
| **Vitamins** | | | |
| Vitamin A (IU/g) | <1 | 0.31-14.7 | Finke 2005, Sawczuk et al. 2022 |
| Beta-carotene (µg/g) | <0.2 | - | |
| Vitamin B1 (µg/g) | 4.1 | - | |
| Vitamin B2 (µg/g) | 9.1 | - | |
| Vitamin B3 (µg/g) | 36.7 | - | |
| Vitamin B5 (µg/g) | 11.9 | - | |
| Vitamin B6 (µg/g) | 1.2 | - | |
| Vitamin B7 (µg/g) | 0.23 | - | |
| Vitamin B12 (µg/g) | <0.0012 | - | |
| Choline (µg/g) | 1684 | - | |
| Vitamin C (µg/g) | 38.0 | 650-3360 | |
| Vitamin D (IU/g) | <0.25 | - | |
| Vitamin E (IU/g | <0.005 | - | |
| **Antioxidants** | | | |
| Fumaric acid (µg/g) | 5.03 | - | Hryniewicka et al. 2016, Silici 2019, Gosh et al. 2020, Sidor et al. 2021a, 2021b, Kosum et al. 2022, Sawczuk et al. 2022 |
| *trans*-Aconitic acid (µg/g) | 11.20 | - | |
| *p*-Benzoquinone (µg/g) | 0.95 | - | |
| Catechin hydrate (µg/g) | 1.85 | - | |
| α-tocopherol (µg/g) | 7.2-8.4 | 0.53-24.1 | |
| Coenzyme Q10 (µg/g) | 19.4-21 | 0.03-114 | |
| Total phenolic (mg GAE/g) | 1.8-3.2 180.05- | 0.61-9.4 | |
| Total flavonoid (mg QE/g) | 320.43 | 0.63-5.8 | |
| Total antioxidant activity(mg | 0.04-0.1 | 90.91 | |
| AAE/g) | - | - | |
| (µmol TE/g) | 0.008-0.016 | 1.01-81.6 | |
| Antiradical activity (%DPPH) | 6.91-24.76 | 2.2-3 | |
| (FRAP, µmol TE/100 g) | 0.79-1.63 | | |
| **Hormones** | | 45.6-51.32 | |
| Testosterone (pmol/g) | 0.47-9.1 | 10-151.25 | Bogdanov 2017, Shoinbayeva et al. 2017, Yucel et al. 2019, Sidor et al. 2021a |
| Estradiol (nmol/g) | 2.18-6.8 | 0.81-457.87 | |
| Progesterone (nmol/g) | 0.51 | 8.0 | |
| Prolactin (nmol/g) | 4.11 | | |

At this point, we should also emphasize that as any natural product, chemical components of apilarnil may vary depending on the age of larvae collected, season, vegetation of the collection location, handling methods or the methodological differences used in the detection (Gosh et al. 2020, Moraru et al. 2024). For example, a recent study (Abd El-Whaed et al. 2024) showed that the flavonoid content (13.16 ± 0.94%) and the antioxidant activity (DPPH $IC_{50}$ = 179.93 ± 2.46 µg/ml) of lyophilized apilarnil may be much higher than those previously reported (in Table 1). Additionally, researchers reported different number of volatile metabolites with two different spectrometric detection approaches (Abd El-Whaed et al. 2024). Another study focusing on the phytochemical content with anticholinergic, antiglaucoma, antiepilepsy and antioxidant properties and the antioxidant activity of apilarnil reported that it showed generally lower antioxidant activity in comparison to the standard molecules (namely butylated hydroxyanisole, butylated hydroxytoluene, trolox, α-tocopherol and vitamin C) with the methods used (Inci et al. 2023). However, except vitamin C, it had higher radical scavenging activity than the standard antioxidants. Furthermore, it showed higher anticholinergic, antiglaucoma, antiepilepsy enzyme inhibitory activities than the standard antioxidants, indicating that it can be used in treatment of these diseases. Upon these outcomes, the researcher concluded that apilarnil has a more effective antioxidant profile compared to standard antioxidants (Inci et al. 2023).

***Use of Apilarnil as Food and in Health Area***

Apilarnil is recommended to be considered as a complete food in human and animal nutrition because it contains all essential amino acids and is a rich source of vitamins and minerals (Topal et al. 2018). In fact, products containing bee larvae have begun to be developed in the field of gastronomy. Examples of these developments are products such as snacks called "Bienengrammeln" or "bee crackle", or chocolate mousse and ice cream containing bee larvae (Ramos-Elorduy et al. 2007, Mishyna et al. 2019). A product that can be used as a meat substitute in foods such as hamburgers has also been developed by combining drone pupae with soya bean concentrate (Ulmer et al. 2020).

A recent study (Ghosh et al. 2020) suggested that late pupae and adult drones, which have high amino acid and mineral content and low fatty acid content, are beneficial for human health and therefore should be used as human food, while larvae and early pupa stages can be used in animal feeds. However, it is recommended that all drone products, regardless of developmental stage, be subjected to processes such as drying, blanching, etc. before consumption, thus increasing safety in consumption (Ghosh et al. 2020). Additionally, they can only be used as human food or in animal feeds if they are produced in accordance with standard production protocols that ensure hygiene and food safety (Ghosh et al. 2021). At this point, it is worth emphasizing that EU legislation requires regular microbiological tests and examinations for risky compounds, and therefore insects must be subjected to risk-reducing processes before consumption. In this respect, the International Platform of Insects for Food and Feed (IPIFF, 2022) has published guidelines on the cultivation of insects for human and animal consumption and instructions for food production. Drone brood intended for consumption is notified under the definition of "food" in Regulation (EC) No 178/2002. It is classified as a new food under Regulation (EU) 2015/2283 and can only be placed on the market after safety assessment and approval by the European Food Safety Authority (EFSA). In addition, other regulations specify legal provisions generally applicable to food safety, production and processing and to products on the market (e.g. Regulation (EC) No. 178/2002; in Germany, for the requirements of the Food Hygiene Regulation (Lebensmittelhygiene-Verordnung - LMHV); for labelling requirements, Regulation (EU) No. 1169/2011; for hygiene regulations, Regulation (EU) No. 1169/2011; for hygiene regulations, Regulation (EC) No. 852/2004 and Regulation (EC) No. 853/2004; and for the assessment of microbiological criteria, Regulation (EC) No. 2073/2005) (Schiel et al. 2022). In addition, both EU and non-EU countries are required to legislate on the use of apilarnil.

Another important point is that apilarnil often contains honey components such as glands, wax containing propolis, nectar and pollen. Although bee allergy is rare but possible, consuming bee products can lead to the development of food and respiratory allergies that begin with the development of sensitivity. For this reason, it is of great importance to investigate the allergenicity of bee products that will be offered for consumption through comprehensive tests and to determine the scope and frequency of the risks posed by their consumption. In addition, necessary legal regulations should be established to ensure that

products offered for consumption carry labels with appropriate warnings for consumers who are allergic to bee products. It should also always be recognized that, unlike other edible insect species, honey bees reared in an open environment cannot be strictly managed.

In apitherapy, drone larvae are commonly used to treat psychotic and neurodegenerative diseases in the elderly, reproductive problems and to enhance libido (Bolatovna et al. 2015, Shoinbayeva et al. 2017). It has also been used to lower cholesterol and triglyceride levels (Vasilenko et al. 2002), maintain liver health and support the immune system (Vasilenko et al. 2005), treatment of mental and nervous disorders (Meda et al. 2004, Bogdanov 2017), thyroid irregularities (Osnicewa et al. 2009), and promote youth and vigor (Bieljajew and Safonowskaja, 2009).

It is well known that pro-oxidants, which are a natural product of aerobic metabolism and whose levels increase under stress, negatively affect reproductive success, especially in males (Schreck 2010, Ubilla and Valdebenito 2011, Baskaran et al. 2021). Apilarnil contains essential amino acids, minerals and vitamins, as well as flavonoids and polyphenols and has a high degree of antioxidant activity (Silici 2019). It is also rich in reproductive and sex hormones. Indeed, drone brood has been used for many years as a natural medicine in some Eastern European, Far East, African and South American countries to support fertility and to eliminate male sexual problems such as sperm deficiency and immobility, and erectile dysfunction (Sidor and Dzugan 2020, Kekecoglu et al. 2021). Recently, it has also been evaluated as an alternative to testosterone replacement therapy (Erdem and Ozkok 2017). In addition, studies to standardize its production and application as a fertility booster were conducted. For example, a company called Vitaliter has carried out studies to purify the lipid part of apilarnil to produce gel capsules (ApiREX) that can be used in testosterone treatment (https://silo.tips/download/apilarnil-lipid-zt-ile-testosteron-artrc-doal-gda-takviyesi-gelitirilmesi). Two other companies submitted patent applications for their already developed products (Erdem et al. 2017, Vakina et al. 2017).

Nowadays, the tendency to meet the needs of the body from natural products, which has increased with the concept of healthy living, has led to a rapid process of developing new commodities with added value from different bee products (Cosmia et al. 2016, Marangoz and Dolu 2019). Under the influence of this trend, many food supplements under various names containing apilarnil in powder, viscous liquid or tablet form have begun to be produced in some European, Far Eastern and South American countries (Hroshovyi et al. 2021, Kekeçoğlu et al. 2021). In a recent study on the development of dietary supplements containing apilarnil (Dzugan et al. 2023), a product containing frozen drone brood (DB) enriched with calcium ions from calcium carbonate (CC) or eggshell (ES) was designed. It was shown that the bioavailability of DB components was better in DB + ES than in DB + CC and DB capsules. It was reported that the two-component food supplement proposed in this study, which demonstrated the synergistic effect between DB and ES calcium, may be an effective therapeutic alternative for balancing osteoporosis-related hormone and calcium deficiency (Dzugan et al. 2023).

**Experimental Studies on the Biological Activities of Apilarnil**

Many studies have been conducted on various animal groups to investigate the effects of apilarnil from different aspects. In an earlier study, Kogalniceanu et al. (2010) reported that apilarnil is an agent that increases glycogen consumption in muscle tissue and has a catabolic effect on the carbohydrate metabolism of white Winstar rats. Yucel et al. (2011) reported that male broilers given 4 g apilarnil per day had better body weight gain. Researchers also observed that daily application of apilarnil enhanced the secondary sexual characteristics such as crown length and beard width. Thereupon, they stated that apilarnil may have an androgenic effect rather than an anabolic effect (Yucel et al. 2011). In their later study, they investigated the possibility of stimulation of sexual development at an earlier age by administering apilarnil to 28 and 55-day-old male and female broilers in the prepubertal period (Altan et al. 2013). In that study, low (2.5 g/animal) and high (7.5 g/animal) dose daily oral apilarnil administration showed no significant effect on the growth performance of male and female broilers. However, increases in testicular weight, plasma testosterone level and crest size were observed in apilarnil-treated males and apilarnil reported to decrease the age at sexual maturity and reduce stress and fear behaviors. In addition, significant decreases in total cholesterol and glucose levels and increases in good

cholesterol levels were detected (Altan et al. 2013). Based on these results, the researchers stated that apilarnil have a higher biological activity in males. Similarly, feeding fresh drone larvae for a month before attempting to spawn has been reported to be more effective in improving reproductive performance in virgin yellow princess (*Labidochromis caeruleus*) males than in females, and spawning began approximately 10 days earlier in aquariums with males and females fed fresh apilarnil (Sahin 2020).

Seres et al. (2014) investigated the androgenic effect of apilarnil by giving drone milk, which is used in larvae and adult nutrition of male bees, to castrated male rats. They also observed that the relative weight of androgen-related organs (glans penis and seminal vesicle) and plasma testosterone levels increased in the rats fed male royal jelly. In addition, they determined that the milk exerts this effect by increasing the expression of Spot14-like androgen-inducible protein in the prostate and that its active components with androgenic effects may be palmitate and oleate methyl esters. In another study, Bolatovna et al. (2015) reported that the weight of the seminal glands increased by 20.1–21.9%, the weight of the epididymis increased by 21.8–25.8%, and sexual dysfunction decreased by 83.3% when piglets administered apilarnil extract via parenteral injection. In addition to increasing the weight of the seminal glands and epididymis, apilarnil injection was reported to improve reproductive functions in terms of ejaculate volume, spermatozoa density, sperm motility, fertility rate, offspring survival rate, and the rate of acrosome-damaged spermatozoa. Moreover, researchers observed that apilarnil calmed injected animals, suggesting that it may have a stimulatory effect on the central nervous system (Bolatovna et al. 2015). Apilarnil extract given to wild boars was also found to improve semen productivity quantitatively and qualitatively (Bolatovna et al. 2015). Similarly, Yemets et al. (2020) showed daily feeding male piglets with 0.5 g of drone homogenate stimulates reproductive functions and improves fertility during puberty. Kosum et al. (2018) gave 2 ml apilarnil twice a day to 75-day-old Sanen goats found larger testicles and higher testosterone hormone levels in the apilarnil group compared to the control group. In follow-up studies, they also observed that the effect size was directly proportional to the dose of apilarnil administered, but no doses of apilarnil had an effect on growth (Kosum et al. 2022).

In addition to having an androgenic effect on sexually mature or immature animals, apilarnil has been found to stimulate the immune system and improve general health in pigs by increasing the antibody production and the response of T-lymphocytes (Mitrofanov and Budnikova 2021). A study conducted on dogs (Efanova et al. 2019) showed that the number of red blood cells and leukocytes, as well as the levels of thyroxine, testosterone, hemoglobin, total protein and globulin in the blood, increased in animals fed apilarnil at a rate of 15 mg/kg per day for two months. The preparation called Apistimul, which consists of apilarnil and sodium chloride, was also increased the amount of hemoglobin and erythrocytes in ram's blood, improved the qualitative and quantitative characteristics of ejaculate, and had a general stimulating effect on all their reproductive functions (Shoinbayeva et al. 2017).

Besides the androgenic effect, Seres et al. (2013) investigated the estrogenic effect of drone milk. They reported that male royal jelly increased uterine weight in juvenile female rats by inducing the expression of estrogen-linked peptide complex component C3 and the active component that may cause this estrogenic effect is E-dec-2-enedioic acid (Seres et al. 2013). An increase in body weight and ovarian length was also observed on day 145 in white sows fed DB homogenate (Kistanova et al. 2020). Animals fed DB homogenate appeared to have a larger pool of primordial follicles with dense growth, as well as ovaries with larger diameter primary and tertiary follicles. Atresia symptoms were also observed in the Graafian follicles of the animals. Based on these findings, the researchers reported that DB homogenate supplementation stimulated the early stages of folliculogenesis in the ovaries, but triggered atresia in the final stage of follicular development (Kistanova et al. 2020).

Many researchers focused on the antioxidant and cell protective effects of apilarnil. Kuzmenko et al. (2018) reported that apilarnil supplementation helps to maintain antioxidant-prooxidant balance in the uterus of pregnant pigs and supports normal embryonic development, especially by increasing non-enzymatic antioxidant levels. At the end of the study investigating the effect of apilarnil on prooxidant-antioxidant homeostasis in pigs during puberty, it was found that the administration of apilarnil to pigs has significantly positive effect on the formation of reproductive function during puberty and had antioxidant effects that significantly slowed

the course of peroxidation processes (Shostya et al. 2019). Therefore, it was inferred that apilarnil can be used as a gonad protector by the breeders. This property of apilarnil has also been demonstrated in a recent toxicology study (Elashal et al. 2024). Researchers experimentally showed that apilarnil supplementation may ameliorate a widespread environmental pollutant (Bisphenol A) induced reproductive impairment symptoms in adult male rats. A 0.6 g/kg body weight daily apilarnil administration was effective to restore the serum glutathione, testosterone and gonadotropin levels, improve the counts, motility and morphology of sperm. Additionally, it increased the proliferating cell nuclear antigen gene expression while decreasing the malondialdehyde levels in testis (Elashal et al. 2024).

In the hepatitis model induced by exposure to carbon tetrachloride in rats, apilarnil was determined to improve liver functions as well as stimulating the immune system (Vasilenko et al. 2002, 2005). Doganyigit et al. (2019a) investigated the effects of different doses (0.2-0.8 g/kg) of apilarnil in the diabetes model induced by the intra-abdominal lipopolysaccharide (LPS) injection. They reported that simultaneous apilarnil injection reduces the DNA damage in kidney tissue 6 h after LPS injection and shows the highest protection at a dose of 0.8 g/kg. Additionally, they observed increased amounts of sperm in the testicular lumen sections of adult male rats given LPS, depending on the dose of apilarnil (Doganyigit et al. 2019b). Consistent with this, subsequent studies supported that apilarnil prevents apoptosis by dose-dependently reducing the expression of precursor genes related to cytokine production in liver and brain tissues, reduces DNA damage, and protects cells against oxidative stress by increasing enzymatic antioxidant levels (Doganyigit et al. 2020a; Hamamcı et al. 2020). Apilarnil also inhibited apoptosis and DNA damage in lung cells (Doganyigit et al. 2020b) and induced autophagy pathway in liver cells (Doganyigit et al. 2020c). Under an LPS-induced sepsis model, apilarnil was reported to reduce inflammation in the kidneys and exhibit anti-apoptotic effects, again by suppressing the expression of inflammatory cytokines in the TLR4/NF-κB pathway (Inandiklioglu et al. 2021).

Okan et al. (2022) investigated the protective effect of apilarnil in endotoxic shock, which is one of the important causes of mortality in intensive care units, through histopathological changes and immune system-related gene (tumor necrosis factor-alpha (TNF-α) and natriuretic peptide (BNP)) expression changes in the heart tissue of male rats with LPS induced sepsis. In this study, where differences in TNF-α expression in heart tissue and BNP expression in brain tissue were evaluated immunohistochemically, edema, bleeding and infiltration were observed in the LPS-administered control group, while these damages were significantly reduced in the LPS-administered apilarnil (0.8 g/kg) group. Additionally, while the expression levels of TNF-α and BNP genes increased significantly in the LPS-administered control group, the expression of these genes was reported to be suppressed in the LPS-administered apilarnil group. Based on these results of the study, the researchers concluded that apilarnil had a therapeutic effect against heart damage caused by LPS due to its anti-inflammatory and antioxidant contents.

Finally, a new study examining the effects of dietary bee product supplementation on reproductive success and oxidative stress levels showed that adding apilarnil and royal jelly to the diet or calorie restriction could be implemented to delay the age-related decline in semen production. It has also been shown that it slows down the aging process and extends reproductive life in male breeder broilers (Seremet-Tugalay and Altan 2020).

**Conclusion:** As implicated by the animal studies summarized above, apilarnil is a bee product with antioxidant, anti-inflammatory, antitumor, anti-apoptotic, androgenic and anabolic effects due to its rich content in amino acids, fatty acids, vitamins, minerals, hormones and antioxidants. It supports general health by strengthening the immune system and antioxidant defense mechanism. Therefore, this bee product has a high potential to make serious contributions to the fields of health and nutrition. However, it should not be overlooked the fact that more detailed studies still need to be carried out on its usage areas, production and usage standards.

It is also important to note that, despite apilarnil or apilarnil-containing various products are being marketed on a global scale via the internet, neither the FAO nor local organizations maintain records of bee products other than honey and beeswax. The lack of records pertaining to the production of alternative bee products hinders the full realization of the potential yield of beekeeping and the accurate quantification of the production of such bee

products. Furthermore, it impedes the broader utilization of these products or raw materials, as it engenders uncertainty regarding their continuity, sources and supply. It is hoped that in the near future, the production quantities of alternative bee products, such as apilarnil, will also be recorded.

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## REFERENCES

Abd El-Wahed AA, Khalifa SAM, Aldahmash B, Zhang H, Du M, Zhao C et al. Exploring the chemical constituents and nutritive potential of bee drone (Apilarnil): Emphasis on antioxidant properties Chem. Biod. 2024;21: e202400085, DOI:10.1002/cbdv.202400085

Akcicek E, Yucel B. Apiterapi'de apilarnil. Arı Ürünleri ve Sağlık (Apiterapi). Sidas Yayınevi, İzmir, 2015 p. 183-190.

Altan O, Yucel B, Acikgoz Z, Seremet C, Kosoglu M, Turgan N et al. Apilarnil reduces fear and advances sexual development in male broilers but has no effect on growth Br. Poultry Sci. 2013;54(3): 355-361, DOI:10.1080/00071668.2013.791382

Balkanska R, Karadjova I, Ignatova M. Comparative analyses of chemical composition of royal jelly and drone brood Bulgarian Chem. Comm. 2014;46(2):412-416.

Barnutiu LI, Marghitas L, Dezmirean D, Bobis O, Mihai C, Pavel C. Physicochemical composition of apilarnil (bee drone larvae) Lucrări Ştiinţifice-Seria Zootehnie 2013;59:199-202.

Baskaran S, Finelli R, Agarwal A, Henkel R. Reactive oxygen species in male reproduction: A boon or a bane? Andrologia 2021;53: e13577, DOI:10.1111/and.13577

Bieljajew WA., Safonowskaja JW. Adaptogenic relationship training based on drone brood Beekeeping 2009; 6:51-52.

Bogdanov S. The royal jelly book, Royal jelly and bee brood: Harvest, composition, quality Bee Prod. Sci. 2012; www.bee-hexagon.net

Bogdanov S. The royal jelly book, Royal jelly, bee brood: Composition, health, medicine Bee Prod. Sci. 2017; www.bee-hexagon.net/fles/fle/flE/Health/RJBookReview. pdfMay2017

Bolatovna KS, Omirzak T, Akhanov UK, Rustenov A, Eleuqalieva N. Improving reproductive qualities of pigs using the drone brood homogenate Biol. Med. 2015;7(2):BM-091.

Borkovcova M, Mlcek J, Adamkova A, Adamek M, Bednarova M, Musilova Z, Sevcikova V. Use of foods based on bee drone brood: Their sensory and microbiological evaluation and mineral composition Sustainability 2022;14 (5): 2814, DOI:10.3390/su14052814

Cosmia M, Gallenti G, Marangon F, Troiano S. Reprint of "Attitudes towards honey among Italian consumers: A choice experiment approach" Appetite 2016;106:110-116, DOI:10.1016/j.appet.2016.08.005

Doganyigit Z, Silici S, Kaymak E, Okan A, Pandir D. LPS'nin böbrek DNA'sı üzerine akut toksik etkisi ve apilarnilin koruyucu rolü Eurasian J. Biol. Chem. Sci. 2019a;2:111-114.

Doganyigit Z, Silici S, Kaymak E, Okan A, Akın A T, Pandır D. Apilarnilin'in erkek sıçanlarda lipopolisakkarite (LPS) bağlı testis toksisitesine karşı koruyucu rolünün belirlenmesi determination of the protective role of apilarnil against testicular toxicity due to lipopolysaccharide (LPS) in male rats Bozok Tip Derg. 2019b;9(2):146-154.

Doganyigit Z, Okan A, Kaymak E, Pandir D, Silici S. Investigation of protective effects of apilarnil against lipopolysaccharide induced liver injury in rats via TLR 4/ HMGB-1/ NF-κB pathway Biomed. Pharm. 2020a;125:109967, DOI:10.1016/j.biopha.2020.109967

Doganyigit Z, Kaymak E, Okan A, Pandir D, Silici S. Investigation of protective effects of apilarnil

against lipopolysaccharide induced lung injury in rats Mellifera 2020b;20:3-15.

Doganyigit Z, Koklu B, Uner A, Okan A, Kaymak E, Silici S. The Effect of apilarnil on the autophagia against lipolysaccarite-based sepsis in liver New Trends in Med. Sci., 2020c;1:84-89.

Dzugan M, Sidor E, Milek M, Tomczyk M. The possibility of using bee drone brood to design novel dietary supplements for apitherapy *Appl. Sci.* 2023;*13*:4687, DOI:10.3390/app13084687

Efanova N, Osintseva LA, Osina LM, Batalova SV, Mikhailova DS. Correction of endocrine and metabolic status of dogs with the help of drone homogenate Innovat. Food Safety 2019;2(24):64-68, DOI:10.31677/2311-0651-2019-24-2-64-68

Elashal MH, Abd El-Wahed AA, Mohamed MA, Hamad R, Abd Eldaim MA, Khalifa SAM et al. Apilarnil ameliorates bisphenol A-induced testicular toxicity in adult male rats via improving antioxidant potency and PCNA expression Reprod. Toxic. 2024;125:108570, DOI:10.1016/j.reprotox.2024.108570

Erdem B, Arslan OC, Mulayim MS. Testosterone enhancer containing lipid extract of apilarnil Türk Patent Appl. 2017;TR 2016014275 A1 20170821.

Erdem B, Ozkok A. Can food supplement produced from apilarnil be an alternative to testosterone replacement therapy? Hacettepe J. Biol. Chem. 2017;45(4):635–638, DOI: 10.15671/HJBC.2018.207

Erdem S, Inci H. Apilarnilin yağ asidi özelliklerinin belirlenmesi Türk Tarım Doğa Bil. Derg. 2022;9(4):900-6, https://doi.org/10.30910/turkjans.1111152

FAO (Food and Agriculture Organization). Production, Crops Primary, https://www.fao.org/faostat/en/#data/QCL

Finke MD. Nutrient composition of bee brood and its potential as human food Ecol. Food Nutri. 2005;44(4):257-270, DOI:10.1080/03670240500187278

Ghosh S, Herren P, Meyer-Rochow VB, Jung C. Nutritional composition of honeybee drones of two subspecies relative to their pupal developmental stages *Insects* 2021;12(8):759, DOI:10.3390/insects12080759

Ghosh S, Sohn HY, Pyo SJ, Jensen AB, Meyer-Rochow VB, Jung C. Nutritional composition of *Apis mellifera* drones from Korea and Denmark as a potential sustainable alternative food source: Comparison between developmental stages Foods 2020;9:389, DOI:10.3390/foods9040389

Hamamci M, Doganyigit Z, Silici S, Okan A, Kaymak E, Yilmaz S, Inan LE. Apilarnil: A novel neuroprotective candidate Acta Neurologica Taiwanica 2020;29(2):33-45.

Hroshovyi T, Dobrynchuk M, Pavliuk B, Chubka M. Drone brood—As a raw material for the manufacture of medicines and dietary supplements Sci. Europe 2021;63:36-39.

Hryniewicka M, Karpinska A, Kijewska M, Turkowicz MJ, Karpinska J. LC/MS/MS analysis of α-tocopherol and coenzyme Q10 content in lyophilized royal jelly, beebread and drone homogenate J. Mass Spectro. 2016;51(11):1023-1029, DOI:10.1002/jms.3821

Ilieşiu NV. Apilarnil, Editura Apimondia, Bucuresti 1991.

Inandiklioglu N, Doganyigit Z, Okan A, Kaymak E, Silici S. Nephroprotective effect of apilarnil in lipopolysaccharide-induced sepsis through TLR4/NF-κB signaling pathway Life Sci. 2021;284:119875, DOI:10.1016/j.lfs.2021.119875

Inci H, Izol E, Yilmaz MA, Ilkaya M, Bingol Z, Gulcin I. Comprehensive phytochemical content by LC/MS/MS and anticholinergic, antiglaucoma, antiepilepsy, and antioxidant activity of apilarnil (drone larvae) Chem. Biodiv. 2023;20:e202300654, DOI:10.1002/cbdv.202300654

IPBES (Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services). The assessment report of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services on pollinators, pollination and food production. S.G. Potts, V. L. Imperatriz-Fonseca, and H. T. Ngo (eds). 552 pages, 2016, DOI:10.5281/zenodo.3402856

IPIFF (International Platform of Insects for Food and Feed). Guide on food hygiene practices for European Union (EU) producers of insects as food and feed. 2022, https://ipiff.org/wp-content/uploads/2019/12/IPIFF-Guide-on-Good-Hygiene-Practices.pdf

Isidorov VA, Bakier S, Stocki M. GC-MS investigation of the chemical composition of honeybee drone and queen larvae homogenate J. Apicultural Sci. 2016;60(1):111-120, DOI:10.1515/jas-2016-0011

Jensen AB, Evans J, Joans-Levi A, Benjamin O, Matrinez I, Dahle B, Roos N, Lecocq A, Foley K. Standard methods for *Apis mellifera* brood as human food J. Apicult. Res. 2019;58:1-28, DOI:10.1080/00218839.2016.1226606

Kekecoglu M, Keskin M, Birinci C, Birinci E, Kolayli S. Effects of honeybee race and season on propolis composition J. Agricult. Sci. 2021;27(3):292-297, DOI:10.15832/ankutbd.619996

Kistanova E, Zdoroveva E, Nevitov M, Nosov A, Vysokikh M, Sukhanova I, Boryaev G. Drone brood fed supplement impacts on the folliculogenesis in growing gilts Veterinarski Arhiv. 2020;90(6):583-592, DOI:10.24099/vet.arhiv.0886

Kogalniceanu S, Lancrajan I, Ardelean G. Changes of the glucidic metabolism determined by the physical effort of the treatment with the Aslavital and Apilarnil Arad Med. J. 2010;3:33-41.

Kosum N, Taskin T, Kandemir C, Yucel B, Ekren Asici GS, Kiral F. Effects of Apilarnil on growth, body measurement and testes characteristics for Saanen male kids. *Agrifood Conference*, 26-28 September, İzmir. 2018;P 40-47.

Kosum N, Yucel B, Kandemir C, Taskin T, Duru M.E, Kuçukaydın S, Cornea-Cipcigan M. Chemical composition and androgenic effect of bee drone larvae (Apilarnil) for goat male kids. Chem. Biodiv. 2022;19(8):e202200548, DOI:10.1002/cbdv.202200548

Kuzmenko LM, Polishchuk AA, Usenko SO, Shostya AM, Bulavenko RV. Prooxidant-antioxidant homeostasis in the tissues of the uterus of pig, depending on the periods of the reproductive cycle World Med. Biol. 2018;64(2): 198-203, DOI:10.26724/2079-8334-2018-2-64-198-203

Lazaryan DS. Comparative amino acid analysis of bee brood Pharma. Chem. J. 2002;36(12):680-682.

Lecocq A, Foley K, Jensen AB. Drone brood production in Danish apiaries and its potential for human consumption. J. Apicult. Res. 2018;57(3):331-336, DOI:10.1080/00218839.2018.1454376

Lipinski MJ, Froenicke L, Baysac KC, Billings NC, Leutenegger CM, Levy AM, Lyons LA. The ascent of cat breeds: Genetic evaluations of breeds and worldwide random-bred populations Genomics, 2008;91(1):12-21, DOI:10.1016/j.ygeno.2007.10.009

Marangoz M, Dolu ZT. Tüketicilerin arı ürünlerine ilişkin bilgi ve güven düzeyleri ile satın alma davranışlarının araştırılması U. Ari. Derg. - U. Bee J. 2019;19(2):110-125, DOI:10.31467/uluaricilik.537602

Margaoan R, Marghitas LA, Dezmirean DS, Bobis O, Bonta V, Catana C et al. Comparative study on quality parameters of royal jelly, apilarnil and queen bee larvae triturate. Bull. U. Agricult. Sci. Vet. Med. Cluj-Napoca-Anim. Sci. Biotech. 2017;74(1):51-58, DOI:10.15835/buasvmcn-asb:12622

Meda A, Lamien CE, Millogo C, Romito M, Nacoulma OG. Therapeutic uses of honey and honeybee larvae in central Burkina Faso J. Ethanopharm. 2004;(95):103-107, DOI:10.1016/j.jep.2004.06.016

Mishyna M, Martinez JJI, Chen J, Benjamin O. Extraction, characterization and functional properties of soluble proteins from edible grasshopper (*Schistocerca gregaria*) and honeybee (*Apis mellifera*) Food Res. Intern. 2019;6:697-706, DOI:10.1016/j.foodres.2018.08.098

Mitrofanov DV, Budnikova NV. Influence of technology on the quality indicators of the composition of drone brood and royal jelly. *International Conference on Agricultural Science and Engineering*, 2021;845:1-6, DOI:10.1088/1755-1315/845/1/012060

Moraru D, Alexa E, Cocan I, Obistioiu D, Radulov I, Simiz E et al. Chemical characterization and antioxidant activity of apilarnil, royal jelly, and propolis collected in Banat region, Romania Appl. Sci. 2024;14;1242, DOI:10.3390/app14031242

Okan A, Kaymak E, Uner AK, Silici S, Doganyigit Z. Apilarnil protects the LPS induced endotoxemic heart Turk. Bull. Hyg. Exp. Biol. 2022;79(4):720-729, DOI: 10.5505/TurkHijyen.2022.78200

Olas B. Bee Products as Interesting Natural agents for the prevention and treatment of common cardiovascular diseases Nutrients. 2022 May 28;14(11):2267, DOI:10.3390/nu14112267

Osnicewa LA, Efanowa NW, Kabyszewa WW. Homogenate of drone in the diet of dogs Beekeeping 2009;10:50-51.

Ramos-Elorduy J, Costa Neto EM, Pino JM, Cuevas Correa MS, Garcia-Figueroa J, Zetina D.H. Conocimiento de la entomofauna útil en el poblado La Purísima Palmar de Bravo, Estado de Puebla, México Biotemas 2007;20(2):121–34.

Sahin P. Sarı prenses balığı *(Labidochromis caeruleus* Fryer, 1956*)* anaçlarının erkek bal arısı larvası (Apilarnil) ile beslenmesinin üreme performansı ve vücut kompozisyonuna etkilerinin araştırılması. OU, Graduate School of Natural and Applied Sciences, Master's thesis, Ordu, 2020, (accession date.20.07.2024), https://tez.yok.gov.tr/UlusalTezMerkezi/tezDetay

Sawczuk R, Karpinska J, Filipowska D, Bajguz A, Hryniewicka M. Evaluation of total phenols content, anti-DPPH activity and the content of selected antioxidants in the honeybee drone brood homogenate Food Chem. 2022;368:130745, DOI:10.1016/j.foodchem.2021.130745

Sawczuk R, Karpinska J, Miltyk W. What do we need to know about drone brood homogenate and what is known J. Ethnopharm. 2019;245:111581, DOI:10.1016/j.jep.2018.10.042

Schiel L, Wind C, Ulmer M, Braun PG, Koethe M. Honey bee drone brood used as food Ernahrungs Umschau 2022;69(7):96-104, DOI:10.4455./eu.2022.019

Schreck CB. Stress and fish reproduction: the roles of allostasis and hormesis Gen. Comp. Endocrinol. 2010;165(3):549-556, DOI: 10.1016/j.ygcen.2009.07.004

Seres AB., Ducza E, Bathori M, Hunyadi A, Beni Z, Dekany M, Gaspar R. Raw drone milk of honeybees elicits uterotrophic effect in rats: evidence for estrogenic activity J. Med. Food 2013;16(5):404-409, DOI:10.1089/jmf.2012.0232

Seres AB, Ducza E, Bathor M, Hunyadi A, Beni Z, Dekany M, Gaspar R. Androgenic effect of honeybee drone milk in castrated rats: Roles of methyl palmitate and methyl oleate J. Ethnopharm. 2014;153(2):446-453, DOI:10.1016/j.jep.2014.02.050

Shoinbayeva KB, Omirzak T, Bigara T, Abubakirova A., Dauylbay A. Biologically active preparation and reproductive function of stud rams Asian J. Pharm. 2017;11(3):184-191.

Shostya AM, Yemets YM, Kuzmenko LM, Moroz OG, Stupar II. The influence of drone larvae homogenate on prooxidant-antioxidant homeostasis in gilts in the period of puberty Bull. Poltava State Agricult. Acad. 2019;4:134-140.

Sidor E, Dzugan M. Drone brood homogenate as natural remedy for treating health care problem: A scientific and practical approach Molecules 2020;25(23):5699, DOI:10.3390/molecules25235699

Sidor E, Milek M, Tomczyk M, Dzugan M. Antioxidant activity of frozen and freeze-dried drone brood homogenate regarding the stage of larval development Antioxidants, 2021b;10(5):639, DOI:10.3390/antiox10050639

Sidor E, Milek M, Zagula G, Bocian A, Dzugan M. Searching for differences in chemical composition and biological activity of crude drone brood and royal jelly useful for their authentication Foods 2021a;10(9):2233, DOI: 10.3390/foods10092233

Silici S. Chemical content and bioactive properties of drone larvae (Apilarnil) Mellifera 2019;19(2):14-22.

Silici S. Honeybee products and apitherapy Turk. J. Agricult.-Food Sci. Tech. 2019;7(9):1249-1262.

Silici S. Drone larvae homogenate (Apilarnil) as natural remedy: scientific review J. Agricult. Sci. 2023;29(4):947-959, DOI:10.15832/ankutbd.1293015

Seremet-Tugalay C, Altan O. Anti-ageing effects of dietary bee products and calorie restriction on semen production and oxidative damage in older broiler breeder males Slovenian Vet. Res.2020;57:149–57, DOI: 10.26873/SVR-954-2020

Topal E, Strant M, Yucel B, Kosoglu M, Margaoan R, Dayioglu M. Biochemical properties and apitherapeutic usage of queen bee and drone larvae J. Anim. Prod. 2018;59(2):77-82, DOI:10.29185/hayuretim.455478

Ubilla A, Valdebenito I. Use of antioxidants on rainbow trout *Oncorhynchus mykiss* (Walbaum, 1792) sperm diluent: Effects on motility and fertilizing capability Latin American J. Aquatic Res. 2011;39(2):338-343.

Ulmer M, Smetana S, Heinz V. Utilizing honeybee drone brood as a protein source for food products: Life cycle assessment of apiculture in Germany Resour. Conser. Recycl. 2020;154:104576, DOI: 10.1016/j.resconrec.2019.104576

Vakina TN, Petrova EV, Trifonov VN, Fedorov EN, Fedorov AV, Andreeva ES, et al. Method for restoring male sex drive (Libido). United States Patent Application Publication 2017;US 9730973 B2.

Vasilenko YK, Klimova OV, Lazaryan DS. Biological effect of drone brood under chronic hyperlipidemia conditions Pharm. Chem. J. 2002;36(8):434-436, DOI:10.1023/A:1021214728006

Vasilenko YK, Klishina II, Lazaryan DS. A comparative study of the immunotropic and hepatotropic action of beekeeping products in rats with drug-induced hepatitis Pharm. Chem. J. 2005;39(6):319-322, DOI:10.1007/s11094-005-0144-6

Yemets YM. Dietary effects of drone larves homogenate on the homeostatic constants and the reproductive capacity of large white gilts Translat. Res. Vet. Sci. 2020;3(2):27-39, DOI: 10.12775/TRVS.2020.008

Yucel B, Acikgoz Z, Bayraktar H, Seremet C. The effects of apilarnil (Drone bee larvae) administration on growth performance and secondary sex characteristics of male broilers J Anim. Vet. Adv. 2011;10(17): 2263-2266, DOI:10.3923/javaa.2011.2263.2266

Yucel B, Sahin H, Yildiz O, Kolayli S. Bioactive components and effect mechanism of apilarnil J. Anim. Prod. 2019;60(2):125-130, DOI:10.29185/hayuretim.591007