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DERLEME /REVIEW

APITHERAPY AND APPLICATIONS IN VETERINARY MEDICINE

Veteriner Hekimlikte Apiterapi ve Uygulamaları

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ABSTRACT

The use of bees and bee products for therapeutic purposes in human and veterinary medicine is called apitherapy. Natural products have been used throughout human history to protect against and treat diseases. In recent years, the emergence of drug resistance and the occurrence of adverse effects associated with the indiscriminate and irregular use of pharmacological agents have prompted humanity to pursue alternative solutions. One of the most significant solutions is the administration of bee products. The use of bee products in apitherapy applications includes honey, bee venom, pollen, propolis, beeswax, royal jelly, perga and apilarnil (bee larvae). In general, apitherapy products with a wide range of indications are widely used in various system diseases and some dermatologic problems and various effects of these products such as antibacterial, antifungal, antiviral, antioxidant, anticarcinogenic, anti-inflammatory, antidiabetic and immunomodulatory effects *in vitro* and *in vivo* have been investigated in many different studies. Apitherapy is less common in veterinary practice than in human medicine. Additionally, bee products are employed in the treatment of other animal diseases, including gastrointestinal disorders, otitis, sinusitis, ophthalmic conditions, dermatological disorders, and skin care. Additionally, bee products are employed as food supplements for animals. The most prevalent additive in animal food is bee pollen. It has been demonstrated to promote growth, reduce mortality and prevent morbidity. Apitherapy has gained importance in the field of veterinary medicine in recent years in order to prevent both human health and economic losses, especially in the treatment of animals consumed as food.

Keywords: Apitherapy, Bee Products, Veterinary Medicine

ÖZ

Arı ve arı ürünlerinin insan ve veteriner hekimliğinde tedavi amaçlı kullanımına apiterapi denir. Doğal ürünler, insanlık tarihi boyunca hastalıklara karşı korunmak ve tedavi etmek için kullanılmıştır. Son yıllarda ilaç direncinin ortaya çıkması ve farmakolojik ajanların gelişigüzel ve düzensiz kullanımıyla ilişkili olumsuz etkilerin ortaya çıkması, insanlığı alternatif çözümler aramaya yöneltmiştir. En önemli çözümlerden biri de arı ürünlerinin uygulanmasıdır. Arı ürünlerinin apiterapi uygulamalarında kullanımı bal, arı zehri, polen, propolis, balmumu, arı sütü, perga ve apilarnil (arı larvaları) içerir. Genel olarak, çok çeşitli endikasyonlara sahip apiterapi ürünleri çeşitli sistem hastalıklarında ve bazı dermatolojik problemlerde yaygın olarak kullanılmaktadır ve bu ürünlerin antibakteriyel, antifungal, antiviral, antioksidan, antikarsinojenik, antiinflamatuar, antidiyabetik ve in vitro ve in vivo immünomodülatör etkileri gibi çeşitli etkileri birçok farklı çalışmada araştırılmıştır. Apiterapi, veteriner hekimliğinde insan hekimliğine göre daha az yaygındır. Ayrıca, arı ürünleri gastrointestinal bozukluklar, otitis, sinüzitis, oftalmik durumlar, dermatolojik bozukluklar ve cilt bakımı dahil olmak üzere diğer hayvan hastalıklarının tedavisinde kullanılır. Ayrıca, arı ürünleri hayvanlar için gıda takviyesi olarak kullanılır. Hayvansal gıdalardaki en yaygın katkı maddesi arı polenidir. Büyümeyi teşvik ettiği, ölüm oranını

azalttığı ve morbiditeyi önlediği gösterilmiştir. Apiterapi, özellikle gıda olarak tüketilen hayvanların tedavisinde hem insan sağlığını hem de ekonomik kayıpları önlemek amacıyla son yıllarda veterinerlik alanında önem kazanmıştır.

Anahtar Kelimeler: Apiterapi, Arı Ürünü, Veteriner Hekimlik

GENİŞLETİLMİŞ ÖZET

Amaç: Son yıllarda gelişen ilaç direnci ve ilaçların yan etkiler nedeni ile hem insan hem de hayvan sağlığında tıbbı alternatif çözümler aranmaktadır. Arı ürünleri de bu alternatif tedavi seçeneklerinin en önemlileri arasında yer almaktadır. Hayvanlarda apiterapi uygulamaları insanlarda olduğu kadar yaygın değildir. Antik uygarlıklar arı ürünlerini hayvanlar için de kullanmıştır, ancak günümüzde arı ürünlerinin pahalı, üretimin sınırlı olması, üretimin güvenilirliği ve canlılarda yan etkisi olup olmadığı konusundaki kuşkular sonucu uygulamalar sınırlı kalabilmektedir. Arılar, yüzyıllardır farklı medeniyetler tarafından çeşitli hastalıkların tedavisinde kullanılan bal, propolis, arı sütü, arı poleni, balmumu ve arı zehri gibi biyoaktif bileşenler içeren çok sayıda ürün üretir. Doğal ürünlerin araştırılması, çeşitli hastalıkları önlemek veya tedavi etmek için son zamanlarda önem kazanmıştır. Arı ürünlerine ve apiterapiye olan ilgi de artmıştır. Apiterapi, hastalıkları önlemek veya ilerlemelerini kontrol etmek için terapötik/profilaktik ajanlar olarak arılar veya ürünleriyle yapılan tedavidir. Günümüzde, apiterapi birçok ülkede tamamlayıcı ve bütünleştirici tıbbın bir parçasıdır. Ayrıca, içerdikleri besin maddeleri nedeniyle, arı ürünlerinin nutrasötik ve diyet takviyesi olarak tüketimi artmıştır. Arı ürünlerinin farmakolojik aktivitesi üzerine yapılan araştırmalar son yıllarda artmış ve çok sayıda biyolojik özellik ortaya çıkmıştır. *In vitro* ve *in vivo* çalışmaların yanı sıra klinik deneyler, arı ürünlerinin çeşitli hastalıkların tedavisinde ve sağlık dengesi ve homeostaz için endike olabileceğini göstermiştir. Buna ek olarak, arı ürünleri gıda, kozmetik ve ilaç endüstrisi tarafından yeni ilaç arayışlarında sürekli olarak kullanılmaktadır. Apiterapi veteriner hekimlikte farklı hayvan türlerine uygulanabilmektedir; Evcil hayvanlar, egzotik hayvanlar, çiftlik hayvanları, vahşi hayvanlar, kuşlar, sürüngenler. Apiterapi ile tedavi edilen hastalıklar çok çeşitlidir ve arı ürünlerinin yaygın kullanımı, anti-mikrobiyal, anti-enflamatuar, anti-radyoaktivite, anti-kanser ve yara iyileştirici özellikleri nedeniyle dikkat çekicidir. Balın floral kaynaklarına ve içeriğine bağlı olarak, antimikrobiyal, antiparaziter, antitümoral, immunmodülatör, antienflamatuar, antioksidan, gastroprotektif, kardiyoprotektif, hepatoprotektif, boğaz ağrısı, öksürük, astım, alerji, semtoplarını azaltıcı, analjezik, antianemik, antiosteoporotik, prebiotik, performans arttırıcı, fertilite arttırıcı ve yara iyileştirici birçok özelliği bulunmaktadır. Polenin antibakteriyel, antifungal, antioksidan ve antikanser özelliklere sahiptir. Polenlerin antimikrobiyal özelliği quersetin, mirsetin, kampferol gibi yapısında bulunan fenolik bileşiklerden kaynaklanmaktadır. Genellikle doğal antibakteriyel özellikleri nedeniyle, binlerce yıldır hem insanların hem de hayvanların sağlığını desteklemeye yardımcı olmak için kullanılmıştır. Evcil hayvanlardan çiftlik hayvanlarına kadar birçok hayvan arı propolisinden faydalanabilir. Genellikle solunum ve bağışıklık sistemlerinin sağlığını desteklemek ve antibakteriyel özelliklerinden dolayı daha spesifik hastalıklar için kullanılır. Arı propolisinin, hayvanlarda ve evcil hayvanlarda kanseri, inflamation ve tümörleri önlemede iyi bir doğal takviye olduğu gösterilmiştir. Birçok hastalıkta infilamasyona sebep olan T hücrelerinin üretimini engeller. Arı sütü, işçi arılar tarafından üretilen bir salgıdır ve yalnızca kraliçe arıya verildiği için etkili bir şekilde bir "süper besin"dir. Ayrıca çeşitli vitaminler ve amino asitler içerdiği anlaşılmıştır ve yüzlerce yıldır sağlığı desteklemek için kullanılmıştır. Arı sütünün koyun gebelik oranları ve kuzulama oranları üzerindeki etkilerini, incelenmiş ve etkili bulunmuştur. Hücre yenilenmesi, üretimi ve metabolizma üzerinde etkilidir. Bütün vücut dokularında canlılık, sağlık, enerji ve bağışıklık sağlamaktadır. Evcil hayvanlar için bal ve arı zehri karışımı uygulanan köpekler, kediler ve safkan yarış atları dahil olmak üzere evcil hayvanlardaki artritis ağrısını azaltmıştır. Eklem, kas hastalıkları ve kasların fonksiyonel bozuklukları bulunan evcil hayvanlarda etkili bulunmuştur. Arı zehiri çok güçlü bir ağrı kesici ve anti-inflamatuar etki sağlar. Düzenli olarak alındığında, zamanla eklem rahatsızlığını en aza indirmeye yardımcı olur, eklem hareketliliğini korur ve geri kazandırır. Apilarnil yüksek oranda protein, vitamin ve hormon içerir. Yapısındaki bileşikler sayesinde androjenik, anabolik, anti-lösemik, anti-anemik, antiaterosklerotik, renoprotektif, hepatoprotektif, nöroprotektif, hipolipidemik, üretrotropik, biyolojik

uyarıcı, immünmodülatör, enerji verici ve hücre yenilenmesini uyarıcı etkilerinden yararlanarak hayvan besleme, hayvan sağlığını koruma ve tedavide kullanılabilir.

Sonuç: Arı ürünleri hayvanlarda farklı etkiler gösterebilir. Arı ürünleri uygulandıktan sonra hayvanların ürüne olumlu tepki gösterme süresi değişiklik gösterebilir. Uygulanacak arı ürünlerini seçerken, mümkün olduğunca saf ve doğal bir ürün seçilmelidir. Eğer ürün uygulanacak hayvana bir tedavi uygulanıyorsa, arı ürünü kullanılmadan önce veteriner hekime danışılmalıdır. Arı ürünleri genellikle güvenli olsa da henüz tam olarak uzun hatta kısa vadede etkileri bireysel ya da tür olarak farklılık gösterebilir. Bazı insanlar ve hayvanlar, özellikle arı sokmalarına alerjisi olanlarda, arı ürünlerine alerjik olabilir. Uygulanacak arı ürününün hayvanların diyetine küçük miktarlardan başlayarak kademeli olarak arttırmak güvenli olur. Ayrıca doğal arı ürünlerinin renginde farklılıklar görülebilir. Bu durum normaldir, çünkü doğal ürünler oldukları için, renklerinde farklılıklar olabilir ve doğa tarafından standart şekilde üretilmemiş olmaları oldukça normaldir.

Bu ürünler geçmişten günümüze insanlar tarafından gıda maddesi olarak kullanılmaktadır. Bununla beraber sağlık üzerine olumlu etkileri olan bu ürünlerin tedavi amaçlı kullanımı da gün geçtikçe artmaktadır. Bu derlemenin amacı apiterapi ürünlerinin hayvanlar üzerinde, sağlıklı yaşamı korumak, desteklemek ve çeşitli hayvan hastalıkları üzerine olan etkilerini kullanım alanlarıyla birlikte vurgulamaktır. Bir arı ürünü bir hayvanda etkili olmasına rağmen bir sonraki hayvanda etkili olamayabilir. Her hayvanın ilaca ve diğer takviyelere tepkisi farklılık göstermektedir. Hayvanların apiterapi ürünlerine farklı sürede tepki verirler. Genel olarak, arı ürününü seçerken, doğal olması amaçlanan ürünlerden maksimum potansiyeli elde etmeye yardımcı olmak için mümkün olduğunca saf ve doğal bir ürün seçmeye çalışılmalıdır. Tüm tamamlayıcı tedavilerde olduğu gibi, bir arı ürününü kullanmadan önce, özellikle de hayvanların mevcut ilaçlarını kullanıyorsa, öncelikle veteriner hekim tavsiyesine başvurulmalıdır

INTRODUCTION

Recently, there has been an increasing focus on alternative medical solutions, driven by the need to address the challenges posed by drug resistance and adverse effects. These developments have been observed across both human and animal health. Of these alternative treatment options, bee products represent one of the most significant and promising areas of research. The use of apitherapy in animals is less prevalent than in humans. Ancient civilisations also used bee products for animals, but today applications may be limited due to the high cost of bee products, limited production, doubts about the reliability of production, and side effects that are not fully understood (Boukraâ 2023).

Apitherapy is an alternative treatment that uses honey, pollen, propolis, royal jelly and bee venom for health benefits. It has been used for thousands of years. The diseases treated with apitherapy are very diverse. Bee products are used for their antimicrobial, anti-inflammatory, anti-radiation, anti-cancer and wound healing properties. The medical treatments applied to humans and animals are similar. In this context, the concepts of human and animal health are not different. From a broad perspective, veterinary medicine aims to protect both human and animal health. It is reported that complementary and alternative therapies are not very common in basic veterinary education and practice worldwide.

Honey

Honey has a highly variable structure, comprising carbohydrates (glucose, fructose, maltose, sucrose, maltulose, isomaltose, and turanose), a water fraction, and a range of other components, including flavonoids, amino acids, phenolic acids, antioxidants, enzymes, vitamins and minerals (Alvarez-Suarez et al. 2014, Cengiz et al. 2018). One of the most important properties of honey is its antimicrobial effect. This activity is based on two principal sources. The first of these is the effect of H_2O_2 produced by glucose oxidase in honey in the presence of light and heat; the other is the non-peroxidal activity that inhibits microbial growth independently of light and heat. Honeys have two different characteristics as nectar and secretion honeys. Nectar-sourced honeys exhibit a higher concentration of glucose and fructose than their secretion-sourced counterparts. Secretory honeys are characterised by a higher mineral content. Furthermore, the pH of nectar-derived honeys is more acidic than that of secretion-derived honeys (Öner and Usta 2022).

The antimicrobial, antiparasitic, anti-inflammatory, antitumour, immunomodulatory, antioxidant,

gastroprotective, hepatoprotective, cardioprotective, respiratory system, cough, allergy, asthma, sore throat, painkiller, antianemic, performance enhancer, prebiotic, antiosteoporotic, fertility enhancer and wound healing properties of honey depend on the source and content of the honey in question (Sorucu 2019).

The most well known and demonstrated effectiveness of honey in animals, especially in treating burns and wounds resistant to conventional therapies (Chatzimisios et al., 2023, Lukanc et al. 2020, Vogt et al., 2021).

In clinical trials, the effects of honey on a wide variety of animals, including cattle, horses, dogs, cats, and swine have been extensively studied (Vogt at al, 2021).

Wound Treatment

When incorporated into an animal's diet, honey has been shown to accelerate wound healing and provide health benefits. It is hypothesised that the health-promoting properties of honey assist the immune system, including in animals with seasonal allergies. The health-promoting effects of honey are beneficial to a wide range of animals, including horses, dogs, other domestic animals and farm animals. A combination of honey and silver sulphadiazine has been employed in the treatment of burns in 15 adult dogs aged 4-5 years. Honey was applied to burn wounds in the dorsolateral region of the body. The reepithelialisation process was more pronounced in the dogs treated with honey, with the affected collagen fibres forming more regularly (Jalali et al., 2007). In cats, dogs, horses, and other animals, the administration of honey in conjunction with other therapeutic modalities has demonstrated efficacy in the management of laminitis, digestive problems, diarrhea, irritability, liver pathology (hepatopathy), arthritis, chronic cough, sinusitis, dermatological conditions, respiratory disorders, cardiac issues, hoof quality (hoof health), and renal dysfunction (Boukraâ 2023).

In one study, honey dressings were applied to canines with dermal wounds. The researchers reported that the healing of the wounds was rapid, that bacterial infections were successfully controlled, that necrotic wounds required less surgical intervention, and that honey was well tolerated by patients. In this study, the standard wound treatment applied to a 12-year-old Mechlin Shepherd dog with diffuse myiasis was unsuccessful in curing the disease. Subsequently, a honey compress treatment was initiated, and upon the animal's return for a follow-up examination five days later, it was observed that the superficial back wounds had almost completely healed, the deep wounds had diminished in size, and healthy granulation tissue had formed (Boukraâ 2023, Rooster and Declercq 2008).

The second case was a 9-year-old shar-pei referred for poor general condition, ulcerations on the tongue and a swelling on the medial side of the left heel marked by skin discolouration. The only treatment that was applied was honeydressing. By the seventh day, a clear granulation layer had formed at the wound site, and by the time that the sixth week had elapsed, the defect was almost completely healed with less scarring. (Boukraâ 2023, Rooster and Declercq 2008).

A nine-month-old boxer was burned on all four paws while playing with a plastic bottle containing a sodium hydroxide-based chemical in powder form. The dog developed exudative, malodorous necrosis, digital and interdigital skin loss, tendon exposure and large foot pad defects in all four paws. The wounds were treated with the application of gauze compresses impregnated with honey, which were then covered with a bandage. The bandages were changed on a daily basis. Initially, the animal showed pain for a short time after honey application, but after 7 days necrotic tissue and odour disappeared, and a clear granulation layer was formed at the wound sites on the paws (Boukraâ 2023, Rooster and Declercq 2008).

A five-year-old male Bernese mountain dog developed a parapreputial fistula following a celiotomy and prostate operation. Despite intravenous broad-spectrum antibiotic treatment, deep sampling and culture of the fistula was performed 5 days after the last surgical intervention and antibiotic-resistant Enterobacter cloacae was isolated. Topical treatment was initiated, given that the general condition was not impaired. Honey was applied to the fistula as deeply as possible with a 1mL syringe. During the first week, drainage from the fistula was significantly reduced. When the fistula was sampled and cultured again, E. cloacae did not grow. It took approximately 1 month for the fistula to disappear completely (Rooster and Declercq 2008).

Additionally, honey has been employed in the treatment of wounds in horses. The application of honey to leg wounds in horses has been

demonstrated to result in a reduction in wound size and an acceleration of the healing process. The healing time was found to be approximately 27% shorter (Bischofberger et al., 2011).

In one study, medicinal honey was used to treat an 8-year-old cat with complete skin loss over 100% of the limb circumference from elbow to claw and a contemporary ulnar fracture. In 49 days, 80% regression of the wound was observed. The wound fully healed with hair regrowth and minimal scarring. Furthermore, full functionality was restored to the affected limb (Figür 1) (Lukanc et al. 2020).

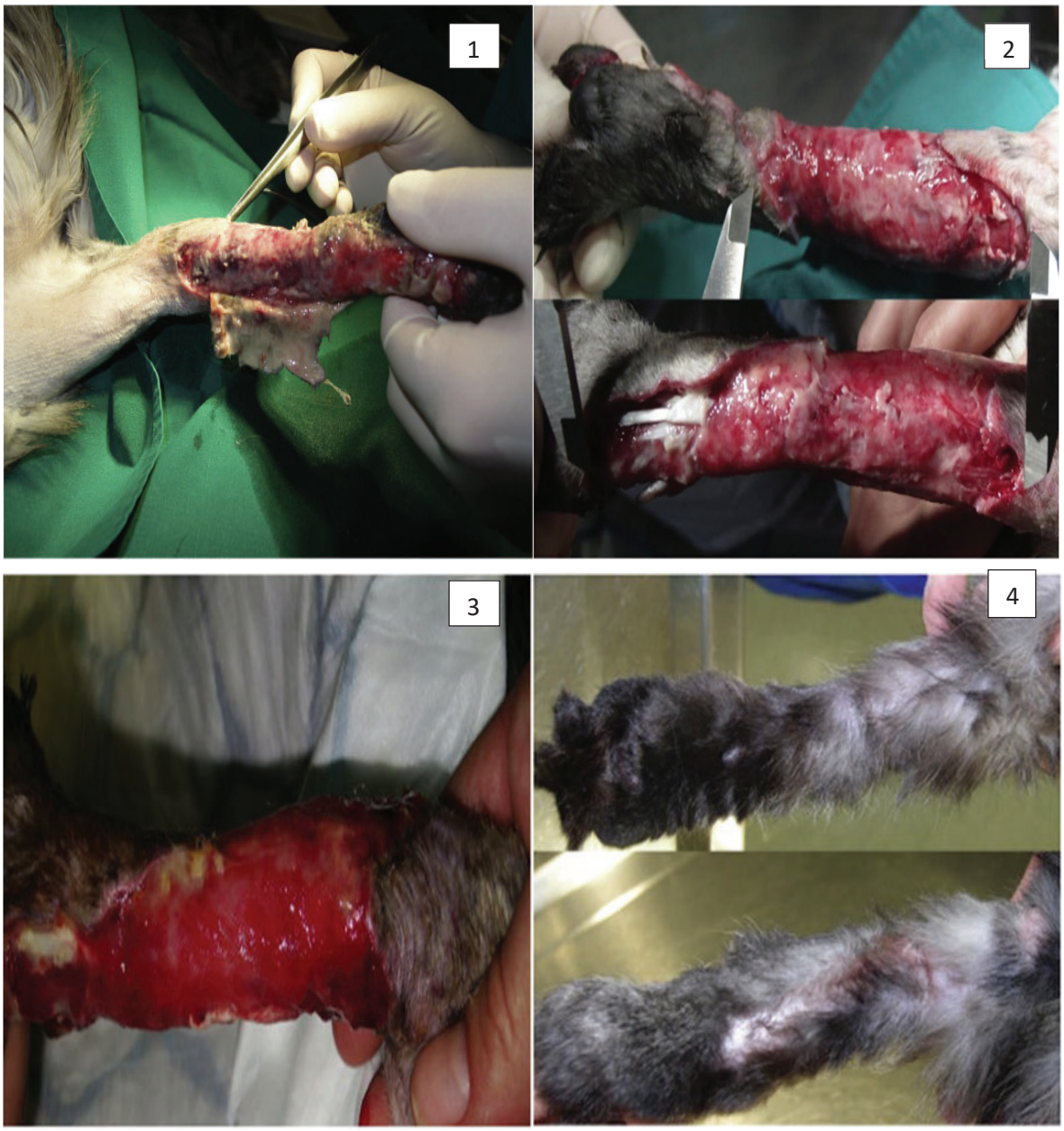

Figure 1. Wound healing after honey treatment application: **1.** Following the necrotomy, 2. On the seventh day following the application of honey, 3. On the fourteenth day following the application, 4. On the one hundred and fifth day (Original photo, V.Erjavec).

Honey has been used as a topical treatment for wounds in humans and animals for a considerable period of time due to its beneficial healing properties. In addition to its healing properties, honey has also demonstrated deodorising effects in malodorous wounds (Boukraâ 2023). The results of these studies demonstrate that honey is an effective and beneficial substance for promoting healing in wounds. Furthermore, it has been established that the treatment of such wounds with honey is more efficacious and cost-effective than other conventional ointments and wound dressings (Boukraâ 2023, Lukanc et al. 2020, Rooster and Declercq 2008).

Mastitis

Mastitis is defined as the inflammation of the mammary gland, which typically occurs in response to an intramammary bacterial infection. Mastitis represents a significant challenge globally, particularly within the context of dairy cow breeding. A study was conducted to assess the efficacy of honey in treating various bacterial strains associated with mastitis. The findings indicated that honey demonstrated sensitivity to these bacteria. Mastitis can be treated by administering honey via the udder duct to the infected udder. Honey does not damage the udder tissues and does not leave any unwanted residues in the milk. The administration of honey to animals with mastitis, even when it exhibits comparable efficacy to antibiotics, represents a viable and innocuous alternative to antibiotic treatment (Molan 2002).

The in vitro activity of different honeys against some mastitis-causing bacterial strains was investigated by Minimum Inhibitory Concentration (MIC) method and found to be effective. (Table 1).

Table 1. Efficacy on some strains of bacteria causing mastitis of natural and artificial honey

Bacteria species	Manuka Honey (%)	Rewarewa Honey (%)	Artificial Honey (%)
Actinomyces pyogenes	1-5	1-5	5-10
Klebsiella pneumoniae	5–10	5–10	>10
Nocardia asteroides	1–5	5–10	>10
Staphylococcus aureus	1–5	1–5	>10
Streptococcus agalactiae	1–5	5–10	>10
Streptococcus dysgalactiae	1–5	5–10	>10
Streptococcus uberis	1–5	5–10	>10

Source: Molan, P.C. 2002

Honey can be used for many purposes in veterinary medicine. The objective of the study was to assess the combined and individual effects of grayanotoxin-rich Turkish mad honey and 5-fluorouracil (5-FU) on colon cancer modelling in rats using N-methyl-N-nitrosourea (MNU) as a carcinogen. The findings indicated that mad honey and 5-FU reduced anaplastic cell growth and oxidative stress by inhibiting antiapoptotic activity. Additionally, the histopathological examination of the liver and kidney revealed no evidence of toxicity associated with the metabolism of mad honey and 5-FU. Consequently, it can be postulated that the concurrent administration of these two agents may represent a promising approach for the management of colon cancer (Kurtdede, et al. 2023).

Pollen

Pollen is a substance collected by bees from flowers with nectar, and it is a bioactive structure formed by flowering plants for the purpose of reproduction. It is notable for its high protein content. It has been demonstrated to possess anti-inflammatory, antioxidant and immunostimulatory properties. While it has the potential to be an effective treatment for allergic diseases, there is also a risk of an allergic reaction due to its protein density (Mărgăoan et al., 2019).

Pollen has antibacterial, antifungal, antioxidant and anticancer properties. This antimicrobial property of pollen is due to phenolic compounds such as quersetin, myrcetin, campferol (Onbaşlı 2019).

Bee pollen is frequently administered to animals for the purposes of bolstering immunity, enhancing digestive health, providing energy, and as an antibiotic. Furthermore, it is frequently employed as a means of mitigating the effects of pollen allergies.

Bee pollen is typically available in tablet or granule form. Pollen has been demonstrated to stimulate ovarian function. It has been determined that laying increased in hens whose ration was supplemented with 2% pollen and 5% animal proteins. Concurrent with the observed increase in egg-laying behaviour, there was also a notable enhancement in the resilience of eggs to the rigours of incubation. (Boukraâ 2023).

The sperm quality, fertility and blood profiles of male rabbits that were administered bee pollen demonstrated a notable enhancement. Furthermore, the offspring of rabbits that were administered bee pollen exhibited increased body weights and superior survival rates. The administration of bee pollen has been demonstrated to enhance reproductive performance in animals, as evidenced by increased rates of both birth and live offspring (Boukraâ 2023).

Bee pollen fed chickens had better development of duodenum, ileum and jejunum villi. The results of this study indicate that bee pollen may play a role in the early development of the digestive system (Boukraâ 2023).

There is some evidence to suggest that the ingestion of pollen may offer protection against the adverse effects of X-ray radiation treatments for both animals and humans (Schmidt and Buchmann 1992). The addition of pollen to the diet has been demonstrated to enhance the health, growth and utilisation of nutrients in domestic animals (Crane 1990). The addition of 2.5% pollen to the diets of chickens and piglets was observed to enhance their capacity to utilise feed (Ettle et al., 2006, Rodrigues et al., 2018). Furthermore, beekeepers provide their colonies with pure pollen, pollen supplements, or pollen substitutes when the availability of natural pollen sources is limited (Boukraâ 2023).

In a study examining the impact of pollen on immunity, it was reported that the addition of 1.5% pollen to the diet of broiler chickens over a 21-day period resulted in an increase in IgM levels (De Oliveira et al., 2013). It has been documented that the addition of pollen to poultry diets has been observed to have a stress-reducing effect and to positively influence animal performance (Seven et al., 2010).

Propolis

Trees secrete a resinous substance, which is collected by bees. Following a series of processing steps, the substance is transformed into propolis, a substance known to have beneficial properties. Bees utilise propolis to protect the colony against microorganisms by neutralising and coating the hive or creatures entering the hive from outside. The substance exhibits antibacterial, antifungal and anti-inflammatory properties (Prabhakar et al., 2016). It has been demonstrated that propolis is effective in the eradication of *Penibacillus larvae*, which are the causative agents of American foulbrood. (Sonmez et al., 2023, Toutiaee et al., 2023). The use of this substance has been documented for thousands of years, with a focus on its beneficial effects on human and animal health. Its natural antibacterial properties have been identified as a key factor in this regard. The benefits of bee propolis are not limited to humans; many animals, including pets and farm animals, can also derive advantages from it. The substance is frequently employed in the treatment of immune system and respiratory disorders, as well as more particular diseases, due to its antibacterial properties. The utilisation of bee propolis in the form of a natural supplement has been demonstrated in animal and veterinary studies to constitute an effective methodology for the prevention of cancer, inflammation and tumour formation in a variety of animal species. It has been demonstrated that this substance inhibits T cell production, which is responsible for the inflammatory processes observed in numerous pathological conditions. Propolis is a natural medicine that is safe for use in animals. No adverse effects apart from allergic reactions have been documented. Bee propolis is available in tablet form and can also be incorporated into toothpastes and skin care lotions (Abu-Seida 2023, Almuhayawi 2020, Kasote et al., 2022). Additionally, propolis has been demonstrated to enhance the immune system of animals. The administration of propolis to the diet of laying hens resulted in an increase in the production of immunoglobulin G (IgG) and immunoglobulin M (IgM). This consequently led to an enhancement of the immune system (Cetin et al., 2010).

The effects of propolis treatment on weight gain, growth rate, reproduction and meat quality were investigated (Bogdanov 2011.).

The utilisation of water-extracted propolis (WPP) as a treatment for Cushing's syndrome in canines represents a promising avenue of investigation, particularly given that there is currently no known cure for this syndrome. Moreover, the cost of treatment is considerable, and the efficacy of

available therapies is often limited. In certain instances, it has been associated with significant adverse effects, including mortality. The administration of propolis was observed to result in the remission of Cushing's syndrome after a period of three months (Glenn 2006).

It has been demonstrated that the incorporation of 500 ppm propolis into the diet of broiler chickens can lead to a notable increase in body weight, with a potential gain of up to 20% (Ghisalberti 1979).

The incorporation of 30 ppm propolis into the dietary regimen of laying hens led to a 5-6% enhancement in egg production, feed conversion efficiency, and chicken weight (Bonomi et al.,1976).

Staphylococcus aureus, which is an important pathogen for human and animal health, is an etiological factor causing mastitis in dairy cattle farms. It is very difficult to destroy *S. aureus* with antibiotics. In a study investigating the effect of propolis on mastitis, it was reported that propolis extract may be effective against the *S. aureus* species causing mastitis. However, milk components may reduce the effects of propolis. (Santana et al., 2012).

In order to investigate the effects of propolis on newborn calf diarrhea, a solution of propolis prepared with 2 cc of 96% ethyl alcohol was administered to the calves. Neonatal diarrhoea was not observed in calves at the end of one month (Tolon et al., 2002).

In a study, the antiparasitic effect of propolis in sheep was investigated. In this study, sheep naturally infected with *Trichuris* spp., *Trichostrongylus* spp. and *Ascaris* spp. were treated with a solution of 33% propolis extract. The total number of eggs in faeces was found to have decreased by 59.7% in the group of animals that had been treated with propolis, in comparison to the control group, which exhibited an increase of 63.6% in the same parameter (Morsy vd., 2013).

A study conducted by Aguiar et al. (Aguiar vd., 2014) to determine the effects of propolis on milk yield and quality showed that cows fed with propolis supplementation had higher protein content in milk and also had higher milk yield. Propolis is a rich source of flavonoids. In a study, an ethanol extract of propolis was administered at a dosage of 150 mg/kg in the form of a diet supplement. The results demonstrated that this treatment led to an increase in sexual activity, sperm concentration, sperm quality, and testosterone concentration (Hashem et al., 2013).

Dogs afflicted with a superficial dermal infection, attributable to pathogenic dermatophytes of the genera *Epidermophyton*, *Trichophyto*n and *Microsporum*, were subjected to a therapeutic regimen comprising weekly baths with a commercial soap formulated with propolis, along with a daily topical ointment for a period of three to eight weeks. Following a two-week course of treatment, all microbial cultures yielded negative results, and all three dogs were found to be free of lesions at the conclusion of the treatment period (Sánchez et al., 2014).

It has been used in dogs and cats with blepharitis, keratoconjunctivitis sicca, infectious conjunctivitis, corneal ulcers, corneal edema, tear duct obstruction, and glaucoma. A study was conducted to investigate the efficacy of propolis in the treatment of eye diseases in 25 dogs and 5 cats. A comparison of the recovery time for animals treated with allopathic eye washes and those treated with propolis revealed a notable difference. Those treated with propolis demonstrated a recovery time of five to seven days for acute cases and 10 to 15 days for chronic cases. It can be reasonably proposed, therefore, that propolis may prove an efficacious therapeutic agent for ophthalmic disorders without the attendant risks and at a relatively modest cost (Giral et al., 2007).

Propolis application was performed in periodontal diseases which are frequently seen in dogs, cause recurrent gingivitis and periodontitis and can cause tooth loss if left untreated. t was established that the utilisation of ethanol extracts of propolis in the treatment of dental caries in canines has the capacity to diminish inflammatory processes, facilitate the reorganization of tissue at the surface level and reduce bacterial activity. It is hypothesised that propolis may be utilised as an oral antiseptic without the potential for adverse effects (Ahuja and Ahuja 2011, Ilewicz vd., 1979).

Information on different clinical events and effects of propolis in dogs are shown in Table 2.

Notably, propolis, in its aqueous or ethanolic extract form, has been demonstrated to be an effective adjuvant in veterinary vaccines. Its efficacy in this role has been shown to be superior to that of conventional vaccine adjuvants (Ma et al., 2011). Additionally, propolis has been incorporated into canine parvovirus and canine coronavirus vaccines

(Das Neves Ferreira et al., 2012), as well as a vaccine against porcine parvovirus (Ma et al., 2011) and a vaccine against the bacterium *Aeromonas salmonicida*, the causative agent of furunculosis in fish. (Liu et al., 2020) resulted in a notable increase in antibody production.

Table 2. Areas and modes of action of propolis in dogs*

Therapeutic effect	Disease or microorganism
Antimicotic	**Canine otitis** *Malassezia pachydermatis* *Candida spp.* **Dermatophytosis** *Microsporum canis* *Microsporum gypseum*
Antineoplasic	Transmissible venereal tumor Osteosarcoma Cushing's syndrome
Bactericide	*Staphylococcus aureus* *Pseudomonas* ssp. *Proteus* ssp. *Escherichia coli*
Immunostimulant	Canine distemper Canine parvovirus
Oftalmic Blefaritis	Conjuntivitis Keratoconjuntivitis
Peridontal Clinical	Gingivitis Peridontitis
Metabolic	Liver diseases
Antiparasitic	Giardiais Trypanosomiasis

*(Betancourt et al. (2015)

Different forms of propolis have been used in various problems in animals and found to be effective. The efficacy of propolis has been demonstrated in the treatment of mastitis, gynaecological disorders, gastrointestinal and respiratory system problems, diarrhea in malnourished calves, wound management, local anaesthetics in surgical procedures, paratyphoid in ducks, foot-and-mouth disease and enzootic pneumonia in pigs. Additionally, propolis has been shown to stimulate growth in animals, with favourable outcomes (Bogdanov 2011).

Royal Jelly

A secretion of worker bees, royal jelly is a 'superfood' as it is only given to the queen bee. It has been used for hundreds of years to promote health and is known to contain a wide range of vitamins and amino acids. The impact of royal jelly on ewe pregnancy and lambing rates has been the subject of scientific investigation and has yielded positive results (Kridli et al., 2006). It provides vitality and therefore health, energy and immunity in all tissues of the body by influencing cell regeneration, production and metabolism (Aydın and Tekeoğlu 2018). It has been found that royal jelly can reduce cholesterol levels in the blood plasma, triglyceride levels and cholesterol deposits in the arteries of rabbits (Nakajin et al., 1982). Royal jelly has been reported to inhibit tumour growth in mice following prophylactic and therapeutic oral administration (Tamura et al., 1987). Furthermore, research has shown that royal jelly can reduce the healing time of skin lesions, exert an anti-inflammatory effect and accelerate wound healing. In rats, these effects have been evidenced by the acceleration of wound healing and the reduction of inflammatory responses (Fujii et al., 1990).

A study investigating the effect of royal jelly on the yield characteristics of laying hens revealed that the administration of lyophilised royal jelly at doses of 10 and 15 ppm led to a significant increase in egg production (10.5%–11%), feed consumption (21%–22%), egg weight (5%–4.8%), live weight gain (7%–6.5%), and yolk pigmentation (9.5%–9.7%) compared to the control group (Bonomi et al., 2000).

The combination of royal jelly and honey demonstrated a synergistic effect against pathogenic bacteria, indicating a potential use as an antimicrobial agent (Boukraa 2008).

In an experimental study, royal jelly was administered to mice with perforated eardrums for therapeutic purposes. Following the administration of royal jelly, it was observed that the eardrum tissue fibres and connective tissues of the mice exhibited a greater degree of fusion than in the control group. It was thus concluded that royal jelly application resulted in the successful healing of eardrum rupture (Calli et al., 2008).

A study examining the effects of royal jelly on reproduction reported that it increased spermatozoa density and spermatozoa motility, decreased the rate of abnormal spermatozoa, and positively affected semen quality in mice (Temamoğulları et al., 2006). It has been determined that royal jelly has positive effects on oestrus and fertility in sheep (Atabay 2012).

Royal jelly can help animals live a longer and healthier life. It has been demonstrated that royal jelly can mitigate the effects of cellular stress, which is a contributing factor in the development of age-related illnesses and diseases. Especially congenital joint, arthritis, osteoarthritis, disorders obesity or old age problems in pet animals can be reduced by giving royal jelly. Royal jelly early free radical

protection can slow down the development and reduce the severity of the disease. It should be noted that royal jelly may cause allergic and adverse reactions in some individuals. It is therefore advised that royal jelly should not be administered to pregnant animals or nursing mothers. The prevalence of allergic reactions in animals that consume royal jelly remains inconclusive. Nevertheless, it has been hypothesised that the likelihood of developing an allergy to royal jelly is increased in animals with a history of allergic disease (Boukraâ 2023).

It should be noted, however, that royal jelly has a limited shelf life. The process of refrigeration and freezing causes chemical changes that delay and reduce the favourable effects of the substance in question. It is recommended that royal jelly be cooled to a temperature between 0°C and 5°C. However, the optimal storage temperature is below -17°C. The average recommended storage period for products produced after this date is 18 months in the refrigerator. The recommended storage period for products stored at -17°C is 24 months, as this is the temperature that offers optimal stability. Freeze-dried royal jelly and royal jelly-based products can typically be stored at room temperature, with the potential for prolonged storage periods, sometimes exceeding several years (Boukraâ 2023).

Bee Venom

Bee venom is a secretion produced by the abdominal glands of honey bees. It contains a variety of bioactive peptides, including melitin, apamin and adolapin, as well as other components such as histamine, noradrenalin and dopamine. Additionally, it comprises enzymes (Aydın and Tekeoğlu 2018).

A range of biochemically and pharmacologically active substances have been identified in bee venom. These include polypeptides, including melittin, apamin, and mast cell degranulating peptides; amines such as histamine, serotonin, dopamine, and norepinephrine; and enzymes such as phospholipase, hyaluronidase, and histidine decarboxylase (Khalil et al. 2021).

Bee venom has been demonstrated to possess a number of beneficial biological activities. Of particular note is its efficacy in modulating the immune system. For a considerable period, this substance has been utilised in alternative medicinal practices with the aim of alleviating a range of pathological conditions, including those associated with discomfort and inflammatory responses (Jung et al., 2013).

A combination of honey and bee venom has demonstrated efficacy in alleviating arthritis pain in a range of animal species, including dogs, cats and thoroughbred racehorses. The treatment has been demonstrated to be efficacious in the management of joint and muscle diseases, as well as functional muscle disorders. Bee venom has been demonstrated to possess potent analgesic and anti-inflammatory properties. When administered on a regular basis, it has been demonstrated to reduce joint discomfort over time, while also maintaining and restoring joint mobility (Boukraâ 2023).

A study investigating the efficacy of bee venom in alleviating hip dysplasia in canines with arthritis revealed that cage activity in the treated group exhibited a marked increase, reaching up to 70% compared to the control group. Nevertheless, it should be noted that the use of this treatment is contraindicated in animals with a known allergy to bees (Vick, and Brooks 1972).

It has been reported that the application of cream containing 0.06% bee venom in corneal injury in dogs has high biostimulative, antiseptic and anti-inflammatory effects and provides faster and better quality healing compared to those in the control group (Krylov and Bardahchieva 1997).

The effect of bee venom supplementation on the performance, antioxidant activity and liver functions of broiler chicks was investigated in a scientific study. The findings indicated a notable increase in live weight gain by the 28th day. A notable increase in feed consumption was observed (Han et al., 2010).

The objective of the study was to assess the efficacy of bee venom in the treatment of mastitis. A total of 15 cows with confirmed mastitis were selected for participation in the study and were randomly divided into four groups. Each group received a different dose of bee venom administered subcutaneously: group 1 received 3 mg, group 2 received 6 mg, group 3 received 12 mg, and group 4 received 24 mg of the venom. The results of the analysis of milk samples collected three and six days after administration demonstrated a reduction in the levels of pathogens across all administered doses (Rahimjanova et al., 2022).

Perga (Bee Bread)

The main ingredient of perga, known as bee bread, is pollen. The worker bees mix the pollen with

enzymes they secrete and use it in the nutrition of the young and the queen. The distinction between pollen and perga is that the latter is fermented with bee enzymes. Perga is three times more nutritionally dense than pollen (Mărgăoan et al. 2019). It contains a higher concentration of free amino acids and readily assimilated sugars. Consequently, it has a high digestibility. It has been demonstrated to exert a beneficial influence on reproductive hormones. Thus, it is used to increase reproductive ability and to increase muscle strength and volume. It is employed in the management of blood pressure and chronic constipation as a result of the acetylcholine it contains (Parlakpınar and Polat 2021).

The bactericidal and bacteriostatic properties of bee bread are noteworthy characteristics. This study was conducted with the aim of evaluating the antimicrobial activity of bee bread extracts at varying concentrations against a range of bacterial strains. The bacterial strains tested were *Staphylococcus aureus*, *Escherichia coli*, *Bacillus cereus*, *Pseudomonas aeruginosa* and *Salmonella enterica*. The results of the study indicate that the initial two dilutions of bee bread extract (33% and 16.66%, respectively) demonstrated heightened antimicrobial activity, while the remaining dilutions exhibited diminished yet discernible activity contingent on the pathogen under examination. The highest antimicrobial efficacy was observed in the case of the *S. aureus* strain, with all dilutions demonstrating an inhibitory effect at both time points, 8 and 12 hours. (Urcan et al., 2018).

Apilarnil

It is a bee product called drone brood homogenate. The product is obtained by collecting and homogenising larvae of the drone larvae, which are approximately seven to eight days old and have not yet completed their development (Parlakpınar and Polat 2021). Apilarnil can be used in animal nutrition, animal health protection and treatment by taking advantage of its androgenic, anabolic, hepatoprotective, renoprotective, neuroprotective, hypolipidemic, anti-anemic, anti-leukaemic, antiatherosclerotic, urethrotropic, biological stimulant, immunomodulatory, energising and cell regeneration stimulating effects thanks to its high protein, vitamin and hormone levels (Sawczuk et al., 2022, Sidor and D˙zugan 2020).

In a study, it was determined that apilarnil had no effect on growth performance in broiler chickens. However, it was observed to stabilise blood glucose and cholesterol levels and to induce premature sexual maturity in male broiler chickens (Altan et al., 2013). Apilarnil is a highly androgenic compound that exerts a dual influence on the body, both androgenic and anabolic (Altan et al., 2013, Erdem and Özkök 2018).

Apilarnil has been demonstrated to increase blood testosterone levels, promote the development of secondary sexual characteristics, enhance the weight of sexual organs, improve sperm quality and quantity, and alleviate reproductive difficulties when administered to a range of animals, including rats, pigs, rams, and poultry (Bolatovna et al., 2015, Shoinbayeva 2017, Yucel et al., 2011).

It can have a direct effect on the quantity and quality of the sperm, allowing the male breeding animals to be used for a longer period. Apilarnil has been demonstrated to stimulate spermatogenesis in males due to its androgenic properties (Altan et al., 2013, Bolatovna et al., 2015). It has been found to increase the amount of sperm, improve sperm quality and quantity and relieve reproductive difficulties. As a result, Apilarnil has both an androgenic and an anabolic effect and can be used as a natural alternative to drugs and chemicals for the stimulation of growth and sexual development. Additionally, apilarnil can be employed as a natural substance due to its anabolic effects, which have been demonstrated to positively influence growth rate, feed conversion, and meat quality in animals (Yucel et al., 2011). The administration of Apilarnil to young pigs resulted in a 20.1-21.9% increase in seminal gland weight and a 21.8-25.8% increase in epididymis weight. Additionally, sexual dysfunction parameters in pigs exhibited an 83.3% improvement. Additionally, there was a 54.3% increase in ejaculate volume, a 27.1% increase in germ cell density, a 51.2% increase in survival rate, and a 14.2% increase in mobility. The percentage of damaged spermatozoa acrosomes decreased by 2.1%, while fertility increased by 76.4% (Bolatovna et al.,2015).

The study on correcting endocrine and metabolic conditions in dogs using apilarnil showed that administering apilarnil to dogs at a daily dose of 15 mg/kg for two months resulted in a significant increase in blood levels of thyroxine, testosterone, erythrocytes, haemoglobin, total protein, globulins and leucocytes (Efanova et al., 2019).

The beneficial effects of bee products on animals have been established through clinical studies, as evidenced in Table 3.

Table 3. A list of bee products whose positive effects have been demonstrated in animal studies*

Bee Product	Animals studied in vivo	Effects
Honey	Horse	Wound healing
	Cat	Wound healing
	Dog	Wound healing
	Mouse	Wound healing
	Rat	Gastroprotective effect Gastric ulcer treatment Hypoglycaemic and antioxidant effects Pancreas protection Cardioprotective effect Antidiabetic effect Anti-atherogenic effect
Propolis	Mouse	Antifungal activity in vulvovaginal candidiasis Antiparasitic (anti-malarial activity) against *Plasmodium chabaudi* Antiparasitic (anti-malarial) action against *Plasmodium falciparum* and *P. berghei* Antiparasitic effect against *Schistosoma mansoni* Anti-carcinogenic potential Reduction of oxidative stress to reduce hepatotoxicity and nephrotoxicity
	Honey bee	Antiparasitic effect against *Nosema ceranae*
	Rat	Antiparasitic effect against *Trypanosoma brucei* and *T. congolense* Wound healing Anti-carcinogenic potential Gastro-protective properties due to antioxidant and anti-*Helicobacter pylori* activity Protective role in the early stages of tongue cancer development Antimicrobial activity against mutans streptococci Prevention of tooth decay Effects of anti-caries Effects on chemoprevention and gastroprotection Healing of corneal wounds
	Dog	Wound healing Storage medium (in the case of tooth replacement) Antimicrobial effects for otitis externa
	Pig	Healing of burn wounds
	Chicken	Protective effect on kidneys and liver
Bee Venom	Dog	Anti-inflammatory and analgesic effects Healing effect on otitis externa caused by *Malassezia* Healing effect for facial paralysis
	Mouse	A neuroprotective effect in Parkinson's disease Neuroprotection in multiple sclerosis Antiviral activity against a wide range of viruses Neuro-protective effects
	Rabbit	Positive effects on the reproductive performance and on the immune response of the male animal Improving reproductive characteristics (sexual stimulant), immune response and health
	Chicken	Promoters of growth Effects as an immunoprophylactic
	Pig	Stimulation of antibody production and viral clearance in cases of infection with the PRRS virus Positive effects on growth, survival and the immune system

	Rat	Gastro-protective effect Anti-diabetic activity Analgesic activity Anti-bacterial activity against *Staphylococcus aureus*
Pollen	Rat	Anti-inflammatory and protective effects for treatment of prostatitis Healing effects in cases of prostatic hyperplasia and inflammation Protective role in diabetes-related problems with blood glucose control and sexual dysfunction in men
	Chicken	Positive effect on colonisation of intestinal microflora Promoters of growth Improvement of the growth performance and the immune system Improvement in weight gain and the rate at which food is digested Positive effect on daily gain, feed conversion and gut microbial composition
Royal Jelly	Rat	Liver and kidney protection during chemotherapy Nephro-protective effect Anti-fibrotic effect against pulmonary fibrosis Stimulation of the folliculogenesis and the secretion of the steroid hormones Improvement of bone strength after ovariectomy Prevention of osteoporosis after ovariectomy Improving male fertility and reproductive success
	Mouse	Immunomodulatory, antioxidant and anticancer effects Antioxidant, anti-inflammatory, apoptotic and anticancer effects Anti-aging effect Improving male fertility and reproductive success
	Rabbit	Relieving neurological problems after ovariectomy Improving male fertility and reproductive success
Apilarnil	Sheep	Reproductive stimulation in rams
	Rat	Androgenic effect on castrated male animals Hepatoprotective effects Neuroprotective effect
	Broiler	Androgenic effects, Reduced levels of blood glucose and cholesterol
	Pig	İncrease in the production parameters of the females Anabolic effect on females Improves fertility; stimulates reproductive function (by reducing time to first estrous cycle for insemination)

*Source: Stevanović J. et al. (2024)

The effects of a bee product on animals may exhibit variability. Following the administration of bee products, the time required for animals to demonstrate a favourable response to the product may vary. In selecting bee products for application, it is advisable to opt for those that are pure and natural to the greatest extent possible. In the event that a treatment is to be applied to the animal, the advice of a qualified veterinarian should be sought prior to the use of the bee product. While bee products are typically regarded as safe, the precise long- or short-term effects may vary considerably between individuals or species. It is possible that some individuals and animals may exhibit an allergic response to bee products, particularly those who have previously experienced an allergic reaction to bee stings. It is safe to introduce bee products into the diet of animals gradually, commencing with minimal quantities.

It should be emphasised that in veterinary practice apitherapy can only be administered after examination by a licensed veterinarian. Apitherapy has great potential for use in veterinary medicine. Officially, however, it can only be used as a complementary treatment. A growing body of evidence highlights the value of apitherapy in promoting animal health and vitality. As a result, there is increasing interest among pet owners and veterinarians in the use of bee products. However, they need to be aware of the potential risks

associated with apitherapy, including potentially fatal anaphylactic reactions in certain cases, However, further preclinical and clinical studies are needed to fully understand the basic mechanisms of action of bee products and to determine optimal doses and methods of application in animals.

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