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Review

The use of propolis as an antimicrobial in livestock – an overview

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Abstract. *The purpose of the present study was to review scientific reports on propolis used in livestock, to analyze them and to make appropriate summaries and conclusions. Propolis is a natural resinous substance collected by honey bees (Apis mellifera L.) from different plant parts such as buds, branches, leaves and exudates. Propolis is a known source of polyphenols and the flavonoids which have been widely studied as biochemical markers for botanical origin and to explain their antioxidant capacity as a key factor in chemoprevention. Antimicrobial, anti-inflammatory and anticancer biological activities of propolis are known. Propolis has been used as a remedy in traditional medicine systems all over the world, mainly to treat wounds, burns, sore throat and stomach ulcer, etc. Modern science has confirmed the antimicrobial and antiviral action of propolis and has discovered numerous other beneficial pharmacological properties of bee glue: immunomodulating, anti-inflammatory, antiobesity, antitumor, and many others. For this reason, a significant number of products containing propolis have been developed and commercialized: medical devices, over-the-counter preparations, health foods and beverages, cosmetics. Recently, studies on the effects of propolis on animal husbandry and animal health have increased due to many issues, such as organic animal breeding, feeding or treatment methods, reducing the use of antibiotics. One of these areas is the use of propolis to improve the growth performance and productivity of the livestock. Propolis has been determined to have antibacterial and antiviral effects in humans and animals.*

Keywords: propolis, livestock, antimicrobial activity, animal health and productivity, replacement

Introduction

The emergence and spread of antimicrobial resistance has become a major public health problem, within the EU and world-wide. Overuse and misuse of substances to kill or inhibit the growth of microorganisms (including bacteria, viruses and fungi), and certain parasites (for example protozoa) have favoured the growth of resistant organisms. This so-called "antimicrobial resistance" can spread to other microbial populations. Infections by resistant organisms endanger the human population, animals and plants, including those not previously in contact with antimicrobial agents (Eur-Lex, 2001).

Today, as feed additives in animal feeding, synthetic products, uncontrolled antibiotics and anabolism have been prohibited in European Union countries and in Turkey. EU standards for the authorization of antibiotics and other drugs are implemented in Turkey (Anonymous, 2013). Most of the feed additives used in animal nutrition and the drugs used in the treatment of animals cause residues in nature. Instead of synthetic feed additives and antibiotics, research should be focused on the use of natural products, medicinal and aromatic plants or similar products in animal nutrition in animal husbandry (Duru and Sahin, 2014). It is predicted that the intensive use of antibiotics, especially synthetic products, will increase the number of bacteria resistant to antibiotics and that there may be mass deaths from many bacterial diseases in the world in the next 15-20 years (O'Neill, 2014; Michael et al., 2014; Şenol, 2017). In terms of human health, the world is now turning to more natural ways and products (Carvalho et al., 2015; Yildirim et al., 2015).

Too much antibiotic is consumed in the world. Estimates of the amount of antibiotics used in animal husbandry worldwide vary between 63,000 and 240,000 tons. It is estimated that the use of antibiotics in livestock will increase year by year and the amount of antibiotics to be used in animal husbandry between 2010 and 2030 will increase by 67% (Thomas et al., 2015). For example, 1,173,000 tons of red meat and 2,400,000 tons of poultry meat were produced in 2017 in Turkey. Total meat production is estimated at 3,573,000 tons. It is hard to predict how much antibiotics have been used. It is the reality that 65.1 mg of antibiotic is used for 1 kg of meat. When this is the case, it can be said that the amount of antibiotic used in animal husbandry is about 13-14% of the total amount of antibiotics used in Turkey. Recently, and fortunately, studies on the effect of

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propolis on animal husbandry and animal health have increased due to many factors such as organic animal breeding, feeding or treatment methods and reducing the use of antibiotics.

Apitherapy, or bee-therapy could be described as using bee products in the treatment of diseases or in the prevention of diseases. The main bee products used are honey, beeswax, bee pollen, propolis, royal jelly, apilarnil and bee venom. These products comprise numerous substances, have long been known for their medicinal and health-promoting properties. Their wide biological effects have been known and used since antiquity. Bee products are considered to be a potential source of natural antioxidants such as flavonoids, phenolic acids, or terpenoids (Kocot et al., 2018).

In the studies conducted on animals, the usefulness of using bee products (propolis, bee pollen, and royal jelly) as natural agents that are capable of counteracting the effects of oxidative stress underlying the pathogenesis of numerous diseases or disorders, such as neurodegenerative disorders, cancer, diabetes, and atherosclerosis, as well as negative effects of different harmful factors and drugs have been determined (e.g., cytostatic agents) (Kocot et al., 2018). Therefore, it is necessary to turn to natural products. Propolis includes antiviral, antioxidant, antibacterial, hepatoprotective, antifungal and immuno-stimulating activities and possesses many biological properties (Saeed et al., 2017). Using raw propolis is not very economical and useful. Therefore, it is more economical and useful to make it liquid and use by extraction. Studies on the use of propolis, which is a natural product, should be increased instead of the use of antibiotics and similar chemicals rather than/in order to stop the use of antibiotics and similar chemicals and more studies should be conducted on the use of it.

Propolis is a natural resinous substance collected by honey bees (*Apis mellifera* L.) from different plant parts such as buds, branches, leaves and exudates. Propolis is used by bees to coat the hive, to fill in cracks and the cracked parts of the hive, to harden and to repair the honeycomb edges, to reduce the hive entrance for easy defense, to disinfect and to polish the queen bee before laying and to mummificate the outsider bodies which are large enough to enter and exit the hive (Sun et al., 2015; Pasupuleti et al., 2017; Kocot et al., 2018).

The existence and the usability of propolis date back to ancient civilizations. Greeks and Egyptians first used propolis as an antiseptic. Since the 12th century, propolis has been used in Europe for the treatment of oral and throat infections and skin disorders. During the Anglo-Boer War and World War II, doctors used propolis to heal wounds (Yılmaz and Özcan, 2004; Özturk, 2010; Yavuz, 2011; Silici, 2015; Yonar, 2017). In summary, propolis has been used by humans since ancient times either in the treatment of various diseases or in reducing the effects of the disease.

Modern herbalists recommend propolis for human use in medicine because of its antibacterial, antifungal, antiviral, hepatoprotective and anti-inflammatory properties to increase the body's natural resistance to infections and to treat gastro-duodenal ulcers. For this reason, a significant number of products containing propolis such as medical devices, over-the-counter preparations, health foods, beverages and cosmetics have been developed and commercialized (Pasupuleti et al., 2017).

Propolis contains more than 300 biochemical constituents, including mostly a mixture of polyphenols, flavonoid aglycones, phenolic acid and their esters, and phenolic aldehydes and ketones, terpenes, sterols, fatty acids, vitamins and amino acids (Park et al., 2000; Alencar et al., 2007; Morsy et al., 2015; El Guendouz et al. 2019). Propolis has been used as a remedy in traditional medicine systems all over the world, mainly to treat wounds and burns, sore throat, stomach ulcer, etc. After 2000 close to 4000 scientific studies have been published by Elsevier and about 3000 - by PubMed.

Based on the above mentioned arguments, it is important to know how propolis can be used in livestock farming. The present paper attempts to analyze the available information on the topic and to draw conclusions and recommendations.

The propolis use in animal husbandry

In the last years many investigations have been conducted in order to discover new alternative feed additives which are considered natural products that consumers would accept. Propolis is one of them and can be considered among the natural feed alternatives to antibiotics in ruminant diets. Propolis extracts were found to have a promising effect on decreasing the energy lost as methane (CH_4) and total nitrogen (N) losses in ruminant production systems that may limit production performance and contribute to the release of pollutants to the environment. However, these effects are diverse among propolis types. Because of the higher antimicrobial activity of propolis against gram positive than against gram negative bacteria, propolis might be a natural useful alternative to antibiotics supplementation for modifying microbial fermentation in the rumen to reduce the loss of energy as methane (CH_4) (Yavuz, 2011; Morsy et al., 2011, 2015).

In a study conducted to evaluate the prevention of diarrhea and feed evaluation in piglets, it was found that the diarrhea rate seen in the piglets fed with the ration including propolis was 52% less than in the control group (Guo and Ding, 2010). In another study conducted to determine the effects of propolis on diarrhea seen in newborn calves, red propolis supplementation was determined to have some potential to improve calf health and reduce the incidence of diarrhea and, as a consequence, the use of antibiotics in calf rearing systems (Slanzon et al., 2019). Propolis serves to rear healthy calves and also improve live weight gain and growth. It is evident that propolis is a suitable natural product for ecological animal production (Yucel et al., 2015).

Gubicza and Miller (1987) established that diarrhea problems of milk-fed calves are less common with propolis usage. In another study, the calves were given 2cc propolis (prepared with 96% ethyl alcohol solution). Neonatal diarrhea was not seen in the propolis group calves. At the end of the study, the average live weight was found to have increased in the propolis group by 46.07 g/day, which was more than the live weight gain in the control group calves (Tolon et al., 2002).

Due to the high content of propolis in flavonoids, it can affect the reproductive performance of the animals. Propolis administration was found to have a good impact on pregnant ewes' health and may be a promising feed additive during critical

periods such as flushing (Morsy et al., 2013). According to another study by Marsy et al. (2016), propolis supplementation increased average daily gain and milk conversion ratio but had no effect on lamb birth and weaning weights

Mohamed (2017) established that propolis had positive effects on the sperm properties in ram as a natural antibiotic and that it influenced the enzymatic activities, the penetration ability and protection from bacterial contaminations. There are some studies claiming that it could be an alternative to the synthetic antibiotics used in freezing and storing the sperms (Gloria et al., 2014; Mohamed and Zanouny, 2017; Mohamed, 2017).

Propolis was found to be an effective natural alternative to parasitological drugs to control helminthiasis and to decrease significantly the total fecal egg count (FEC) in grazing Santa Inês ewes (Morsy et al., 2013) using ethanolic extract of red propolis (3 g/ewe/day) during the flushing period. Using alcoholic extract of propolis at 33% in 20 cattle (12 months) naturally infected with *Trichuris* sp., *Trichostrongylus* sp., and *Ascaris* sp., which were administered in single doses once or twice a day for three consecutive days and, 30 days after the start of treatment, an average reduction of 59.7% was found in the FEC count between animals receiving treatment and an average increase of 63.6% was found in the control group of animals that did not receive any treatment (Dürrewald et al., 2008). Thus, it can be concluded that propolis can enhance the oxidative status of the blood plasma and it may indicate an activation of the animal's immune system since propolis has anti-inflammatory and immune modulatory activities. Propolis can modulate lipid and protein metabolism and has hepato protective effect.

Propolis application also provides positive results against the mastitis which is a significant problem in milk breeding. Mastitis treatment is usually done with antibiotics. In a study done on quails, propolis was concluded to have decreased the microbial activity on the shell surface (Aygun and Sert, 2013).

The addition of propolis to the feed of egg-laying hens influenced the egg quality and some serum parameters positively (Silici et al., 2018). It was reported that propolis is effective on antibody production in poultry farming and that the usage of propolis particularly in vaccination processes makes the vaccine more effective and results in antibody increase (Wang et al., 2006; Kong et al., 2006; Freitas et al., 2011). Propolis supplementation increased the antibody response to Newcastle disease virus, infectious bursal disease, and avian influenza (Taheri et al., 2005; Ziaran et al., 2005), but had no effect on infectious bronchitis (Taheri et al., 2005). Similarly, Freitas et al. (2011) stated that supplementation of propolis in laying hen feed (50 mg/kg) increased the production of IgG specifically to red blood cells of the laying hens and natural antibodies; indicating that propolis could be used to increase antigen-specific antibody responses to vaccines. In some studies, the addition of propolis to broilers and laying hens feed reduced mortality rates (Mahmoud et al., 2016). Broilers fed diets supplemented with propolis showed reduced mortality, decreasing by 3 to 7% (Omar et al., 2004; Shalmany and Shivazad, 2006; Tatlı Seven**,** 2008; Tatli Seven et al., 2008; Tatli Seven and Seven, 2008; Mahmoud et al., 2016). Similarly, mortality rate was reduced by 3.34% in heat stressed laying hens treated with 2 or 5g propolis/kg diet (Tatli Seven, 2008; Seven et al., 2011; Mahmoud et al., 2016).

The propolis extract demonstrated to possess bactericidal properties against studied microorganisms in descending order as follows: *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pyogenes*, *Pasteurella haemolytica* and *Salmonella* spp. All these results show the possibility of using propolis in either treatment alone, as a natural alternative, or being associated with an appropriate antibiotic for the potentiating effect in the event of serious infections in animals. Using a remarkable natural product of bees, propolis provided more health beneficial actions, including antibacterial effect, against 6 bacterial species responsible for severe infections in farm animals (Schnitzler et al., 2010; Mot et al., 2014).

Propolis is made up of complex chemical compounds, which is the most important group of phenolic acid components, which play a significant role in antiviral activity. Propolis was tested for the activation of it against several animal viruses, such as infectious bursal disease virus and avian reovirus (Hegazi and Abd El Hady, 2001; Abd El Hady and Hegazi, 2002; González-Búrquez et al., 2018) in addition to Newcastle virus disease, bovine rotavirus (Bernal, 1991; González-Búrquez et al., 2018), pseudorabies virus (Burquez et al., 2015), and bovine viral diarrhea virus (Cueto et al., 2011; González-Búrquez et al., 2018). It was also demonstrated that the flavonoid possesses extensive pharmacologic effects, including antimicrobial (Pepeljnjak et al., 1985; Del Rayo Camacho et al., 1991; González-Búrquez et al., 2018), antioxidant (Santos et al., 1998; María et al., 2018), antimutagenic, and anti-inflammatory properties (Sala et al., 2003; González-Búrquez et al., 2018).

Conclusion

The conducted studies demonstrated that propolis has natural anti-bacterial, anti-viral, anti-fungal, anti-oxidant, and anti-inflammatory properties. Numerous scientific investigations have been focused on the biological activities of propolis and its functions as a health supplement in humans. It could have similar function in livestock. For this purpose, many studies on the subject have been done on different animals and poultry. In studies on farm animals, the positive effect of propolis supplementation on reproduction, digestion, semen and live weight was determined. Again, in animals, propolis has been reported to have therapeutic or protective effect instead of antibiotics against certain diseases. The remnants of feedstuffs used in animal husbandry, and especially the antibiotic residues, are considered to be an important public health problem. It should be seen as a problem not only for humans but also for animals. Propolis is a natural product for human and animal health and therefore, more studies on the use of propolis in animal husbandry should be done.

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