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Nanotechnology and nano-propolis in animal production and health: an overview

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ABSTRACT

Nanotechnology is the science and technology of small and specific things that are <100 nm in size. Because of the size of nanomaterials, new changes in their chemical and physical structure may occur, and indicate higher reactivity and solubility. Many of nanotechnology applications in food and agricultural production are being developed in research and development settings. Global challenges are related to animal production, including environmental sustainability, human health, disease control, and food security. Nanotechnology holds promise for animal health, veterinary medicine, and some areas of animal production. Nanotechnology has had application in several other sectors, and its application in food and feed science is a recent case. Especially, natural nano antimicrobials obtained from different techniques such as nano-propolis are useful to veterinary medicine in terms of health, performance, and reliable food production. Nano-propolis is a nano-sized (1–100 nm in diameter) propolis particles tied together to make it more effective without changing its properties by changing the size of propolis by different methods. Propolis have many advantages such as anti-inflammatory, antioxidant, anticancer and antifungal activity, etc. The consumption of free form of propolis restricts these benefits due to low bioavailability, low solubility, low absorption, and untargeted release. Different nanoencapsulation technologies are used to obtain nano-propolis. Nano-propolis are more easily absorbed by the body because they have a size smaller. Nano-propolis is also more effective than propolis in terms of antibacterial and antifungal activity. This review focuses on some recent work concerning the uses of nanotechnology in animal health or human health using animal models, and the effectiveness of nanotechnology on natural supplements such as propolis used in animal nutrition and animal health.

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Introduction

The term ‘nano’ is derived from a Greek word meaning ‘the dwarf’ and is generally used combined with other words such as nanometre, nanobots, nanotechnology, etc. (Chakravarthi and Balaji 2010). Nanotechnology is the science and technology of small things (<100 nm) with new changes in their chemical and physical structure, and also higher reactivity and solubility (Troncarelli et al. 2013). Stability of the substances is increased because of their protection against oxidising agents, other compounds or enzymes when the active component is nanostructured (Brandão et al. 2011; Troncarelli et al. 2013). Results are promising that will permit scientists to apply processes more rapidly and

efficiently, and, maybe, at a lower risk to consumers. However, more studies are still needed to support the value, and the reliability of nanotechnology, while preventing any damage to the environment or to human beings (Ramírez-Mella and Hernández-Mendo 2010).

Nanotechnology represents advances and developing technology in the molecular, atomic and macromolecular fields (Scott 2005; Troncarelli et al. 2013). It offers scientific advantage with its rapid and specific moves, besides high bioavailability, and biodegradability properties. All these advantages have significant effects on both production and economic losses in livestock animals, and healthier food and feed production. The use of nanotechnology devices for diagnosis

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of animal diseases or as animal models for the diagnosis of human diseases is a great accomplishment in one health initiative (Bentolila et al. 2009; Num and Useh 2013). Advances in nanoscience have a significant potency to solve the problems in the animal health field. It can solve lots of mysteries related to animal health, reproduction, production, good hygienic practices and maintaining of food animals. However, the use of nanotechnology in these area is not widespread [Australian Pesticides and Veterinary Medicines Authority (APVMA 2015)].

Bee glue or propolis is a substance that is collected by honeybees from different plant sources such as eucalyptus, chestnut and oak. Propolis has several biological activities such as antioxidant (Gul Baykalir et al. 2016), anti-inflammatory (Funakoshi-Tago et al. 2015), antibacterial (Seven et al. 2011), antifungal (Shokri et al. 2017) and antiviral (Schnitzler et al. 2010), among others. Nano-propolis that is a natural nano-material can be useful to veterinary medicine in terms of health, performance, and reliable food production. The nanoparticles are more easily absorbed by the body because they have a size smaller (Sahlan et al. 2017), while the nano-propolis is more effective than propolis in terms of antibacterial and antifungal activity (Afrouzan et al. 2012).

The studies related to nanotechnology have been on the consideration to develop improvements in techniques of animal production, it is necessary to enforce this knowledge for animal health. Research focussed on human health is already done using animal models, but sufficient information is not available about nanotechnology. The most important point that should not be forgotten in nanotechnology studies necessary to include ethical, environmental and food safety factors (Ramírez-Mella and Hernández-Mendo 2010).

This review focusses on some recent work concerning the uses of nanotechnology in animal health or human health done using animal models, and also effectiveness of nanotechnology on natural supplements such as propolis used in the animal nutrition and animal health.

Nanoparticles

Nanoparticles are particles with at least one dimension smaller than 1 micron and potentially as small as atomic and molecular length scales (~0.2 nm). Nanoparticles can have amorphous or crystalline form and their surfaces can act as carriers for liquid droplets or gases. To some degree, nanoparticulate matter

should be considered a distinct state of matter, in addition to the solid, liquid, gaseous, and plasma states, due to its distinct properties (large surface area and quantum size effects). Examples of materials in crystalline nanoparticle form are fullerenes and carbon nanotubes, while traditional crystalline solid forms are graphite and diamond (Buzea et al. 2007). In nanotechnology, nanoparticle is described as a small object that behaves as a whole unit for its transport and properties. Particles are further classified by diameter. Ultrafine particles are the same as nanoparticles and between 1 and 100 nanometres in size. Fine particles are sized between 100 and 2500 nanometres. Coarse particles cover a range between 2500 and 10,000 nanometres. Nanoparticle research is currently an area of intense scientific interest owing to a great variety of potential applications in biomedical, optical, and electronic fields (Bagheri et al. 2016).

A series of nanoparticulate systems, which include functionalised fullerenes and carbon nanotubes, iron oxide nanoparticles, liposomes, dendrimers, polymeric micelles, polymeric nanospheres, nanoshells, nanobins, quantum dots, and polymer-coated nanocrystals used to treatment of human diseases (McMillan et al. 2011; Troncarelli et al. 2013). The small-sized nanoparticle contains similar physiological molecules, which also might allow it to utilise the same mechanisms of entry across internal barriers (Troncarelli et al. 2013). On this basis, a comprehensive study regarding the possible use of suitably performing nanoparticles for disease control or diagnosis and treatment of organs protected by internal barriers has been progressing in recent years (Pietrojusti et al. 2013; Troncarelli et al. 2013). Nanostructures are outfitted with smart particles to allow their delivery outside certain biologic barriers such as the brain, skin, eye, mucus, blood, cellular, extracellular matrix placenta, and subcellular organelles (Troncarelli et al. 2013). Smart delivery systems have multifunctional properties for successful marking. In addition, they might have been pre-programmed, time controlled, spatially targeted, self-regulated and remotely organised (Scott 2005; Troncarelli et al. 2013). Especially, smart delivery system is needed for drugs used in the treatment of human and animal diseases. One of the main problems that contribute to a low efficiency in drug delivery is the low drug concentrations to the active location and the very short drug residence time in the cellular and anatomical location. In recent years, smart polymeric nanodelivery systems have shown extraordinary capability to get over many of the anatomical and physiological barriers and deliver drugs locally to sites of interest thus improving therapy. The current focus in the pharmaceutical

industry is moving towards a smart drug, which increases the effectiveness and decreases the toxicity (Venditti 2017).

Nanotechnology in animal health and production

Nanotechnology has the potential to solve many mysteries related to animal health, production, reproduction, good hygienic practices during rearing and maintaining of food animals. The technology application is usable especially with livestock. Nanotechnology is no longer a concept or theory of the new world, but has become a new enabling technology over the years, with enormous potential to revolutionise agriculture and livestock development over the world. It can supply new vehicles for molecular and cellular biology, biotechnology, veterinary physiology, reproduction and much more (Patil et al. 2009). For example, it can be used for pathogen detection, so there are several areas that nanotechnology could be applied in the science and engineering of agriculture, animal, and food systems (Patil et al. 2009; Scott and Chen 2012).

Many applications of nanotechnology for food and agricultural production are being developed in research and development settings. Global challenges are related to animal production, including environmental sustainability, human health, disease control, and food security. Nanotechnology holds promise for animal health, veterinary medicine, and other areas of animal production (Scott 2005; Kuzma 2010). Animal production and nanotechnology are important areas of research and development. However, there is not yet enough common use of nanotechnology in the market (Kuzma 2010). Therefore, careful analysis of the potential technical, societal, and policy implications of these emerging applications is timely. Besides, animal welfare, safety of animal-derived products, risks to the environment and human health, and industry consolidation are among the many concerns that are likely to be derived from biotechnology to nanotechnology. Furthermore, for many of the newest nanotechnology products proposed for livestock production, biotechnology and nanotechnology are inseparable, and the two converge in particular products or applications. It is important to the public as nanotechnology and livestock production matures (Kuzma 2010). Lately, nanotechnology has a range of potential applications for animal production systems, including new tools to aid animal breeding, targeted disease treatment delivery systems, new materials for pathogen detection, and identity preservation systems (Buyukkilic and

Konca 2010). For example, micro and nanofluidic systems are used for the mass production of embryos for breeding; drug delivery systems able to diffuse inaccessible parts of an animal's body; more biologically active drug compounds; and sensors for monitoring livestock health and locations (ETC Group 2004).

The development of agriculture and animal husbandry are important for animal health. Therefore, nanotechnology has become more important for veterinarians. Likewise, nanotechnology has a significant potency to solve the problems in the animal health field (Scott 2005). Nanoparticles have been used in treating poultry infections. Poultry is a key source of *Campylobacter* infection in humans and its prevalence in carcasses is very high (Keener et al. 2004; Manuja et al. 2012). Researchers have hypothesised about reducing *Campylobacter in vivo* using polymeric nanoparticles fed to turkeys (Franklin et al. 2003; Manuja et al. 2012). Nanoparticles consisting of a polyethylene glycol linker, polystyrene base and a mannose targeting biomolecule that adheres to *Escherichia coli* have been developed (Manuja et al. 2012). The particles bind the pathogens in the gut of livestock to prevent colonisation and growth, and are removed in the waste. The nanoparticles could replace traditional sub-therapeutic uses of antibiotics and reduce the development of antibiotic-resistant bacteria. Silver nanoparticles have been used as an additive in diets for weanling pigs resulting in an increase in their growth (Fondevila et al. 2009; Manuja et al. 2012).

The Cu (II)-exchanged montmorillonite nanoparticles (MMT-Cu) have been used to investigate the effect on growth performance, digestive function and mucosal disaccharase activities of weaned pigs (Tong et al. 2007; Manuja et al. 2012). The potential effect has been reported to be mediated through antimicrobial properties of the nanoparticles. The addition of MMT-Cu to the diet increased the average daily weight gain, feed efficiency, and digestibility as compared with those of the control and copper sulphate groups (Tong et al. 2007; Manuja et al. 2012). Nano-sized minerals, vitamins or supplements developed for food application in human beings can also be used for animal feed. Nano-sized additives have also been specifically developed for animal feed. Nano-sized liquid vitamin mixes are available for use in poultry and livestock feed (Manuja et al. 2012).

One of the important targets in livestock is to have a good control mechanism developing new systems to ensure early diagnosis by farmers or veterinarians. The smart treatment delivery systems are considered in nanotechnology, and these systems include biological and bioactive systems such as useful feed

supplements, drugs, nutraceuticals, and implantable cell bioreactors (Scott 2005).

Natural products and nanotechnology has had a developing application in several other sectors, and its application in food and feed science is a recent case (Jelinek et al. 1989; Manuja et al. 2012; Hamad et al. 2017). Moreover, nanotechnologies used to improve food quality and food safety [Nanotechnology Industries Association (NIA 2015)]. Particularly, nanotechnology has been utilised to improve finding of a range of chemical and microbial contaminants in feeds. Especially, feed spoilage by fungi can be a problem for feed security. It may result in heating and mustiness, reduced palatability and the loss of nutritive value (Bryden 2012). Due to poor storage conditions of animal feeds, many fungi grow easily and produce toxins causing mycotoxicosis. The economic effects of this contamination on the agriculture sector is enormous, because it reduced the nutritional value of food and feedstuff, decreased animal meat production, and toxified the users of dairy products. A nanocomposite of MgO–SiO₂ has been used as an effective adsorbing agent for removal of aflatoxin from wheat flour (Manuja et al. 2012). Similarly, a modified montmorillonite nanocomposite has been used to reduce the toxicity due to aflatoxin in feeds of broiler chicks (Shi et al. 2006; Manuja et al. 2012).

Li et al. (2008) reported that several natural and synthetic nanomaterials have showed powerful antimicrobial properties through different mechanisms, including photocatalytic production of reactive oxygen species that damage cell components and viruses (for example zinc oxide and titanium dioxide), compromising the bacterial cell cover [for instance, silver nanoparticles (nAg), chitosan, carbon nanotubes, carboxyfullerene, peptides and zinc oxide], interruption of energy transduction [e.g. aqueous fullerene nanoparticles (nC60) and nAg], and inhibition of enzyme activity and DNA synthesis (such as chitosan) (Wassel and Khattab 2017). The use of antimicrobial nanoparticles produced with natural actives indicates significant safety and efficiency outcomes against bacterial infections in animals, without causing residues in animal products, with no need for withdrawal.

Naturally, occurring chitin and certain peptides have been long recognised for their antimicrobial properties (Li et al. 2008). As known, inorganic arsenic (As-III) is a common component of the Earth's crust. It can be introduced into drinking water sources through different activities. The natural occurrence of inorganic As (III) in drinking water causes significant concern because of its marked negative effects on human health (Zavareh et al. 2015).

Various adsorbents are being used to remove As (III) from drinking water. Nowadays, for this purpose, the use of nano-sized metaloxide and hydroxide adsorbents (such as oxides/hydroxides of iron, aluminium, manganese and zirconium) is effective and attractive. Makwana et al. (2014) reported that cinnamaldehyde is a principal ingredient of cinnamon which contains an essential oil which is 60–75% of the total oil. Cinnamaldehyde is one of the molecules of importance for development as a food antimicrobial agent due to its demonstrated activity against both Gram-positive and Gram-negative bacteria, including organisms that are of concern for food safety. Cinnamaldehyde is recorded as a flavouring agent by the food and drug administration and is permitted to be added to food (Makwana et al. 2014). Makwana et al. (2014) informed that cinnamaldehyde was found to be an effective antimicrobial against *Escherichia coli* W1485 and *Bacillus cereus* ATCC 14579 in buffer solutions. In addition, researchers reported that the antimicrobial effect of cinnamaldehyde rose by encapsulation in nanoliposomes. This study showed that the potential usefulness of progressive antimicrobial glass surfaces coated with nano-encapsulated cinnamaldehyde for active packaging of liquid foods.

Nano-propolis in animal health and production

Propolis (bee glue) is a substance that is an adhesive and dark yellow to brown-coloured balsam. It is collected from some parts of trees and plants such as eucalyptus, chestnut and oak by bees and obtained by mixing with their wax (Tatli Seven et al. 2012; Hasan et al. 2014). It is used today in drug and personal products. Besides, the antimicrobial action of propolis known as a natural product is recognised worldwide (Troncarelli et al. 2013). Propolis and nanostructured systems which are known as antibiotics, hormones, probiotics, prebiotics, and immunomodulators can be used as growth promoters in animals. The use of antibiotics as growth promoters in animals brings out problems associated with microbial resistance and antibiotic residue (Fahri 2009). Propolis has also effects antioxidative, antimutagenic, immunomodulatory, and cytostatic properties. These effects of propolis are associated with its structure including rich flavonoid, terpenoid, and phenolic acid (Prytyk et al. 2003; Tatli Seven et al. 2009, 2012). Antioxidant, antibacterial and antifungal properties of propolis, colligate with the fact that several of its contents are present in food and/or food additives, and are recognised and generally known as safe (Burdock 1998), which makes it an

indispensable candidate as a natural preservative in new food applications. This meets the demand for natural-based antioxidants and antimicrobials, fuelled by the increasing user demand for natural, minimally processed foods with traditional preservatives at no or at very low concentrations (Han and Park 1995; Tosi et al. 2007).

Propolis is potentially very beneficial. It was reported that propolis has an efficacy against the inhibitory effects of free radicals and as an antibacterial (Hasan et al. 2014; Schmidt et al. 2014). Barud et al. (2013) determined that the ethanol extract of propolis is 70% effective at inhibiting the growth of microorganisms. It was reported that propolis has antibacterial effects. *Streptococcus mutans* is a bacteria that causes dental caries. Propolis can be used as an alternative in the prevention of dental caries reducing the number and growth of *S. mutans* (Dziedzic et al. 2013). Hasan et al. (2011) reported that propolis can be used as an antibacterial agent for *Salmonella thipymurium*. Besides, propolis is able to inhibit *E. coli* and *Staphylococcus aureus* (Popova et al. 2013). It was found that propolis is an active compound against the bacteria *S. aureus* (Trusheva et al. 2010). The results of the study showed a larger clear-coloured zone with an increase in the concentration of propolis. However, how propolis inhibited the bacteria is unknown (Hasan et al. 2014). Sabir (2005) hypothesised that some constituents in propolis could limit the bacterial enzyme RNA polymerase ability to attach to the DNA. Consequently, bacterial DNA replication does not occur. At the same time, important compounds of propolis have the ability to prevent the action of the enzyme restrictive endonucleases that do not occur in RNA transcription ending with disrupted cell division. Fatoni (2008) noticed that flavonoids and tannins are the most effective components on bacteria of propolis. In addition, Sabir (2005) stated that the hydroxyl group of flavonoids may be able to decrease toxic effects of bacteria, the changing transport systems of nutrients and structure of organic compounds.

Nano-propolis is a nano-sized (~1–100 nm in diameter) propolis particles which are tried to be made it more effective without changing its properties by changing the size of propolis by different methods. Nano-propolis can result in better efficacy in the fields of medical science and biology (Afrouzan et al. 2012). Propolis does not have a good solubility in water. Nano-propolis would raise the ability to dissolve a substance achieving better solubility compared to propolis. Nano-propolis can more easily enter through the outer membrane of bacteria in order that the active antibacterial compounds can harm bacterial cell walls.

Nano-propolis is obtained using microencapsulation method (Kim et al. 2008; Sahlan and Supardi 2013; Hasan et al. 2014). Sahlan and Supardi (2013) used encapsulation methods to obtain nano- and micro-propolis by casein micelles to improve its handling properties. Researchers noticed that Indonesian propolis was encapsulated by casein micelle with a homogeniser following a sonication, and separated by a micro- and ultra-filtration system, creating micro- and nano-particles. These micro- and nano-particles exhibited high flavonoid and moderate polyphenol capacities (encapsulations efficiency, 94 and 67% for flavonoids and polyphenols, respectively). In a further step, the size of particles was analysed by a particle size analyser which showed that the average size was 1.3 µm and 300 nm. The morphology of particles was analysed by transmission electron microscopy. Researchers stated that micro- and nano-propolis might be used as antimicrobials agents or for other purposes in food or healthcare products (Sahlan and Supardi 2013). In a previous study, Szliszka et al. (2009) reported that propolis had inhibition of matrix metalloproteinases, anti-angiogenesis, prevention of metastasis, cell cycle arrest, and induction of apoptosis. Besides, propolis has shown no systemic toxicity or side effects upon *in vivo* administration to both rats and humans. Therefore, there is a pressing need to find new techniques to increase the potential of propolis. Recent studies (Jayakumar et al. 2013; Do Nascimento et al. 2016) reported the encapsulation of propolis extract in nanoparticulate systems. Chitosan was used to obtain nanoparticles. Elbaz et al. (2016) investigated chitosan-based nano-in-microparticle carriers for enhanced oral delivery and anticancer activity of propolis. *In vitro* cytotoxicity studies showed that the propolis-loaded nano-in-microparticles induce more cytotoxic effect on human liver cancer cells than human colorectal cancer cells and mediated three-fold higher therapeutic efficiency than free propolis. The propolis-loaded nano-in-microparticles induce apoptosis of human liver cancer cells and significantly decrease their number in the proliferative.

Propolis has already been encapsulated with different methods as in alginate microparticles, by atomisation methods, using gelatine as encapsulant, by the emulsification-solvent evaporation technique at microparticules of poly (ε-caprolactone) and by incorporation in a β-cyclodextrin (Nori et al. 2010). The results presented in the study (Nori et al. 2010) determine that it was possible to encapsulate propolis extract with soy protein isolate and pectin by complex coacervation process and thus to obtain it in the powder form, free of alcohol and with possibility of release

Table 1. The results of some studies related to nanopropolis.

Source	Activity	Size of particles	Target	Type of treatment	Synthesis methods	Findings
Hasan et al. (2014)	Antibacterial (agar well diffusion method)	≤175 nm (SEM-FTIR)	Gram-positive Gram-negative bacteria (<i>in vitro</i>)	Encapsulation (Maltodekstrin)	High-speed homogenisation technique	The nanopropolis showed higher bacterial activity than extract propolis were 205.86% for <i>B. subtilis</i> , 211.83% for <i>S. aureus</i> , 227.01% for <i>E. coli</i> , and 230.29% for <i>Salmonella</i> sp.
Afrouzan et al. (2012)	Antibacterial Antifungal (agar well diffusion method)	<100 nm (SEM)	<i>S. aureus</i> , <i>C. albicans</i> (<i>in vitro</i>)	Encapsulation	Milling media method	Inhabitation zones of propolis and nanopropolis <i>S. aureus</i> ($p < .01$), <i>C. albicans</i> ($p < .05$).
Kim et al. (2008)	Antitumor (soft agar)	50 nm (DLS- TEM)	Human pancreatic cancer, cell mice (<i>in vitro</i> and <i>in vivo</i>)	Encapsulation	FTIR NMR	Inhibits pancreatic cell growth in murine xenograft models and growth of pancreatic cancer cell lines <i>in vitro</i> .
Qurbatussofa (2013)	Antibacterial (disc diffusion method)	176.30, 205.10, 295.80 nm (PSA)	<i>E. coli</i> (<i>in vitro</i>)	Encapsulation	Aimi	Result activity antibacterial nanopropolis with disc diffusion methods against <i>E. coli</i> indicated nanopropolis does not have antibacterial, because nanopropolis does not produce clear zones in disc paper area.
Prasetyo et al. (2011)	Antibacterial (agar well diffusion)	175–873 nm (SEM-FTIR)	Gram-positive Gram-negative bacteria (<i>in vitro</i>)	Encapsulation (Maltodekstrin)	High-speed homogenisation technique and solvent evaporation	Nanopropolis showed higher bacterial activity than extract propolis were 208.86% for <i>B. subtilis</i> , 211.83% for <i>S. aureus</i> , 227.01% for <i>E. coli</i> , and 230.29% for <i>Salmonella</i> sp.
Hasan et al. (2012)	Antibacterial (agar well diffusion method)	100–322 nm (SEM)	<i>E. coli</i> (<i>in vitro</i>)	Mengkapsulasi propolis	Homogenise in high speed	Antibacterial activity evaluation shows on nanopropolis concentration 10–0.02% active on <i>E. coli</i> (inhibit the growth of <i>E. coli</i> at very low concentrations)
Sahlan and Supardi (2013)	Antibacterial	1.3 μm–300 nm (TEM-PSA)	<i>B. subtilis</i> , <i>S. aureus</i> , <i>Micrococcus luteus</i>	Encapsulation (casein micelle)	High-pressure homogeniser	Encapsulated Indonesian propolis has antibacterial activity.

TEM: transmission electron microscopy; SEM: scanning electron microscopy; FTIR: Fourier transform infra-red spectroscopy; DLS: dynamic laser light scattering; NMR: H-nuclear magnetic resonance; PSA: particle size analyser.

under controlled conditions in foods. The authors informed that this process protects antioxidant compounds such as the phenolic and flavonoids present in the free propolis and as well as its inhibitory activity to *S. aureus*. Nano-propolis is expected to supply better antibacterial activity compared to propolis (Hasan et al. 2014). It has been shown that nano-propolis inhibits *E. coli* growth even in very small amounts (Prasetyo et al. 2011; Hasan et al. 2012). Propolis has an antibacterial activity by encapsulation of *Bacillus subtilis* (Sahlan and Supardi 2013; Hasan et al. 2014). It was determined that propolis and nano-propolis of Iranian origin showed different real activity against some bacteria (*S. aureus* and *Candida albicans*) (Afrouzan et al. 2012; Hasan et al. 2014). Hasan et al. (2014) found that nano-propolis was more effective bacterial activity compared to propolis against *Bacillus subtilis*, *S. aureus*, *E. coli* and *Salmonella* sp., 206, 212, 227, and 230% respectively. Antibacterial activity of nano-propolis was examined compared with antibiotics. The same study used ampicillin to compare the antibacterial activity as a positive control. The reason for using ampicillin as a positive control was for a broad-spectrum antibiotic that can inhibit both Gram-positive and Gram-negative bacteria (Hasan et al. 2014). Researchers (Hasan et al. 2014) used the concentration of ampicillin at 10 mg/mL. The efficacy of nano-propolis in comparison with ampicillin (100%) for *B. subtilis*, *S. aureus*, *E. coli* and *Salmonella* sp. was 44, 49, 42, and 38% respectively. The clear area of nano-propolis significantly varied with ampicillin for all test bacteria (Hasan et al. 2014). In a research using tetracycline, nano-propolis was more effective against *S. aureus* than tetracycline, with 20 mm diameter inhibition zone (Gonsales et al. 2006; Afrouzan et al. 2012). Afrouzan et al. (2012) showed that antimicrobial activity of nano-propolis in comparison to propolis was more effective. The inhibition zone diameters of nano-propolis were significantly higher than propolis against both *C. albicans* ($p < .05$) and *S. aureus* ($p < .01$).

Afrouzan et al. (2012) reported that the antimicrobial activity of nano-propolis was more effective against Gram-positive bacteria than yeast. They suggested that the causes for nano-propolis being more effective in antibacterial activity than antifungal activity could be due to the characteristic of cell walls differences present in membranes of bacteria and yeast, the antibacterial activity, and the thickness of the peptidoglycan layer (Afrouzan et al. 2012). Afrouzan et al. (2012) showed that natural nanoparticles have the potential to be used efficiently in the control of bacterial and fungal diseases. Fahri (2009) studied potency of nano-propolis as a growth promoter using *in vivo*

assays on male rats. In this study, encapsulated propolis nanoparticles that had been prepared by the high-speed homogenisation technique followed by encapsulation using maltodextrin with solvent evaporation technique were used. The size of nano-propolis was evaluated by scanning electron microscope. Researcher used the body weight of rats to determine how propolis affects the bacteria. It was found that the highest effectiveness reached by nano-propolis 2%, with effectivity of 109% compared to the positive control, and the most stable count of *E. coli* on faecal material in nano-propolis of 2%.

Chung et al. (2010) investigated the hypoglycaemic effect of nano powder propolis. Streptozotocin-induced diabetic rats were divided into two groups: a diabetic control group and a group to which nano powder propolis (0.9 mL) was administered. After the rats were fed with nano-propolis for 4 weeks, an oral glucose tolerance test was made, and then blood sugar, blood lipid levels and body weights were measured after 16 h fasting. Chung et al. (2010) determined that the nano-propolis was effective in the treatment of diabetes because of the reduction of blood sugar level and the regeneration of damaged β -cells observed in streptozotocin-induced diabetic rats.

The antibacterial effect of Chinese propolis and nano-propolis on common pathogens *in vitro* was investigated (Jingli and Feili 2008). According to the study, while both Chinese propolis and nano-propolis could inhibit bacteria effectively, nano-propolis showed more effective inhibitory activity. However, it was determined that their inhibitory effect on *S. aureus* was weaker than oxacillin and vancomycin. The results of some studies related to nano-propolis are summarised in Table 1.

Conclusions

Nanotechnology is effective in almost every area of concern to human and animal health. Nanotechnology offers scientific advantage with its rapid and specific moves, besides high bioavailability, and biodegradability properties. All these advantages have significant effects on both production and economic losses in livestock animals and more healthy animal production. Nanomedicines against various pathogens in veterinary medicine could be developed. Especially, natural nano-antimicrobials such as nano-propolis are useful to veterinary medicine in terms of health, performance, and reliable food production. There is a need to increase research because of the paucity of research currently being done on this topic.

Disclosure statement

No potential conflict of interest was reported by the authors.

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