



# Potential Role of Propolis Nanoparticles in Medicine and Health: An Updated Review

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**Abstract** | Nanotechnology is defined as the science and technology of small objects with a diameter of less than 100 nanometers. Nanomaterials may undergo novel chemical and physical changes as a result of their size, indicating increased reactivity and solubility. Nanotechnology has a huge potential to make a major change in the agriculture and livestock sector. It can introduce new tools for molecular and cellular biology, biotechnology, veterinary physiology, animal genetics, and reproduction. Nano-propolis is beneficial to veterinary medicine in different aspects by varying the size of propolis using various techniques, nano-propolis can be more effective without compromising its qualities. Propolis has numerous benefits, including anti-inflammatory, antioxidant, anticancer, and antifungal properties. Low bioavailability, solubility, absorption, and untargeted control, the advantages of free form propolis are limited due to previous reasons. Nano-propolis is made using a variety of nanoencapsulation processes. Because of their smaller size, nano-propolis is more utilized by the body than the free one. This study focuses on some current research on the application of nanotechnology in animal health and human health utilizing animal models, as well as the usefulness of nanotechnology on natural supplements like propolis used in animal nutrition and health.

**Keywords** | Nanotechnology, Nano-Propolis, Animal production and health, Natural products

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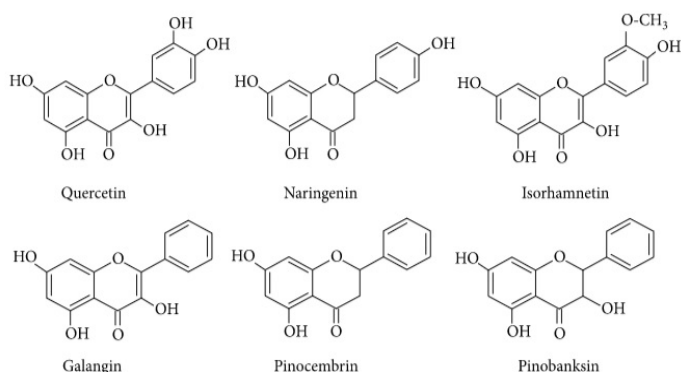
## INTRODUCTION

Nanotechnology is the science of very tiny objects with adjacent chemical and physical structures, as well as increased reactivity and solubility. When the active constituent is nanosized, the substance's stability is boosted due to its protection from oxidizing agents, other chemicals, and enzymes (Kirtane et al., 2021). It is predicted for nanotechnology to do significant advances in medicine, as gene therapy, imaging, and novel drug discovery and drug delivery in the treatment of several diseases as diabetes, cancer, and others, in addition to advances in electronics, material science, space research, and robotics (DiSanto et al., 2015; Mohamed et al., 2021). Nanotechnology has a broad and possible impact on veterinary medicine and improves the safety of domestic animals, production, and income to the farmers by using nanomaterials. Approaches in nanoscience have the potential to solve substantial

challenges in the field of animal health. It has the potential to resolve dozens of new mysteries relating to veterinary fields (Şenel, 2020).

Propolis is a plant resin obtained by bees via variety of plant parts to protect the hive from insects and microbes while also maintaining the hive's appropriate temperature and humidity, it is dark yellow to brown glue and balsam (Drescher et al., 2019). Propolis contains at least 300 components, with resins (50 %), waxes (30 %), essential oils (10 %), pollen (5 %), and other organic compounds (5 %) accounting for the majority. Phenolic parts and esters, as well as various kinds of flavonoids, terpenes, steroids, aromatic beta-aldehydes, alcohols, sesquiterpenes, and stilbenes, can all be found among the organic components. The interaction of these chemicals produces a synergic effect that is crucial to propolis' biological activity. Rutin, caffeic acid phenethyl ester (CAPE), quercetin, p-coumaric

acid, benzoic acid, galangin, pinocembrin, chrysin, and pinobanksin are the active constituents initiating the pharmacological actions of it (Hegazi et al., 2019). Chemical structures of various constituents of propolis were revealed in Figure 1.



**Figure 1:** The examples of flavonoids and their glycosides detected in bee products (Kocot et al., 2018).

CAPE is also known as an immunomodulator, and it should be evaluated as an option for reducing an overactive inflammatory response. Flavonoids and phenolic acids, as well as their esters, are pharmacologically active compounds in propolis. Bacteria, fungi, and viruses are all affected by these components in different ways. Propolis and its constituents also have anti-inflammatory (Inui et al., 2021) and immunomodulatory properties (Yosri et al., 2021). Propolis has also been demonstrated to reduce blood pressure and cholesterol (Sforzin et al., 2017). There are several categorizes of propolis differ in botanic origin, physical-chemical features, and geographic location, green propolis, brown propolis, red propolis, and yellow propolis are all types of propolis (Santos et al., 2020).

Propolis is beneficial in the treatment of gastrointestinal problems in animals (Pasupuleti et al., 2017). Also, propolis is a promising supplement for improving sheep production growth and health via adding it to their milk and improved its antibacterial, antioxidant, and immunological responses (Cécere et al., 2021). Calves fed on diets contain nano-ZnO and propolises in comparison to control diet has caused to decreasing faecal, nasal and ocular excretion scores (Seifdavati et al., 2018). There was a need to reduce or eliminate the use of growth-promoting antibiotics in cattle; in some countries, so it is critical to look for alternatives such as propolis (Fugita et al., 2017).

Health achievement, and consistent food manufacture, nano-propolis, a natural nano-material, can be effective in veterinary medicine. Because of their smaller size, nanoparticles are more utilized by the body than free one and more effective in antibacterial and antifungal activity (Sahlan et al., 2017; Afrouzan et al., 2012). NanoBone graft material is a newly created and authorized granular

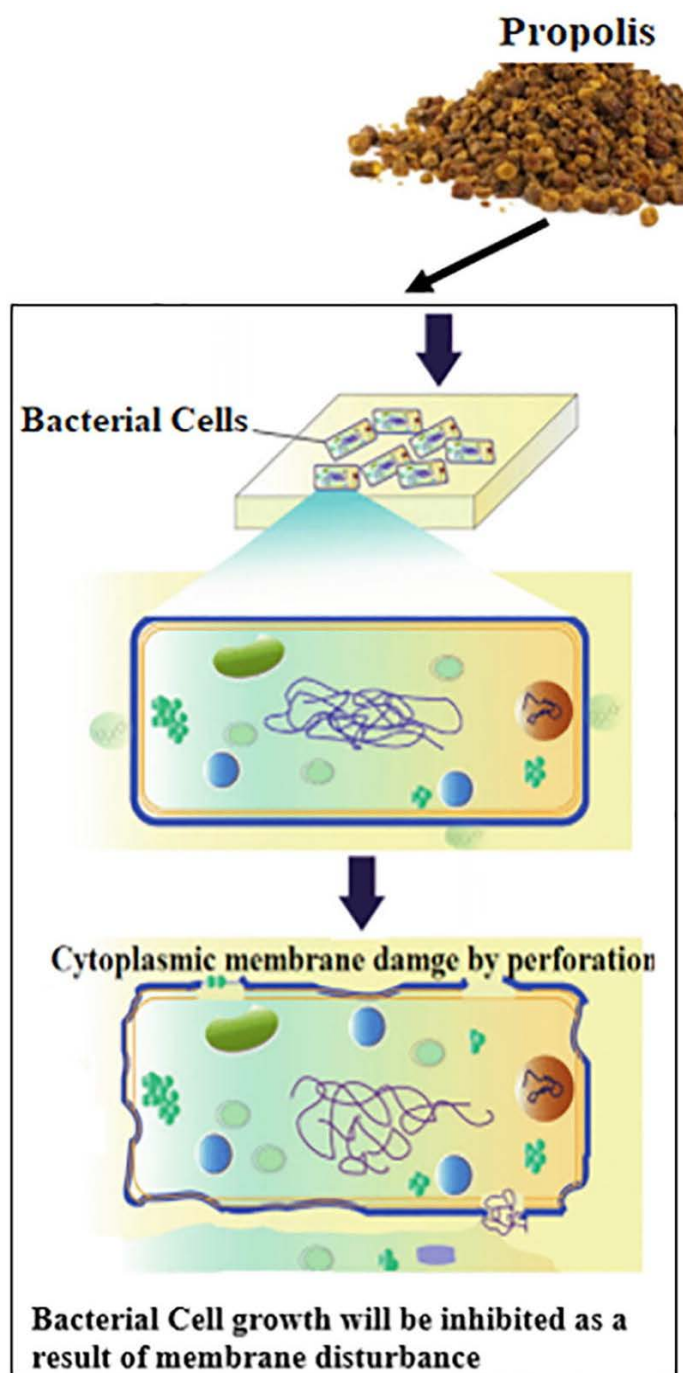
material for bone regeneration that is made up of synthetic nanocrystalline hydroxy-appatite embedded in a silica gel matrix that mimics the structure of normal bone tissue (Soliman et al., 2020). Nanobone and propolis in combination produced better effects than nanobone alone. This could be explained by the surface texture of nanobone, which serves as a propolis reservoir and enables for continuous propolis supply in the regenerated area (Ibrahim et al., 2019). This review article focuses on the different therapeutic properties of propolis and its nanoform.

## ANTIMICROBIAL PROPERTIES

In a study, Brazilian propolis (red propolis), which derives from the *Dalbergia ecastophyllum* plant. The influence of propolis collecting time, chemical makeup, and antibacterial action were investigated. There was seasonal variation in the concentrations of vestitol, neovestitol, and isoliquiritigenin. During the rainy season, the maximum concentration of these components and antibacterial action was observed (the period from January to May) (Bueno-Silva et al., 2017; Zulhendri et al., 2021). Geopropolis is a form of propolis produced by *Melipona mondury* and *M. scutellaris* bees. In both composition and biological function, it is extremely similar to propolis produced by *Apis* spp. Bees. *Melipona quadrifasciata* and *Tetragonisca angustula*, two stingless species of bees, were used to compare two ethanolic extracts of propolis (EEP). Geopropolis extracts were found to have greater efficacy against Gram-positive bacteria than Gram-negative bacteria (Torres et al., 2018). The mechanisms of propolis activity against pathogen were revealed in Figure 2.

To improve the handling properties of nano- and micro-propolis, the microencapsulation process is used to create nano- and micro-propolis by casein micelles. Micro- and nano-propolis, according to the researchers, could be employed as antimicrobials (Sahlan and Supardi, 2013). In comparison to propolis, nano-propolis is predicted to have higher antibacterial properties against *Bacillus subtilis*, *S. aureus*, *E. coli*, and *Salmonella* sp., respectively (Przybyłek and Karpiński, 2019). It was discovered that the antibacterial activity of nano-form was found to be more potent than that of propolis. Nano-propolis had considerably larger inhibitory zone widths than propolis against different types of bacteria (Afrouzan et al., 2012).

The flavonoid composition of propolis, including the presence of pinocembrin, galangin, and pinobanksin, is primarily responsible for its antimicrobial activities. Pinocembrin has antifungal effects as well. Esters of coumaric and caffeic acids are two more substances with well-established effects. Some research has focused on the solvent for propolis extraction, which may alter the potency of its antibacterial impact (Szliszka et al., 2013).



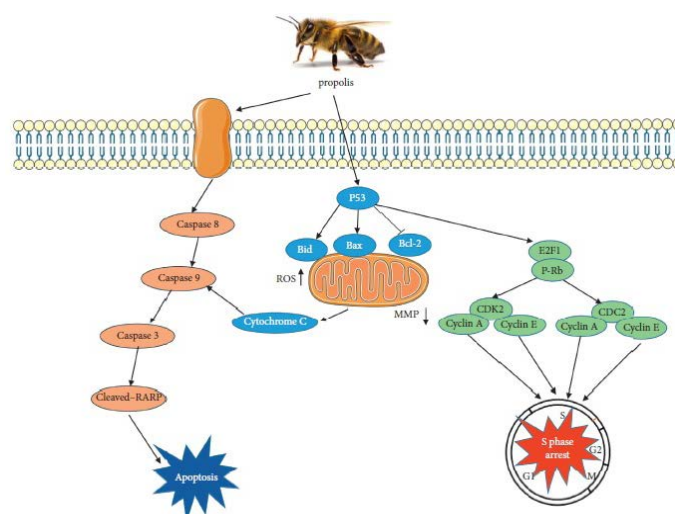
**Figure 2:** Mechanism action of propolis as anti-bacterial agent (Almuhayawi, 2020).

Propolis has antifungal properties against *Candida albicans*, *Candida parapsilosis*, *Candida tropicalis*, and *Candida glabrata*. It has been demonstrated to have aflatoxigenic properties against fungi such as *Aspergillus flavus*, where it suppressed the organism's conidial growth (Mutlu Sariguzel et al., 2016). Both green and red Brazilian propolis have been shown to exhibit antifungal action against distinct *Trichophyton* species that cause dermatophytosis, with red propolis being more effective. Furthermore, the n-hexane extract of Brazilian red propolis displays antifungal effectiveness against *Candida* spp. resistant to fluconazole and other antifungal drugs (Pippi et al., 2015).

Propolis' antifungal effect is thought to be related mostly towards its capacity to trigger apoptosis via metacaspase and Ras signaling. Propolis also interferes with the expression of genes involved in disease, cell adhesion, biofilm formation, filamentous growth, and phenotypic switching. The shift from yeast-like to hyphal development is likewise slowed by propolis. Propolis, namely its phenolic component pinocembrin, has been shown to diminish the levels of phosphorylated adenosine nucleotides in *Penicillium italicum* hyphae, as well as damage the hyphae and cell membrane, resulting in ionic leakage and soluble protein in *P. italicum* (Peng et al., 2012).

### ANTICARCINOGENIC PROPERTIES

It was reported about the inhibition of matrix metalloproteinases, anti-angiogenesis, prevention of metastasis, cell cycle arrest, and induction of apoptosis in propolis in a late study (Botteon et al., 2021; Forma and Bryś, 2021). Furthermore, different studies on rats and humans revealed no toxicity or side effects when propolis administrated. As a result, new strategies for increasing propolis' potential are urgently needed. The techniques of encapsulation of propolis extract into nanosized form have been described in several researches (Jayakumar et al., 2013; Do Nascimento et al., 2016). The influence of propolis and its components on cell proliferation was revealed in Figure 3.



**Figure 3:** The influence of propolis and its components on cell proliferation (Jiang et al., 2020).

Using chitosan carriers to improve propolis anticancer efficacy. In several studies the cytotoxicity of nano propolis was more than free propolis on human liver cancer cells (Elbaz et al., 2016). In comparison to free propolis, propolis nanosuspension exhibits a substantial inhibitory efficacy against tumor growth on the EAC in female mice. Preventing oxidative damage, immunological activation, and apoptotic induction may all play a role in the anti-tumor strategy (Abdo et al., 2019). Studies at the origin



of propolis from five locations in Indonesia were able to suppress the growth of the MCF-7 cell line *in vitro*. When nanopropolis is used instead of propolis, it inhibits the proliferation of MCF-7 cells at very low concentrations (Hasan et al., 2014).

The lung cancer cells treated with propolis nanosized showed a significant decrease in cell survival and scattering, revealing a significant cytotoxic impact and might be used as an efficient nano-vesicle (Ilhan-Ayisigi et al., 2020). The stingless bee propolis (*Tetragonula iridipennis*) sample raised from the Pudukottai district of Tamilnadu was used to synthesize silver nanoparticles. The produced silver nanoparticles were thoroughly described and proved to be efficient against lung cancer cell lines, the IC 50 concentration is 38 g/ml (Varthamanan, 2015).

Another study was evaluating the cytotoxic effects of propolis extracts on human cancer cell lines, including the human bladder cancer cell line 5637 and the hepatic cancer cell line HepG2, as well as L929 cells, as well as their oncogenic and proapoptotic gene expression profiles. Propolis showed selective cytotoxicity against the two cancer cell lines when compared to normal fibroblast L929 cells, according to the authors, and it had no effect on the expression of the Bcl-2 and p53 genes (Sadeghi-Aliabadi et al., 2015).

#### ANTI-OXIDATIVE AND IMMUNOMODULATING PROPERTIES

Flavonoids and other phenolic constituents present in propolis appear to be capable of scavenging free radicals, preventing the oxidation or destruction of lipids and other molecules such as vitamin C during oxidative damage (Attia et al., 2012). Micellar propolis nanoformulation treatment against oxidative stress injury in liver cells appears promising (Tzankova et al., 2019). Propolis has an immunomodulatory impact and increases the response by increasing the phagocytic index, NO generation, and IgG antibody production, according to a prior study (Kalsum et al., 2017). Propolis -loaded SNEDDS had a stronger immunostimulant impact than propolis in several models (Fitria et al., 2021).

Korean propolis had anti-oxidant properties due to its ability to scavenge reactive oxygen species. Furthermore, pretreatment with Korean propolis activated Nrf2 signaling, which increased the expression of anti-oxidant enzymes. These data suggested that using Korean propolis, which had anti-inflammatory and anti-oxidant properties, to prevent *H. pylori*-induced stomach damage could be beneficial (Song et al., 2020). It was discovered that propolis serves as an antioxidative reagent, reducing and inhibiting the effects of lead on rabbit brain (Radhi, 2019).

Propolis boosts the immune system of the host and inhibits biological immune response modifiers. *In vitro* and *in vivo* supplementation of propolis flavonoids liposome with ovalbumin improves cellular immunological and humoral responses in mice, according to a study. Furthermore, it can considerably boost macrophage phagocytic function, the production of interferon-gamma, interleukin-6 (IL-6), and IL-1, as well as induce larger concentrations of a variety of immune cells and immunomodulatory cytokines that are critical for maintaining homeostasis (Tao et al., 2014).

#### ANTI-INFLAMMATORY AND WOUND HEALING PROPERTIES

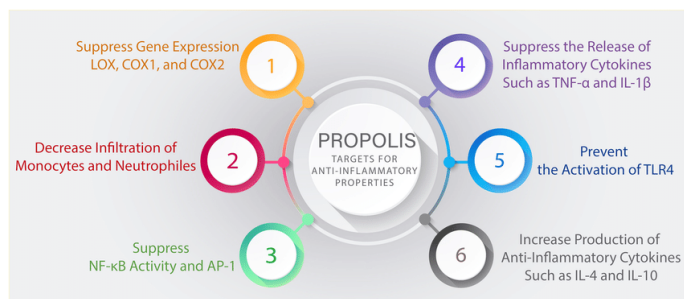
Some results of collagen types I and III expression and degradation in wound matrix certified the potency of propolis, showing that propolis supports re-epithelialization. Propolis' biological effects on wound healing and tissue regeneration could be linked to its antibacterial, anti-inflammatory, and immunomodulatory capabilities. Polyphenols' anti-oxidative activity is mediated through a variety of mechanisms, including the ability to stop ROS, chelating ions of metals thus interfering with the cascade of reactions causing lipid peroxidation with other antioxidants (Olczyk et al., 2013).

Propolis with chitosan biofilm reduced granulation tissue maturation time and wound contraction, implying that it improved re-epithelialization with a substantial influence on inflammatory infiltration and fibroblast population in a time-dependent activity. In conclusion, propolis combined with chitosan nanoparticle biofilm significantly improved full thickness wound healing in rats with excisional wounds (Abbaszadeh et al., 2019).

Propolis has anti-inflammatory characters in acute and chronic inflammation models, but the mechanism by which it achieves this effect is unknown. Others confirmed that propolis reduces COX activity in saline- or LPS-treated rats' lung homogenates in a concentration-dependent manner. Others discovered that applying propolis to diabetic lesions in rodents improves wound healing and re-epithelialization. It has also been suggested that propolis plays a role in reducing neutrophil infiltration and normalizing macrophage influx into injured areas. Furthermore, the nodular forms vanished, and the wounds were quickly healed. Another study indicated a potent impact of chitosan nanoparticles matrix and propolis extract, incorporated in collagen films and showing biological properties suitable for cutaneous wound healing (Toreti et al., 2013).

Another experiment implied that local application of nano-emulsion containing nano vitamin C, E and propolis gel in the mouth cavity during surgical procedures under

local anesthesia appears to promote wound healing, particularly in the first three days after the procedure. It protected patients having oral surgical procedures from early issues from wound healing (such as bleeding) while also providing effective healing and anti-inflammatory esthetic effects (Furukawa et al., 2021). The probable anti-inflammatory effects of Propolis was revealed in Figure 4.



**Figure 4:** The probable anti-inflammatory effects of Propolis (Pahlavani et al., 2020).

### ANTIVIRAL PROPERTIES

Propolis is a natural product that is widely utilized in food and beverages to promote health and inhibit disease, as well as having immunomodulatory effects (Silva-Carvalho et al., 2015). It has the potential to be an effective antiviral agent. Propolis-ALg NPs have a crucial role in the treatment of lumpy skin disease viral infections (LSDV)-infected animals in the clinic. The findings demonstrated that ALg-Propolis NPs were an effective in treatment for LSDV, confirmed via symptom withdrawal. It also aided in the reduction of feverish instances and enhanced the overall health of clinically sick animals (Farag et al., 2020).

Propolis, has been studied as an antiviral agent against herpes simplex virus type 1 (HSV-1) (Schnitzler et al., 2010), infectious Bursal Disease Virus and Reo-Virus, and HSV-1 and HSV-2, which resulted in a significant reduction in viral copies (Yildirim et al., 2016). Other investigations have found that propolis has antiviral effect by entering with virion envelope structures, preventing virus adsorption to host cells or entrance into host cells, or decreasing virus RNA replication (Kwon et al., 2020). The antiviral impact of Mexican propolis was proven in research against Canine Distemper Virus (González-Búrquez et al., 2018).

### ANTI-DIABETIC PROPERTIES

In addition to propolis antioxidant qualities, it has been shown in some studies to have hypoglycemic characteristics (Al-Hariri, 2011). Previous research had shown that ethanol and water extracts of propolis had beneficial benefits on diabetic rats (Zhang et al., 2015). Propolis has been shown to reduce oxidative damage in numerous tissues of diabetic rats caused by alloxan or streptozotocin. Protective impact of propolis against nephropathy Propolis preparations have

been shown to reduce diabetic hepatorenal damage, most likely due to its anti-oxidant properties and detoxification process, decreasing the damaging impacts of free radicals on tissue. Propolis' ability to protect diabetic mice from ROS-induced damage suggests that it may have the same protective impact in humans (Oršolić et al., 2012).

Egyptian propolis (EEP) conjugated with chitosan polyacrylic (CS-PAA) nanoparticles showed promise in controlling blood glucose in type 2 diabetic rats, according to a study (Hegazy et al., 2021). The hypoglycaemic impact of micro powder propolis was studied by Chung et al. (2010). Because of the decrease in blood sugar levels and the regeneration of damaged cells revealed in streptozotocin-induced diabetic rats made propolis-nanoparticles beneficial in the treatment of diabetes (Chung et al., 2010).

Treatment of diabetic rats with propolis resulted in a considerable reduction in fasting blood glucose levels (Al-Saeed and Mohamed, 2015). Another study found that propolis has a favourable effect on lowering blood sugar levels in rats with alloxan-induced diabetes when compared to the control group (Zaahkoun et al., 2016). Propolis may be a nutritional supplement with potential therapeutic for blood glucose control, as well as preventive efficacy against diabetes related liver impairment and non-toxicity in acute toxicity (Wu et al., 2012).

### REPRODUCTIVE IMPROVEMENTS

Propolis conserve the reproductive system against toxicity; due to the flavonoids and phenolic chemicals, that have protective impacts against aluminum chloride, which causes testicular dysfunction, poor sperm quality, and low testosterone levels (Ogretmen et al., 2014). Propolis has been shown in previous research to increase testosterone levels, body and reproductive organ weights, the percentage of motile sperm and normal-shaped sperm, and seminal plasma enzymes, as well as reduce free radicals and lactate dehydrogenase levels in rabbits. Propolis has a crucial role in oxidative stress and its relationship to testicular toxicity, as well as the ability to defend against cyclosporine. Propolis' protection is mediated, at least in part, by reducing testicular lipid peroxidation and raising CAT levels in that region (Yousef et al., 2010).

In rats, propolis use raises testosterone levels while lowering the amount of dead and defective sperm (Baykalir et al., 2018; Seven et al., 2020). In rats, propolis and nano-propolis treatments reduced the negative effects of cisplatin on spermatogenic activity, antioxidant status, and apoptosis, according to a study (Seven et al., 2021). The observed results in another study implied that using Alginate-propolis nanoparticles (ALg-propolis NPs), a successful propolis oral administration nano system might be developed on an industrial scale. Furthermore,

it proposed the use of nanoparticles with Propolis as an excellent replacement for colostrum to avoid any shortages in kids' needs, particularly if the mothering capacity is weak, by raising the twinning rate and so improving the performance of newborn goat kids (Sadek et al., 2020).

### HEPATOPROTECTIVE ACTIVITY

Propolis has hepatoprotective properties. It raises glutathione levels while lowering lipid peroxidation and glutathione oxidation. As a result, propolis boosts antioxidant activity and works as a hepatoprotection against mercury intoxication. Propolis extract has also been shown to protect against CCL4-induced hepatorenal oxidative stress and damage in studies. Humayun et al. (2021) demonstrated that Propolis reduced the amount of kupffer cells which shown its hepatoprotective properties. The ethanolic extract of red propolis had a hepatoprotective

impact as it reduced DNA damage in liver cells *in vitro*, had antineoplastic activity in human hepatocellular carcinoma cell line, did not have bad impact in normal cells, and was able to decrease liver enzyme and the severity of cirrhosis caused by thioacetamide (Silva et al., 2019). Micellar propolis protected rats from CCl4-induced acute liver damage *in vivo* was studied. PEO26-PPO40-PEO26 micelles could be considered a viable oral delivery strategy for propolis to protect liver cells from oxidative stress injury (Tzankova et al., 2019).

Propolis in nano form is more effective at competing for *M. aeruginosa* toxicity and as an antioxidant agent, supplementing may be a promising strategy for reducing *M. aeruginosa*-induced liver damage *M. aeruginosa* is harmful to tilapia, and the mechanism underlying this toxicity could be oxidative stress. A meal enriched with

**Table 1:** Ameliorative influence of nanopropolis in some *in vivo* and *in vitro* studies.

Animals	Concentration	Duration	Effects	References
RPE1 cells	100 -50 -25 -12.5 µg /ml	48 hrs	The clinically infected cattle which treated with the Propolis-ALg NPs revealed a 100 % recovery. Therefore, the Propolis-ALg NPs were shown to be a potential candidate in the therapy against LSDV infections.	Farag et al. (2020)
Infected cattle with lumpy skin disease virus	300 µl/ animal	6 weeks		
Male Wistar rats	Gauzes were immersed in a solution containing nanomaterials (20 g/100 ml)	18 days	ZnO/ Ag/ propolis extract NPs hastens wound healing and upsurges wound closure ratio	Bayrami et al. (2020)
Nubian goats newborn	0.06 ml	20 days	ALg-propolis NPs were proved to improve the immune status by increasing the serum IgG and IgA immunoglobulin and a decrease of the serum cytokine levels of newborn Egyptian-Nubian goats	Hegazi et al. (2021)
Wistar rats	45.0 µg/ml	14 days	Chitosan/propolis/ silver nanoparticles had antimicrobial and wound healing power they help in skin protection, disinfection, and regeneration.	Al-saggaf, (2021)
Albino mice	30 µg/ml	21 days	Chitosan/propolis nanoparticles were used in repairing of epithelial cells, hair follicles and sebaceous glands in the skin of the burn wound of albino-mice model.	Sharaf et al. (2021)
Vero cells (African green monkey kidney epithelium)	0.3-0.6-125-2.5- mg/ kg	24 hrs	Propolis-loaded poly(lactic-co-glycolic acid) nanoparticles mediates a potent anticandidal activity by reducing gene-encoding virulence with <i>C. albicans</i> .	Iadnut et al. (2019)
Nile tilapia	10 g mixed in diet	4 weeks	Propolis nanoparticles showed a significant reduction in total protein, albumin, and globulin levels, lysozyme activity, and total immunoglobulin levels protecting Nile tilapia from glyphosate toxicity.	Abd El-Magid et al. (2021)
HT-29 cell line	30 and 300 mg/Kg 1.3.10.30 and 100 µg/ml	One month 72 hrs	Propolis in combination with Layered double hydroxide (LDH) nanoparticles increased Bax pro-apoptotic gene expression, decreased Bcl-2 anti-apoptotic gene expression, and induced apoptosis.	Azarshinfam et al. (2021)
Sprague-Dawley rats	10 mg/kg	21 days	Nano-propolis treatments mitigated the side effects of cisplatin on spermatogenic activity, antioxidant situation, and apoptosis in rats.	Seven et al. (2021)
Male rabbits	100 mg/kg	7 days	Propolis nanoparticles played as hepatoprotective and antioxidative agents protective role against Eimeria infestation in rabbits.	Abd El Megid et al. (2018)



propolis and nanopropolis scavenges ROS by increasing the activity of the endogenous antioxidant defense system, which confers liver protective benefits. The materials studied reduce liver toxicity through an antioxidant pathway, although propolis and nanopropolis have a stronger ability to counteract the toxic effects of dietary *M. aeruginosa* on the liver of *Oreochromis niloticus* fish (Shaheen and Zahem, 2020).

All authors contributed equally.

### CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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The platform nano-formulation of propolis was found to be more effective than plain propolis and silymarin at suppressing AST, ALT and ALP levels in hepatotoxicity-induced in mice and promoting tissue healing. Finally, the usefulness of liposomes as a key for boosting multi-component propolis' hepatoprotective efficacy was demonstrated (Ambardekar et al., 2012). When rabbits are infected with *Eimeria*, zinc oxide nanoparticles and propolis nanoparticles work as hepatoprotective and antioxidative agents (Abd El-Megid et al., 2018). Table 1 illustrated the ameliorative effect of nanopropolis in some *in vivo* and *in vitro* studies.

### CONCLUSIONS AND RECOMMENDATIONS

Nanotechnology has proven to be useful in practically every aspect of human and animal health due to its quick and precise development, as well as its high bioavailability and targeting. All of these benefits have a substantial impact on livestock animal production and economic losses, as well as healthier animal production. In veterinary medicine, nanomedicines against numerous pathogens could be produced. Natural nano-antimicrobials, anti-viral, anti-carcinogenic, etc. such as nano-propolis, are particularly beneficial to veterinary care in health, performance, and food safety. It was proved that the nano-propolis was more effective than propolis. Due to the presence of flavonoids, which the efficacy of propolis is ascribed to, the proposed formulation could be used as a bioactive medication in which the carrier can exert a complementary effect with the drug loaded. Therefore, in future research, nano-propolis should be examined in terms of drug interactions in multiple diseases. There is a need to increase research in veterinary field because of the scanty of research currently being done on this topic.

### NOVELTY STATEMENT

The role of Nano-propolis in veterinary medicine was mentioned. The information will be helpful for researchers to conduct the researches and find out the outcomes.

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