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Review Article

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Chemical and biological properties and biomaterial applications of Egyptian propolis: A review

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Abstract

Egyptian propolis, a resinous material collected by honeybees from a variety of botanical sources, has received increased scientific attention due to its complex chemical composition and diverse biological activities. Egyptian propolis contains a diverse range of bioactive compounds, such as flavonoids, phenolic acids, terpenoids, and aromatic aldehydes, and its chemical composition varies depending on botanical origin and geographic region. This review conducts a thorough analysis of its chemical constituents and investigates the biodiversity in its composition across various Egyptian ecosystems. The biological properties of Egyptian propolis are thoroughly discussed, including its powerful antimicrobial, anti-inflammatory, antitumor, and antioxidant properties, which have been validated by numerous in vitro and in vivo studies. These properties have enabled their use in various biomaterial domains, including food preservation, wound healing, and dental care. Egyptian propolis has been used in medicine, industry, and in the production of nanoparticles due to its antimicrobial properties. However, more research is needed on Egyptian propolis because there are few studies exploring its various applications. This work is to consolidate current knowledge and identify future directions for the development of Egyptian propolis as a sustainable and multifunctional material.

Keywords: Egyptian Propolis; Propolis; Applications of Propolis; Bee products; Biomaterials

1. Introduction

Propolis is a combination of substances used by bees to protect their hive [1]. This protection involves filling cavities in the hive's walls, reducing the entrance during chilly days, and mummifying the desired intruders to prevent their decay. It is also called bee glue because it acts as a protective sealant in the hive [2]. Because it serves as a protective sealant in the hive, propolis is also known as bee glue [3]. Propolis, in Greek origin, refers to the area at the entrance to a city [4, 5]. Since ancient times, there have been ongoing discussions regarding the origin of the propolis; whether propolis originates from plants or bees remains uncertain. The approximate composition of propolis and the factors that influence it are now known as a result of the advancement of analytical techniques [2]. Propolis is formed through the incorporation of salivary enzymes secreted by bees into plant resins obtained from buds, exudates, and various plant tissues [6, 7]. The variety of plant species, continents, and regions that utilize propolis in their production gives it a distinct composition. Even though it contains different chemicals, propolis has many of the same health benefits as honey, such as being an antioxidant and fighting bacteria, viruses, parasites, inflammation, and promote cell growth [8, 9].

Chemists and biologists are currently focusing on Egyptian propolis as a valuable health-related product due to its numerous biological properties. Some of these properties are antimicrobial, antioxidant, anti-inflammatory, antiulcer, and antitumor [10]. The fact that there are a lot of beekeepers in

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Egypt is one reason for the increased interest. Propolis's high antioxidant content contributes to its numerous health and medicinal benefits. These antioxidants are effective at eliminating reactive oxygen species (ROS) and repairing the tissue damage they cause [11]. Egyptian propolis displays diverse colors and shapes. According to information collected from beekeepers in Egypt, it is typically characterized by a dark color, ranging from brown to black [12, 13].

Propolis is sourced from several governorates and regions in Egypt, including El Beheira, Menoufia, Ismailia, Kafr El Sheikh, Assiut, Sohag, Dakahlia, Banha, Beni Suef, Fayoum, and Gharbia (Figure 1). Egyptian propolis has enormous potential as a bioactive component that enhances the properties of various medical materials. Incorporating it into wound dressings and other medical tools improves their efficacy in killing microbes and aids the body in healing and regenerating new tissue [14, 15]. This review will comprehensively examine the chemical and biological properties of Egyptian propolis, highlighting its potential applications as a biomaterial. The study seeks to augment comprehension of the various bioactive compounds found in Egyptian propolis and their significance for medical and industrial applications through the synthesis of previous research findings.

2. Chemical properties

Samples Research on propolis chemical analysis indicates that the composition of propolis can change depending on where it is collected and the time of year [16, 17]. The composition of propolis is intricate, and additional compounds are periodically discovered [18]. To ensure the quality, safety, and efficacy of propolis in Egypt, it is necessary to establish chemical standardization [19]. The chemical composition of propolis is extraordinarily complex and has not yet been fully elucidated. It typically contains resins, waxes, and minor mechanical impurities. Flavones, flavonols, and flavanones represent the major constituents of propolis. In addition, propolis includes terpenes, isovanillin, aromatic unsaturated acids, caffeic acid, and ferulic acid, whose distinct biological activities allow differentiation among these compounds [19–22]. Raw propolis is not suitable for direct use in analysis or treatment. The substance must first be extracted to dissolve and release its most active components. We employ ethanol, methanol, water, hexane, acetone, dichloromethane, and chloroform as extractants, with a concentration of around 70% [23, 24].

The color of propolis typically ranges from creamy to deep brown; the composition of propolis is contingent upon the bees' environment and is initially determined by the plants in the vicinity [18, 25]. Various plants secrete substances that influence the compounds found in propolis. Aside from the resin, some of these substances are lipophilic materials that are present in the leaves, gums, and lattices [18]. Esters of phenolic acid, beeswax, flavonoid aglycones, triterpenes, and lipids and wax are all present in propolis. It also contains minerals and micronutrients, including zinc, manganese, copper, and pollen [26]. The majority of propolis originates from the buds of black poplar trees in certain regions. Propolis contains many phenolic acids, flavonoids (flavones and flavonones), and esters [18]. Typically, researchers use the capillary zone electrophoresis (CZE) technique to measure the compounds present in propolis (Figure 2) [27, 28].

3. Biodiversity in propolis composition

There are hundreds of different compounds found in propolis, and their bioactivity and chemical makeup depend on two main things: where they come from botanically and where they were collected (Table 1) [29]. Propolis is mostly identified by the name of the plant from which it came. This name acts as proof that the propolis came from a certain place by recognizing the anatomical features of plant tissues [30]. The propolis type and source are typically determined by comparing the chemical properties of propolis to plant materials and tracing bee collection sites. Furthermore, changes in honeybee species, harvesting season, collection techniques, and post-harvest processing have a significant impact on the overall composition and nutritional value of raw propolis [31, 32]. Propolis is typically classified into various groups, including Poplar, Birch, Green, Red, Pacific, Mediterranean, and others, depending on the botanical sources and the presence of primary constituents [20]. Egypt collects propolis, which has a black color, and many of the trees that produce propolis in Egypt are mango, eucalyptus, acacia, cypress, ficus sycomorus, casuarina, ziziphus, and citrus.

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Figure 1. Egyptian locations of propolis across the country's governorates.

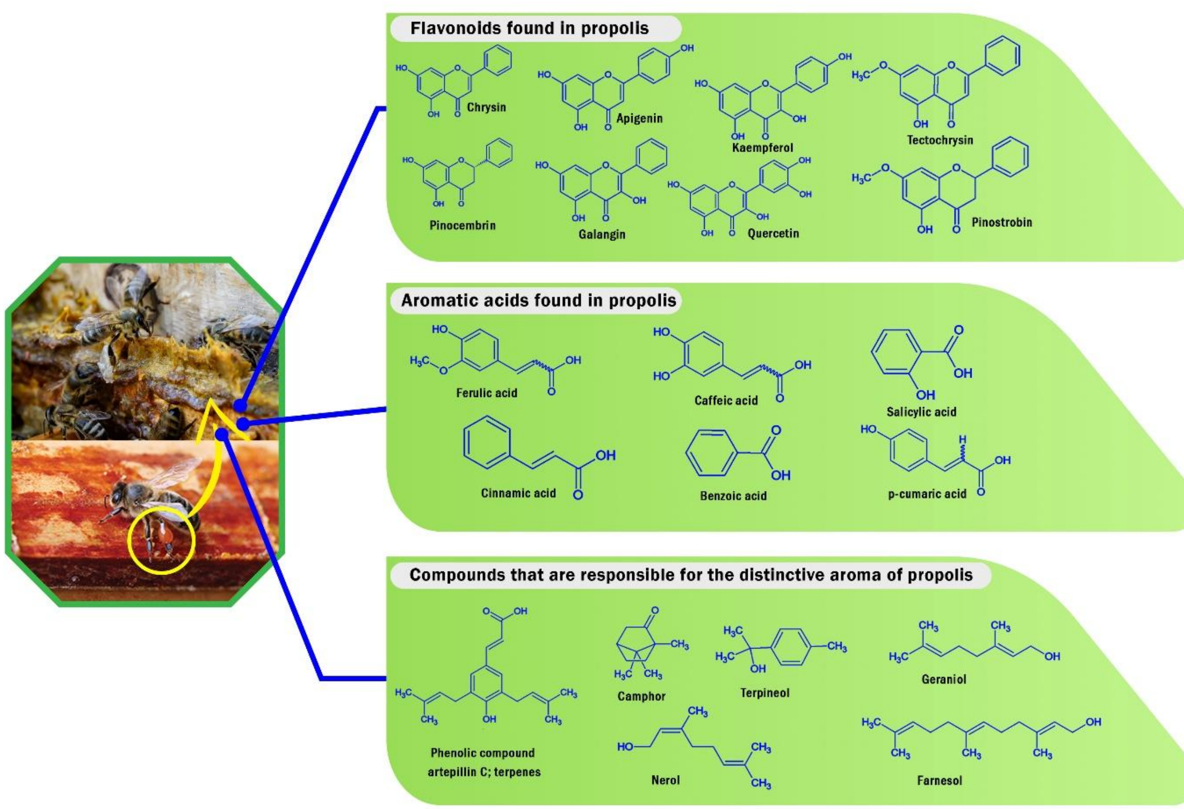

Figure 2. Chemical compounds of the most common components of propolis.

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Table 1. Biodiversity Propolis components in some Egyptian places and Arab countries.

Origins	Techniques	Some identified compounds	Ref.
Egypt (Ismailia, El-Saff, Baniswief, Fayoum, Assiut and Sohag)	GC/MS	Palmitic acid, Oleic acid, Tetracosanoic acid, Malic acid, Lactic acid, Succinic acid, 2-Hydroxy-cyclohexane-l-carboxylic acid, 2-Hydroxy-cyclohexane-l-carboxylic acid, 2.3-Dihydroxypentanedioic acid, 4-Hydroxy-benzoic acid, Caffeic acid, 3,4-di-Methoxy-cinnamic acid, Ethyl palmitate.	[33–35]
Egypt (Dakhahlia)	GC/MS	Hex, propane, octa, 2-hydroxypropanoic acids, 3-hydroxybenzoic acid, 4-hydroxybenzoic acid Hydroxycinnamal Pentanylcaffeate, 3-methyl-3-butenyl-trans-caffeate, Coumarate dimethylallyl.	[36]
Egypt (Kfer- Elsheikh)	HPLC	Catechol (Benzene-1,2-diol), Benzoic acid (Benzenecarboxylic acid), p-Hydroxybenzoic acid, Salicylic acid, Gallic acid, Vanillin, and Caffeine. -4H-chromen-4-one).	[37]
Saudi Arabia	LC–MS, HSCCC, HPLC	Sandaracopimaric acid, Propsiadin, Psiadiarabin, Phenol, Salicylic acid, Protocatechuic acid, Vanillin, Eugenol, Pinocembrin, Pinostrobin, Catechines	[38, 39] [39] [39, 40]
Jordan	HPLC	Chrysin, Galangin, Genkwanin, Alpinone, Naringenin, Apigenin, Tectochrysin, Pinocembrin, cryptomeridio, triterpenoids 24-(Z)-3-oxolanosta-1,7,24-trien-26-oic acid, 1ß,3ß-dihydroxyeupha-7,24-dien-26-oic acid.	[41, 42]
Oman	GC-MS	Fisetinidol, 2,3-trans-3,4-trans Mollisacacidin, 2,3-trans-3,4-cis Mollisacacidin, 7-O-methyl-8-prenylnaringenina, 3′,8-Diprenylnaringenina, 8-Prenyl-5,7-dihydroxy-3′-(3-hydroxy-3-methylbuthyl)-4′-methoxyflavanone, Pinitol,	[38, 39] [39] [39, 40]
Sudan	HPLC, GC/MS	Gallic, b-oh benzoic, caffeic, phenol, p-comaric, salicylic, ferulic, cinnamic, quercetin, eugenol, chrysin, galangin, pinostrobin, vanillin, pyro gallic, kaempherol, catechine, dadzin, genstin, dadazien, genstein	[43]
Algeria	HPLC–MS/MS, TLC	Pinobanksin 3-(E)-caffeine, pectolinarigenin, ladanein, Scopolin, Cistadiol, 18-hydroxy-cis-clerodan-3-ene-15-oic acid, Pagicerine, Demecolcine, Papaver, 5-(4H)-thebenidinone, N,O-dimethyl stephine phenylthioxomethylmorpholine.	[38, 39] [39] [39, 40]
Moroccan	HPLC-DAD	Vanillic, coumaric, ferulic, cinnamic, gallic, chlorogenic, rosmarinic, ellagic, Hesperidin, epicatechin, rutin, apigenin, quercetin, naringin, kaempferol	[44]

HPLC: High-performance liquid chromatography; GC/MS: Gas chromatography/Mass Spectrometry.

4. Biological properties

Human health significantly benefits from the use of propolis, which serves a variety of purposes, as antibacterial, antifungal, anti-inflammatory, antiviral, anesthetic, antioxidant, antitumoral, anticancer, and anti-hepatotoxic properties, among other uses, many studies have also shown that Egyptian propolis is characterized by many of these biological properties (Figure 3) [13, 36, 45, 46].

4.1. Antimicrobial activity

It was found that Egyptian propolis was excellent at killing both Gram-positive and Gram-negative bacteria, even strains that are resistant to many drugs (Table 2).

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Phytochemicals and other chemicals, like pinocembrin, galangin, and pinobanksin, interact with each other to make propolis work [4, 47]. In the same way, the antibacterial activity is a result of the active compounds, which include flavonoids and aromatic compounds (caffeic acid). Propolis affects bacteria by stopping their cells from dividing, damaging their cell wall and cytoplasm (Figure 4) [48], and stopping them from making proteins [27, 49, 50].

Among the 26 or more constituents of propolis, it was reported that p-coumaric acid, pinobanksin-3-acetate, pinocembrin, 3-acetylpinobanksin and caffeic acid exhibit anti-fungal activity (Table 2) [31]. In vitro inhibitory activity against certain fungi and yeasts was observed by certain authors in the range of 4 to 40 mg of total flavones (extracted from propolis). A concentration of 15-30 mg/ml of pure propolis extract was also discovered to inhibit the growth of *Aspergillus flavus, Penicillium virdicatum*, *Aspergillus ochraceus, Candida albicans*, and *Penicillium natatum*. It was also discovered that a concentration of 15-30 mg/ml of pure propolis extract was required to impede the growth of *Candida albicans*, *Aspergillus flavus, A. Ochraceus, Penicillium viridicatum, and P. notatum.* 17 fungal pathogens were treated with 10% propolis extracts. They discovered that propolis extract inhibited *Candida* and all the tested dermatophytes. discovered that the growth of fungus was inhibited by a propolis concentration of 5% or 10%, while the lower concentration did not completely suppress growth. Also discovered that the minimal inhibitory concentration of Egyptian propolis was between 10 and 30 mg/ml [50, 51].

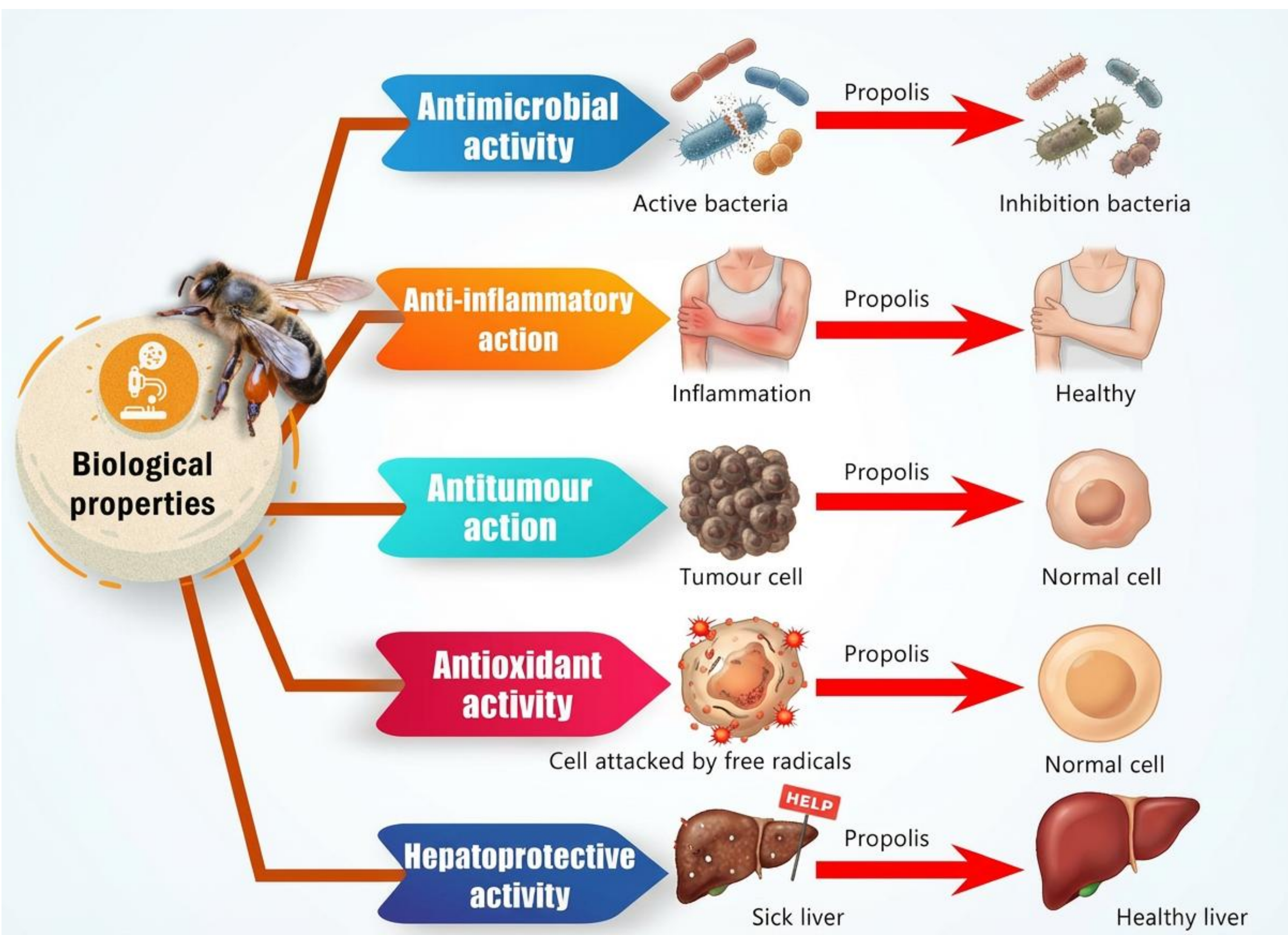

Figure 3. The biological properties of Egyptian propolis.

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Table 2. The inhibitory effect of propolis extract on some bacteria and fungi.

Microbial strain	Growth Inhibition	Extracted	Ref.
Staphylococcus aureus	+	70% ethanol+ ALg NPs	[10, 33, 34, 38, 45, 50, 52]
Escherichia coli	+	70% ethanol+ ALg NPs	
Salmonella enterica	++	70% ethanol + CNF/PVA	
Salmonella senftenberg	+++	70% ethanol	
Proteus vulgaris	+	70% ethanol+ ALg NPs	
Citrobacter diversus	+	70% ethanol+ ALg NPs	
Streptococcus mutans	+++	70% ethanol	
	++	70% ethanol + CNF/PVA	
Bacillus cereus	+++	70% ethanol	
Candida albicans	++	70% ethanol + CNF/PVA	[10, 33, 34, 45, 50, 52, 53]
Listeria monocytogenes	+++	70% ethanol	
Listeria innocua	+++	70% ethanol	
Aspergillus flavus	++++	70% ethanol	
Aspergillus parasiticus	+++	70% ethanol	
Fusarium oxysporum	++	70% ethanol	

*ALg NPs: Alginate nanoparticles. Cellulose nanofiber (CNF)/poly(vinyl alcohol) (PVA).

(++++) indicates the highest growth inhibition, (+) the lowest growth inhibition.

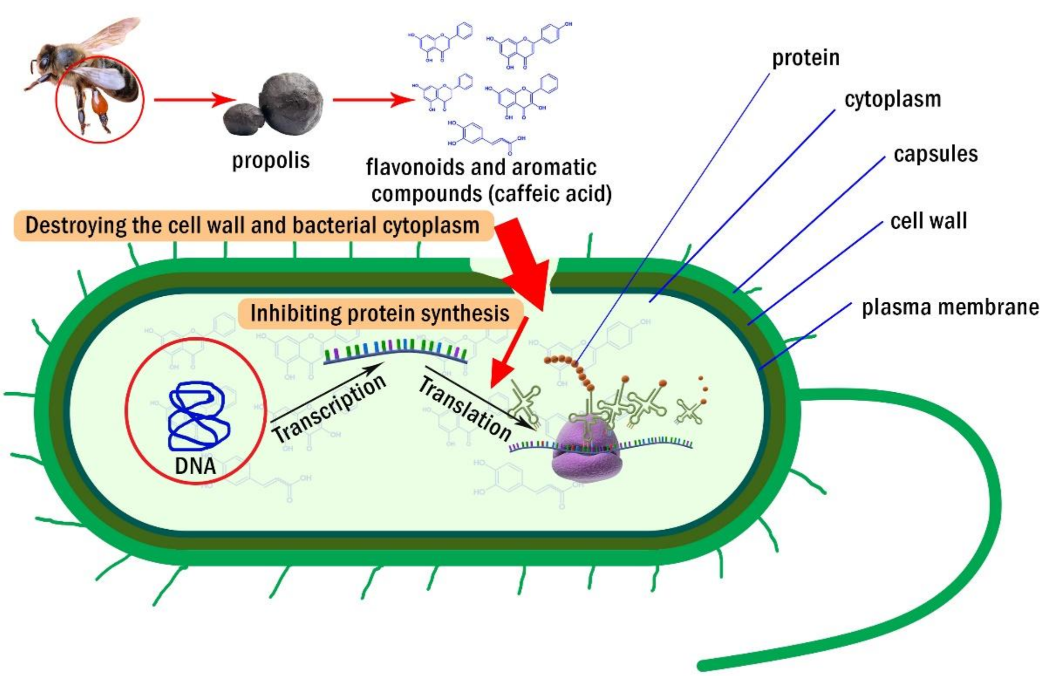

Figure 4. Mechanism of action of propolis as an antibacterial.

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4.2. Anti-inflammatory action

Propolis' anti-inflammatory properties are attributable to the presence of flavonoids [49, 54–56]. It is responsible for the regulation of NADPH-oxidase, ornithine decarboxylase, myeloperoxidase activity, hyaluronidase from guinea pig mast cells, and tyrosine-protein kinase [27]. The mode of action of these compounds is to restrict the production of leukotrienes and prostaglandins by white blood cells [49] and to slow down the activity of myeloperoxidase, ornithine decarboxylase, tyrosine-protein-kinase, and NADPH-oxidase [57]. In rat models, caffeic acid phenethyl ester and galangin, both constituents of poplar propolis, demonstrated anti-inflammatory activity and inhibited carrageenan-induced pleurisy, carrageenan-induced edema, and adjuvant-induced arthritis [4]. Propolis regulates the inflammatory substances that are produced within the cell as a result of pressure, poisonous material, or pathogenicity [58]. An established assay for evaluating the anti-inflammatory properties of implanted biomaterials is the stabilization of erythrocyte membranes. The release of various enzymes from decomposed lysosomal vesicles is the cause of inflammation. Therefore, it was demonstrated that Egyptian propolis stabilizes the erythrocytic membrane, thereby preventing the leakage of these enzymes and the occurrence of inflammation [45].

4.3. Antitumor action

The antitumor properties of propolis' components have been investigated [59–62]. Additionally, components such as caffeic acid phenethyl ester [47] and artepillin C were found to have antitumor effects [63]. These propolis compounds are involved in the cell cycle arrest, matrix metalloproteinase inhibition, anti-angiogenesis effect, and the prevention of disease transmission from one body part to another [64]. Propolis has the capacity to halt DNA synthesis in tumor cells, induce apoptosis in tumor cells, and activate white blood cells to produce agents that regulate the function of B, T, and natural killer cells [4, 65]. To prevent the rapid division of tumor cells, additional compounds, including galangin, cardanol, nemorosone, and chrysin, are involved [64]. The cytotoxic activity of natural killer cells against murine lymphoma was enhanced by the use of propolis for a period of three days [66, 67]. The apoptosis of C6 glioma cells is induced by the presence of tumor suppressor proteins in Caffeic acid phenethyl ester [64, 68, 69]. Caffeic acid and esters, as well as diterpenoids and phenolic compounds, possessed the ability to destroy tumor cells. The combined function of propolis' polyphenolic constituents is responsible for its antitumor effect [67]. Propolis fulfils the synthesis of glutathione in hematopoietic tissues, which is a consequence of the decrease in glutathione production in tumor cells due to radiation [70]. Studies also showed the effect of propolis against liver, breast, and colorectal cancer. The impact was diverse. The inhibitory concentration of Egyptian propolis was 7.87% on liver cancer, 27.73% on breast cancer, and 73.92% on colorectal cancer [13, 71]. Another study on Egyptian propolis from Kafr El-Sheikh Governorate found that it contains a high concentration of natural bioactive and polyphenolic compounds that have been shown to have a strong effect on cancer cells, including breast cancer and non-small lung cancer cell lines. The results were as follows. After 48 and 72 hours of incubation, propolis extract and Bovine Serum-propolis NPs significantly reduced breast cancer growth by ($54 \pm 0.01\%$ and $45 \pm 0.005\%$, $P \leq 0.001$) and ($20 \pm 0.01\%$ and $10 \pm 0.005\%$, $P \leq 0.0001$), respectively. Propolis extract and albumin-propolis NPs significantly inhibit non-small lung cancer growth after 72 hours of incubation ($15 \pm 0.03\%$ and $5 \pm 0.01\%$, $P \leq 0.00001$, respectively) [72].

4.4. Antioxidant activity

Galangin and pinocembrin, two components of propolis, were observed to possess antioxidant properties [49, 54, 73]. The aqueous extract of propolis was more effective than the ethanolic extract due to its higher polyphenol content. Galangin exhibited greater activity in both extracts than pinocembrin, which is attributable to the structural differences between the two [4]. Vitamin C, lipids, and other compounds were also protected from destruction or oxidation by the antioxidants, which were able to reject free radical particles. The primary cause of cell ageing and deterioration in conditions such as Parkinson's disease, Alzheimer's disease, arthritis, cancer, diabetes, cardiovascular diseases, and insufficient liver function is free radicals and other factors [74]. Vanillin and phenolic acids, among other components of propolis, were able to penetrate the epidermis and dermis, shielding them from free radicals that are generated as a result of radiation or prior to the maturation of dermal cells [58].

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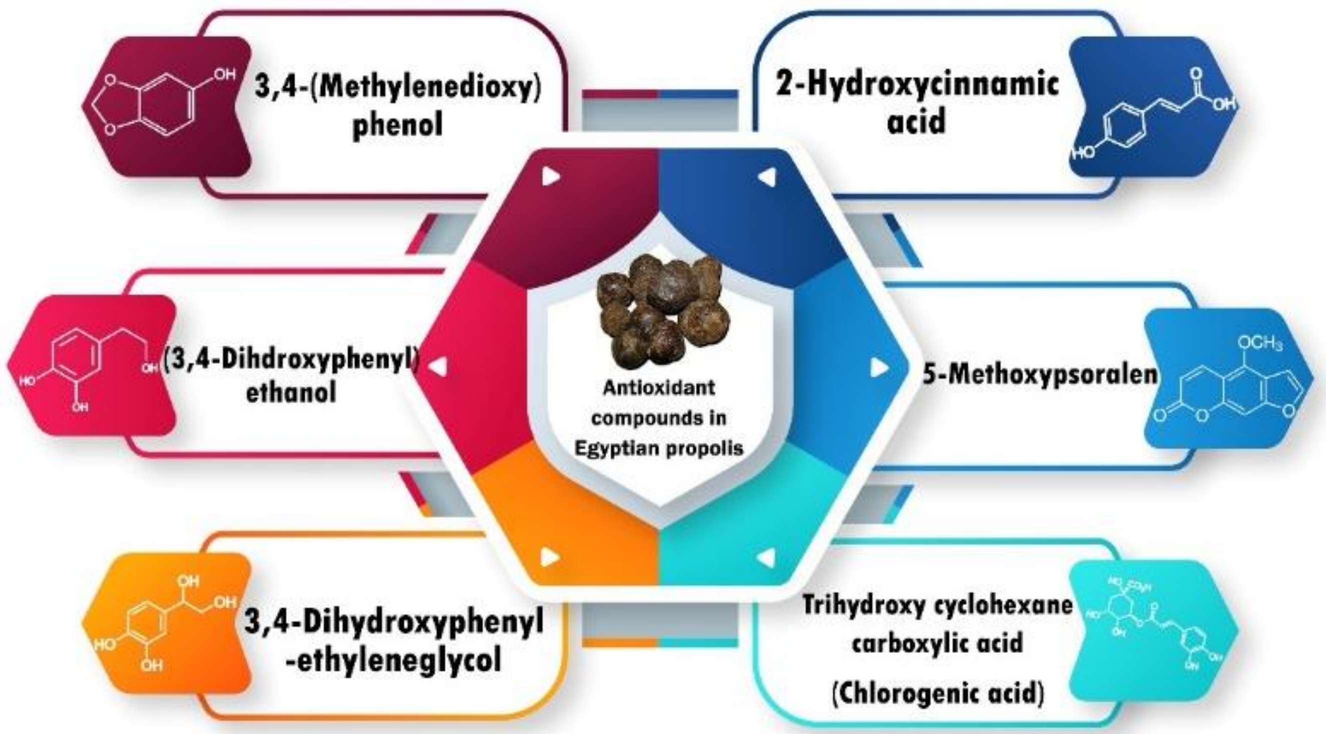

Figure 5. Antioxidant compounds in Egyptian propolis.

Phenolic compounds are responsible for the antioxidant activity of propolis through their ability to donate hydrogen ions to free radicals. This mechanism protects cells against oxidative reactions and contributes to the prevention of oxidative deterioration and contamination during food storage. Propolis has been shown to effectively scavenge free radicals, which are major contributors to the oxidation of lipids, nucleic acids, and proteins [70]. It is known that propolis is characterized by the presence of phenolic compounds, and some of these compounds distinguish Egyptian propolis by being a powerful antioxidant (Figure 5) [50].

The hepatoprotective properties of propolis have been demonstrated in several studies [75–79]. It elevates the glutathione concentration while inhibiting lipid peroxidation and regulates the level of oxidized glutathione. Also, propolis enhances the antioxidant activity against mercury-induced toxicity and functions as a hepatoprotective agent. In a study conducted on male Wistar albino rats using Egyptian propolis extract, the researchers found that propolis has a protective role against Bisphenol-A induced hepatotoxicity [80]. A study on rabbits demonstrated that propolis treatment led to a significant reduction in lipid peroxide levels and an elevation in antioxidant enzymes, including Glutathione peroxidase, Glutathione S-transferase, Catalase, and Superoxide dismutase. These results indicate that propolis may safeguard liver tissues from the detrimental effects of monosodium glutamate. In addition, the combination treatment with propolis effectively reduced the negative impact of Monosodium glutamate on antioxidant enzymes and Thiobarbituric acid reactive substances [81]. This finding is supported by Fadillioglu et al. 2004, who observed that propolis treatment enhanced the repair mechanism of damaged cell membranes [82].

5. Biomaterials applications of propolis

Food preservatives may be derived from either natural or synthetic sources; inclusion in food mitigates spoilage and unwanted alterations, and preservatives are regarded as the primary contributors to carcinogenicity, teratogenicity, and toxicity [83]. The inclination of consumers towards natural preservatives has significantly impacted the food industry [84]. Natural products, including essential oils, plant extracts, and bee products, have been emphasized for their application in foods as natural preservatives [85–88]. Propolis

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antimicrobial and antioxidant properties exemplify food preservative characteristics, and the majority of propolis components, particularly phenolic acids, and flavonoids, are naturally occurring in food. A growing body of research has investigated the use of propolis in food preservation, with a particular emphasis on its effectiveness as a natural and safe antimicrobial and antioxidant preservative. Propolis has been tested in a variety of food matrices, including fruits, vegetables, juices, meat, seafood, oils, and other food commodities [89, 90]. So many studies suggest that Egyptian propolis can act as a natural food preservative [85, 86].

5.1. Food coating applications

Numerous studies have concentrated on the impact of propolis extract on the quality and storage of fruits and vegetables, so that propolis can be applied as a surface coating on foods or incorporated into food formulations to enhance preservation [91]. The addition of propolis to food may offer health benefits. Furthermore, it has been reported to inhibit lipid oxidation and enhance shelf life [92, 93]. Egyptian propolis (Figure 6) can be used and effective as a natural preservative in various food formulations, such as milk and yoghurt [94], egyptian sausage [95], ice cream [96], milk powder [53], tomato [97], orange [98], apple [99], kareish cheese [100], minced beef [101], Nile tilapia "*Oreochromis niloticus*" [102].

5.2. Medical application of Egyptian propolis

Propolis in health and medical conditions is linked to its biological functions, and contains a wide range of biological functions, including antimicrobial [103], antidiabetic [73], anticancer [104], anti-inflammatory activities [105], antiulcer [106], antioxidant [107], and antitumor properties, as previously mentioned in the context of biological characteristics. Propolis is a critical component of wound healing due to these diverse effects [108]. This work reports the application of propolis-based wound dressings for the treatment of various wound types, including burns, ulcers, and healed wounds [15]. In vitro cell viability assays showed that chitosan/propolis nanoparticles incorporated into cellulose nanofibers exhibited a viability of 89.46%. Furthermore, in vivo studies using an albino mouse model demonstrated substantial tissue regeneration after 21 days of treatment, with restoration of epithelial layers, hair follicles, and sebaceous glands in burn-injured skin [109]. A study also demonstrated that the use of propolis was effective in preventing wound infection and promoting wound healing within 14 days. This was done through a hydrogel that was created by combining chitosan with honey, propolis, and venom in varying proportions [110]. Also, propolis has been employed to treat burn wounds caused by diabetes. The results of the study indicated a substantial decrease in both the burn surface area and the bacterial colony count over a 25-day treatment [111, 112].

Some works reported the combined use of propolis and honey for the treatment of urinary tract infections. The findings revealed that the ethanolic extract of propolis (EEP) had antimicrobial activity against five multidrug-resistant uropathogens, with varying degrees of efficacy, whereas honey alone had no detectable activity against these pathogens. Notably, the EEP-honey combination showed strong antimicrobial synergy, as evidenced by a 4:8 fold reduction in minimum inhibitory concentration (MIC) values. Furthermore, during propolis fractionation, ethyl acetate was found to be the most effective solvent for extracting antimicrobial compounds from EEP [113]. Another study investigated whether propolis and nano-propolis creams could help elderly mice heal their wounds. That study confirmed significantly improved wound healing in both the propolis and nano-propolis groups, with a significant increase in wound healing rates and collagen deposition [114] .In a randomized, parallel-arm clinical trial, propolis was used on a sample of 60 children aged 6 to 8 years at high caries risk. The children were randomly divided into two groups. The first group received propolis gum and were instructed to chew it twice daily for at least 20 minutes for two weeks. The second group received propolis mouthwash and were instructed to gargle twice daily for one minute. Data showed that propolis significantly reduced plaque scores and colony counts in both groups [115].

6. Nanoparticles

The development of potential sustainable technology for humankind is contingent upon the use of nanomaterials. The potential of nanotechnology is to optimize the manipulation of propolis, improve its penetration, and enhance its physicochemical properties (Figure 7) [116, 117]. Some researchers from Egypt utilized propolis extract that was

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immobilized in bovine serum albumin conjugated with folic acid. This was done to enhance the control of propolis extract delivery, as well as to enhance its cellular uptake and its impact on cancer cells. The results showed a substantial decrease in the growth of cancer cells, suggesting that propolis extract and albumin propolis nanoparticles possess the capacity to negatively regulate Cyclin D1 and activate caspase-3 and light chain 3. Through its capacity to phosphorylate phospho-GSK3β, propolis extract is increasingly capable of inactivating GSK3β. The nuclear fragmentation after 72 hours of incubation of breast and non-small lung cancer was also observed using acridine orange/ethidium bromide and 4′,6-diamidino-2-phenylindole stains. The results were thus confirmed. The study concluded that propolis and its derivatives can be utilized as natural therapeutic agents to specifically combat cancer invasion [72]. Another study aimed to prepare and characterise propolis nano-capsules derived from propolis collected in the Qalyubia Governorate by extracting with water, ethanol, and supercritical carbon dioxide at 50 °C in the presence of a co-solvent. The bioavailability of propolis was studied and incorporated into cracker formulations to extend their shelf life. The study's findings highlight the critical compounds involved in propolis fractionation, which were previously documented by various authors prior to commercialisation. Propolis nano-capsules made from supercritical fluid-carbon dioxide extracts at 50 °C showed significant inhibitory effects on human tumour growth, potentially preventing oxidative damage while inducing apoptosis and stimulating the immune system. Crackers fortified with these two nano-forms of propolis extract demonstrated overall acceptability, improved stability, and a longer shelf life. This product represents a novel functional food that the food industry can use to improve human health. Finally, various opportunities for nano-capsulation in the food industry will improve people's quality of life [118].

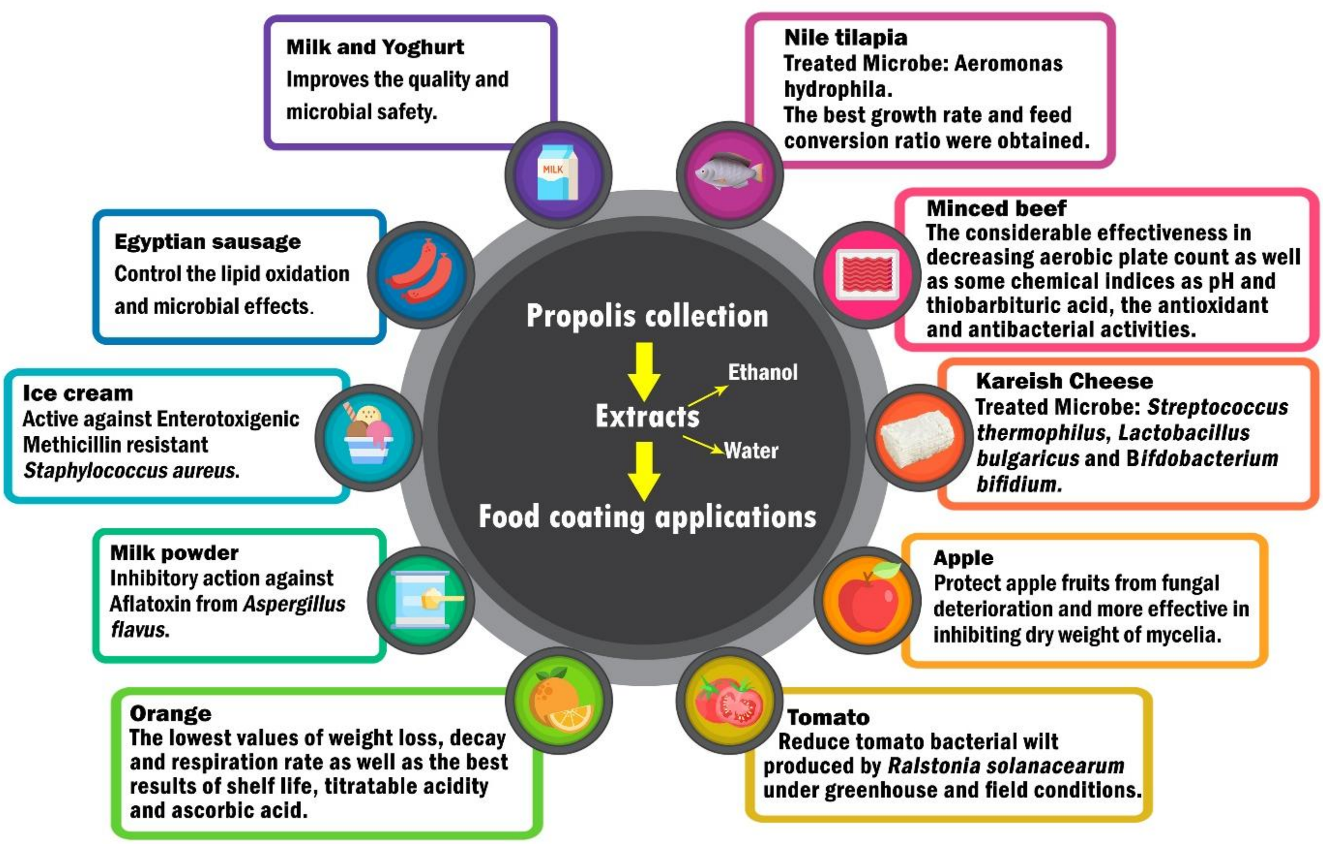

Figure 6. Application and action of Egyptian propolis as a natural preservative in various food formulations.

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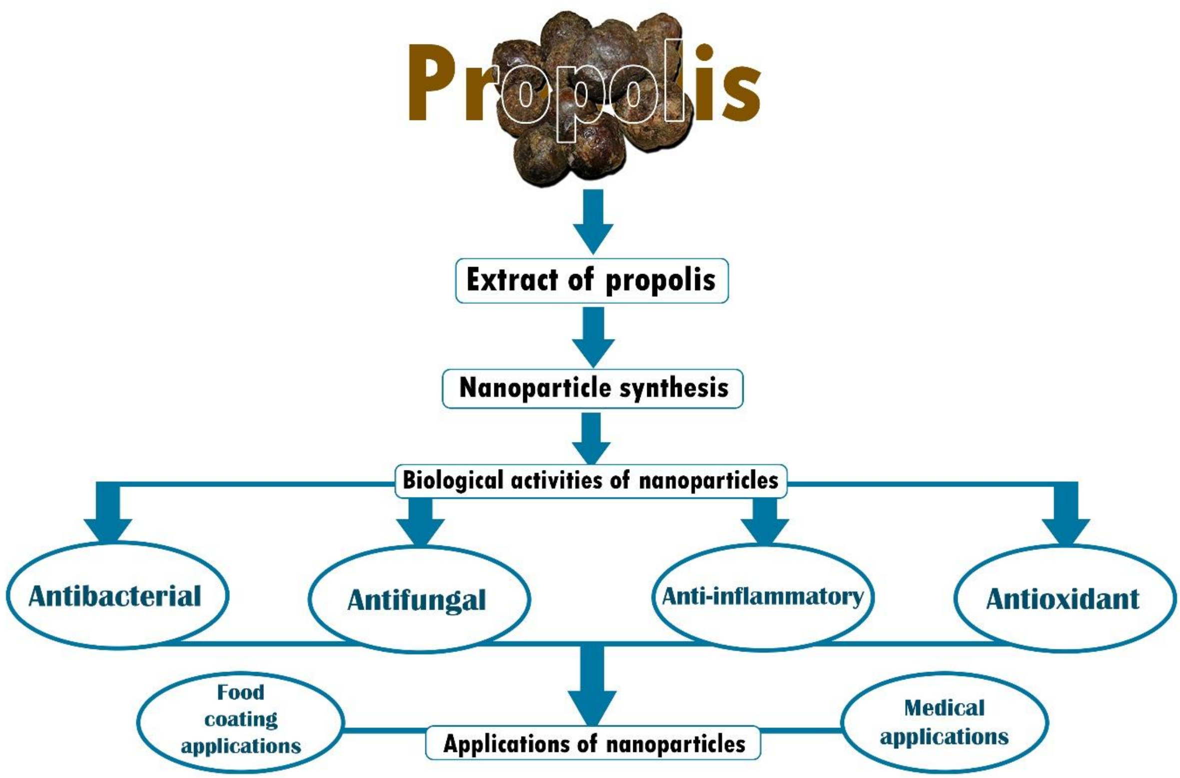

Figure 7. Uses of propolis loaded with nanoparticles.

The Egyptian propolis was used as a reducing and capping agent in a study to produce silver nanoparticles using a simple and environmentally friendly chemistry method. The biosynthesis of silver nanoparticles demonstrated that the preparation process was simple to control in terms of reduction rate within 13 minutes, moderate pH, and temperature of 75 °C. The antimicrobial activity of biosynthesized silver nanoparticles against Staphylococcus aureus and *Escherichia coli* (*E. coli*) was investigated. The results indicated a synergism between propolis and silver nanoparticles, as anticipated, for gram-negative bacteria *E. coli*. However, the extract did not exhibit any effect on the concentration used. The results demonstrated that biosynthesized silver nanoparticles, which were produced using Egyptian propolis, have the potential to be a highly effective antimicrobial product for the treatment of infections and as an active ingredient in the treatment of a variety of human diseases [116]. The study aimed to create bioactive nanomaterials using environmentally friendly methods, motivated by their numerous industrial applications. To produce silver nanoparticles (AgNPs), a simple green synthesis method was used, with Egyptian propolis acting as a reducing and capping agent simultaneously. The results showed that adding silver nanoparticles improved the antimicrobial activity of propolis extracts in a concentration-dependent manner. In addition, all samples had relatively high minimum inhibitory concentrations (MIC) against *Escherichia coli*. Overall, antimicrobial efficacy increased with increasing AgNP concentration in the propolis-based formulations [119].

7. Discussion

This review focuses on Egyptian propolis' significant properties, including its diverse chemical composition, potent biological activities, and growing potential in biomedical and industrial applications. Egyptian propolis, like other global varieties, contains a complex blend of flavonoids, phenolic acids, terpenoids, and aromatic aldehydes [19]. However, the diverse flora of the Egyptian ecosystem, which includes plants such as mango, acacia and citrus, has uniquely shaped its chemical profile, while Egyptian propolis contains some of the same components as Mediterranean and Middle Eastern propolis, such as caffeic acid derivatives, pinocembrin, and

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galangin, it also contains unique phytochemicals, which contribute to its broad bioactivity. Despite these promising characteristics, the chemical composition of the product varies by location, including Ismailia, Sohag, Kafr El-Sheikh, and Fayoum. This makes it difficult to standardize and ensure consistent quality and reproducibility. Most studies on Egyptian propolis use ethanolic extracts, which contain a high concentration of flavonoids and phenolic acids. In contrast, aqueous extracts contain more polyphenols and antioxidant activity [23]. The extraction method used is critical in determining the bioactive profile, highlighting the importance of standardized protocols for consistent results and clinical relevance. Egyptian propolis has well-documented biological activities, including antimicrobial, anti-inflammatory, antitumor, and antioxidant properties, which are primarily attributed to polyphenolic compounds [13, 36, 45, 46]. Its antimicrobial properties are especially impressive, as Egyptian propolis has been shown to inhibit both Gram-positive and Gram-negative bacteria, including multidrug-resistant strains such as *Staphylococcus aureus* and *E. coli*. Flavonoids and aromatic acids have antimicrobial properties because they break down microbial cell walls, inhibit protein synthesis, and prevent biofilm formation. This makes propolis an intriguing natural remedy for wound healing and food preservation. Egyptian propolis has anti-inflammatory properties because it inhibits the activity of key enzymes such as cyclooxygenase and lipoxygenase, reducing the production of pro-inflammatory mediators like prostaglandins and leukotrienes [49, 57]. It also strengthens erythrocyte membranes, reducing the release of lysosomal enzymes that worsen inflammation. These properties suggest that it could be used in the development of anti-inflammatory biomaterials like wound dressings and topical treatments. Caffeic acid phenethyl ester (CAPE), chrysin, and galangin are thought to induce apoptosis, inhibit angiogenesis, and disrupt the cell cycle in cancer cells [64]. Notably, when combined with nanoparticle formulations, Egyptian propolis exhibits synergy, increasing its selective cytotoxicity against tumor cells while minimizing damage to healthy tissues, implying a potential role in integrative oncology. Furthermore, its high polyphenol content confers antioxidant properties, allowing it to scavenge reactive oxygen species (ROS) and protect DNA, proteins, and lipids from oxidative damage. This lends credence to its hepatoprotective and neuroprotective effects, which have been demonstrated in animal studies. Egyptian propolis has numerous industrial and biomedical applications. It has been used successfully as a natural preservative and edible coating for perishable products such as fruits, dairy, fish, and meat [94, 101, 102].

Propolis has two advantages over synthetic preservatives: it inhibits microbial growth while also providing health-promoting antioxidants, making it a safer and more sustainable option. Propolis is used in medicine to promote tissue regeneration, reduce infection, and modulate inflammation. It is found in wound dressings, hydrogels, and chitosan-based composites. Studies have shown that propolis-loaded nanofibers and hydrogels can improve epithelialisation and angiogenesis, further supporting its role in regenerative medicine. Propolis has also been studied in dentistry, with a focus on caries prevention and oral health maintenance, demonstrating its potential as a biomaterial in dental applications. The potential of Egyptian propolis is further enhanced by nanotechnology, which has applications in green nanoparticle synthesis and drug delivery. Propolis has been used as a reducing agent in the synthesis of silver nanoparticles with enhanced antimicrobial properties. Furthermore, propolis-loaded nano-capsules improve drug bioavailability and targeted delivery, highlighting their significance in pharmaceutical and biomedical innovation [118].

Despite its potential applications, Egyptian propolis research faces several challenges and constraints. Much of the current research focuses on in vitro studies or small-scale in vivo models, with few large-scale clinical trials to confirm safety and efficacy in humans. The variability in composition, extraction methods, and dosage complicates result in interpretation, making it difficult to develop clear clinical or regulatory guidelines. Furthermore, the rising demand for propolis raises concerns about its long-term viability, as overharvesting could endanger bee populations and local ecosystems. More detailed mechanistic studies are also needed to better understand the molecular interactions that drive their biological effects. While broad antimicrobial, antioxidant, and anticancer pathways have been proposed, precise molecular mechanisms remain unknown. Advanced multi-omics approaches, such as metabolomics and transcriptomics, could aid in the discovery of the complex networks through which

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propolis works. While propolis is generally regarded as a non-toxic natural product, there have been numerous instances of contact dermatitis and hypersensitivity, particularly among beekeepers. Contact cheilitis, contact stomatitis, perioral eczema, lip oedema, oral pain, lip desquamation, and dyspnoea are signs of allergic reactions [120].

8. Future research directions

Comparative studies of Egyptian propolis with other regional varieties may also reveal distinct bioactive markers that can be used in therapeutic applications. To fully realize the potential of Egyptian propolis, future research should focus on a few key areas. To ensure quality control and reproducibility across studies, first standardize extraction protocols and create chemical fingerprints. Second, large-scale clinical trials must be conducted to determine the safety and efficacy of propolis-based formulations for wound healing, antimicrobial resistance, cancer treatment, and oral health. Third, mechanistic studies, particularly those involving advanced molecular techniques, should be prioritized to better understand the signaling pathways modulated by propolis. Sustainable production practices should also be investigated to ensure that propolis is harvested responsibly and without disrupting bee populations. Further research into propolis-derived nanomaterials for targeted drug delivery, bioimaging, and regenerative medicine may also lead to new therapeutic applications. Finally, cross-regional phytochemical studies will aid in mapping Egyptian propolis' biodiversity and better understanding how its chemical composition varies in comparison to other types of propolis worldwide.

9. Current advancements and challenges

Recent studies on propolis have made big strides in figuring out what chemicals and biological properties it has. It has been shown to work biologically in antimicrobial formulations, anti-inflammatory therapies, and antioxidant systems, and cancer studies have shown promising results. Propolis has also been successfully added to biomaterials like edible films, wound dressings, and dental composites to make them work better. Also, its use in the green synthesis of nanoparticles has opened new possibilities for biomedical uses that are good for the environment. There are still a few problems to solve. It is hard to standardise and reproduce results because the chemical composition changes depending on where and when it is. There aren't enough clinical trials to prove that it is safe and effective for people to use. Regulatory systems for natural products are still not very well connected, which makes it hard for businesses to grow. We also need to find ways to gather and process materials that don't hurt the environment so that we can make a lot of them.

10. Conclusion

Egyptian propolis is a valuable natural resource that can be applied in medicine, food technology, and nanotechnology. It is an excellent candidate for developing new biomaterials and drugs due to its diverse chemical properties and strong biological effects. Future research should focus on developing standardised extraction and characterisation protocols to ensure consistency across studies and applications. Furthermore, combining propolis with nanomedicine, bioengineering, and smart materials could lead to new products that can deliver drugs directly to specific areas, aid in tissue healing, and deal with resistance by addressing these challenges and capitalising on its unique properties, Egyptian propolis has the potential to set a standard for novel natural products and significantly advance the field of biomaterial science.

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Data availability

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