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Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

Journal by Innovative Scientific Information & Services Network

REVIEW ARTICLE BIOSCIENCE RESEARCH, 2020 17(2): 740-752. **OPEN ACCESS**

Composition, functional and medicinal importance of propolis: A review

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Propolis is a product of honeybee and it is used as a traditional medicine since centuries. Propolis is rich in phytochemicals and bioactive components such as, phenolic acids, flavonoids, and enzymes etc. It plays vital role in promoting good health and provided prevention from various diseases. Among bioactive potential of propolis, antioxidant, anti-inflammatory, antibacterial, antiviral, antifungal, anticancer and antitumor activities are widely researched. Propolis has significant functional and nutritional properties and can be used in the formulation of functional foods. Nevertheless, some precautions should be taken as some bee products are associated with allergic potential. The aim of this review study was to report different types of propolis, their composition, bioactive potential and possible applications in food and feed industries.

Keywords: Propolis, functional properties, bioactive potential, antioxidants, preservation

INTRODUCTION

Propolis is used as a traditional medicine since centuries in addition to its nutritional benefits (Andrade et al., 2017). Propolis is a product of honeybee; it is rich in phytochemicals, bioactive components and enzymes (Ferreira et al., 2017). Propolis is a mixture of resinous compounds collected by honeybees, mainly from leaf and flower buds and stems of trees (Andrade et al., 2017). In terms of composition propolis is highly complex and its contents vary greatly and mainly comprised of beeswax, resin, essential oils, and pollens. Bees add the saliva to the resinous plant exudate that leads to the formulation of propolis, consequently the partially digested material is as well mixed with bee wax (De Francisco et al., 2018). Propolis is used by bees as a barrier to keep pathogenic bacteria and fungi out of the hive. Thus, inhibitory effect against microorganisms is an essential characteristic of propolis. Propolis serves as a material to seal pores in the beehive that in turn provides a barrier, maintain the internal aseptic environmental conditions (Belloto de Franciso et al., 2017). The resins and impurities are removed from raw propolis before being used in a variety of pharmaceutical and functional foods (Banskota et al., 2001). Due to waxy nature, bees use propolis as a material for construction and repair of their hives and as a barrier against external invaders or against wind and rain (Freires et al., 2016).

Propolis exhibits a pleasant aroma and varies in color from yellow green to red and to dark brown depending on its source and age (Schmidt et al., 2014). Propolis exhibits several biological and pharmacological properties, such as immuno-modulatory, antitumor, anti-inflammatory, antioxidant, antibacterial, antiviral, antifungal, and anti-parasitic activities (da Silva et al., 2019). Propolis is also used in over the counter preparations for cold syndrome and dermatological preparations in the treatment of boils, acne, herpes simplex and genitals (Freires et al., 2016). Propolis is also used in mouthwashes and toothpastes to prevent caries and to treat gingivitis and stomatitis. Due to antimicrobial and antioxidant potential, propolis is widely used in, food, pharmaceutical and cosmetics industries (Daleprane et al., 2012). The bioactive potentials of propolis are attributed to more than 300, known substances composing propolis (Huang et al., 2014). Various research studies have been reported on isolated compounds responsible for propolis biological functions, and flavonoids are found to be one of the most important bioactive groups (Freires et al., 2016; Mello et al., 2010; Trusheva et al., 2011)

The flavonoid and (hydroxyl) cinnamic acid derivatives are primary bioactive compounds present is propolis (De Francisco et al., 2018). The flavonoids and phenolic acids are mainly attributed to health effects than the other propolis constituents (Huang et al., 2014). Propolis extracts are commonly obtained by conventional ethanol or aqueous extraction or by Soxhlet apparatus (Galeotti et al., 2017). For commercial applications, propolis is added in the form of organic solvent or water extracts. Moreover, various studies have shown the extraction of bioactive compounds with supercritical fluid as an alternative to obtain high yield from natural matrices, including propolis (Machado et al., 2016).

Origin of propolis

The green Brazilian propolis, originates from the leaves of *Baccharis dracunculifolia* and is one of the famous tropical propolis (Boudourova et al., 1997; Tazawa et al., 1998). The red propolis is gathered by bees in Cuba, Mexico and Brazil from *Dalbergia* species and symbolized by the presence of isoflavonoids (Daugsch et al., 2008: Trusheva et al., 2006).

Pacific propolis is originated from the tree *Macaranga tanarius* located in tropical islands in the Pacific Ocean (Taiwan, Okinawa, Indonesia), and characterized by prenylated flavanones (propolins) as major constituents (Huang et al., 2007; Kumazawa et al., 2004; Kumazawa et al., 2008). Different types of propolis, their origin and main constituents are summarized in table 1.

Composition of propolis

Resins, flavonoids, phenolics and various other aromatic constituents are present in propolis (Parolia et al., 2010). Apart from flavonoids, the other components of propolis are terpenes, different amino acids, and caffeic acid phenethyl ester, sesquiterpene alcohols, caffeic acid, ferulic acid, vanillin, benzoic acid, steroid hydrocarbons, cinnamic acid and minerals (Pietta et al., 2002).

Among minerals and vitamins, manganese, iodine, calcium, potassium, sodium, magnesium, zinc, iron, vitamins B2, B1, B6, C, E, D and provitamin A are also present in propolis. Some fatty acids and enzymes such as phosphatases, amylases and lactamases are also present in propolis (Kurek-Górecka et al., 2014).

Bioactive potential of propolis

Propolis exhibits several biological activities that basically result from the anti-oxidative effects of polyphenols (Huang et al., 2014). The bioactive potential of propolis vary with the chemical composition, method of extraction, and geographical distribution. This information helps to interpret the bioactive potential of propolis and provides a direction for identification of new bioactive molecules (Freires et al., 2016); Silva-Carvalho et al., 2015; Sforcin and Bankova, 2011). The therapeutic applications of propolis include therapy of cardiac system (anemia), pulmonary system (for multiple diseases), dental care, dermatology, cancer therapy, immune system enhancement and digestive tract.

For many decades propolis has been choice of treatment in traditional or folk remedies this phytomedicine has been one of the best ways of treatment due to its therapeutic and medicinal effects. The major benefits are potential activity against inflammation and protection of liver cells and tissues (Banskota et al., 2001) anti-bacterial (Koo et al., 2000) anti-viral (Amoros et al., 1994) anti-mycotic (Abd-El-Kareem et al., 2018) and antioxidant effects (Popova et al., 2005).

Table 1: Diversity in propolis types, source, origin and major constituents.

Propolis Types	Geographic Origin	Plant source	Main constituents	References
Poplar	Europe, North America, non-tropic regions of Asia, New Zealand	*Populus spp*. of section *Aigeiros,* most often *P. nigra L.*	Flavones, flavanones, Cinnamic acids and their esters	(Popova et al., 2005)
Green	Brazil	*Baccharis spp.,* predominantly *B. dracunculifolia*	Prenylated p -coumaric acids, diterpenic acids	Salatino et al., 2005)
Birch	Russia	*Betula verrucose Ehrh.*	Flavones and flavonols (not the same as in Poplar type)	(Popravko and Sokolov, 1980)
Red propolis	Cuba, Brazil, Mexico	*Dalbergia spp.*	Isoflavonoids	(Trusheva et al., 2006)
Mediterraean	Sicily, Greece, Crete, Malta,	*Cupressaceae (species unidentified)*	Diterpenes (mainly acids of labdane type)	(Tylkowski et al., 2010)
Clusia	Cuba, Venezuela	*Clusia spp.*	Polyprenylated benzophenones	(Trusheva et al., 2011)
Pacific	Pacific region Okinawa, Taiwan, Indonesia	*Macaranga tanarius*	C-prenyl-flavanones	(Huang et al., 2007; Kumazawa et al., 2008)

Propolis also shows anti-cancer (Lotfy, 2006) and immuno-regulatory activity with enhanced non-specific anti-tumour resistance properties (Oršolić et al., 2004). Despite well-known applications of propolis, its detailed chemical and bioactive characterization needs more attention, to be considered as a therapeutic agent in conventional treatment system. Thus, different types of propolis are characterized by their plant origin and chemical profile (Sforcin and Bankova, 2011; Bankova, 2005). Despite of its association with various biological functions, the exact therapeutic mechanism of propolis is not clear yet (Silva-Carvalho et al., 2015; Steinberg et al., 1996). The different bioactive components present in various propolis, their biological activities, and bioactive potential of propolis from different origins are summarized in table S1 and S2, respectively.

Antimicrobial potential

The antimicrobial property of propolis is extensively studied. All different types of propolis have antimicrobial activities, despite the variations in composition.

Antibacterial properties

Propolis exhibits broad antibacterial potential, including Gram negative and Gram positive bacteria (Kosalec et al., 2005; Park et al., 1998). The antibacterial activity is directed more against gram positive (for example *S. aureus spp, Actinimyces naeslundii, Streptococcus spp*.,) than Gram-negative bacteria (for example, *S. enteritidis, P. aeruginosa, E. faecalis E. coli, Peptostreptococcus spp*) (Kujumgiev et al., 1999: Koru et al., 2007). The ethanol extract of propolis (200 mg/mL) exhibited antibacterial effect against Gram-negative bacteria (*E. coli* and *P. aeruginosa*) but activity against Gram-positive bacteria (*Bacillus subtilis*) was more remarkable (Kumar et al., 2008; Oldoni et al., 2011). It was confirmed that propolis also showed antimicrobial potential against root canal pathogens of primary teeth (Rezende et al., 2008). When ethanol was used as a solvent for extraction of Brazilian propolis larger bacterial inhibition zones were observed as compared to other extraction solvents (da Silva et al., 2019; Rezende et al., 2008). It was reported that *E. faecalis* from infected dentin models could be eliminated by 30% Jordanian propolis (Awawdeh et al., 2009). The effect of propolis on membrane potential and membrane permeability might be the reason for its antibacterial activity (Mirzoeva et al., 1997; Siqueira et al., 2014).

Antifungal potential

Propolis showed fungicide effects against fungi, which cause juice spoilage, i.e., *Candida famata, C. kefyr, Pichia ohmeri, C. glabrata, C. pelliculosa,* and *C. parapsilosis* (Koc et al., 2007). The flavonoids in propolis are associated with antifungal effects (Farnesi et al., 2009). The variations in the composition of propolis affects the antifungal activity. It was reported by different studies that the effect of propolis varies against fungi due to the different geographic origin (Bonvehí and Gutiérrez, 2011; Quiroga et al., 2006). The functional properties of propolis based on geographical origin are summarized in table S2.

The Brazilian PEE has shown great activity against numerous strains of *Candida* (*C. albicans, C. krusei, C. guilliermondii and C. tropicalis*), *C. guilliermondii* being the most resistant and *C. albicans* the most sensitive. Some fungal species of Trichophyton, which cause dermatophytosis showed sensitivity to green and red Brazilian propolis (Da Silva Frozza et al., 2013).

Antiviral properties

Propolis has the capability to prevent virus proliferation. In various in vitro studies, the effect of propolis on the DNA and RNA of different viruses, such as *Herpes simplex type 1, Herpes simplex type 2, poliovirus type 2, adenovirus type 2,* and *vesicular estomatitis virus* have been reported. The viral multiplication was found to decrease after treating with propolis (Amoros et al., 1992).

The water and ethanol extract of propolis from Czech Republic showed the antiviral effect against *Herpes simplex virus type 1* (HSV-1) in cell culture. When cells were treated prior to viral infection, both extracts showed high *anti-HSV-1* activity and the bioactive components were chrysin and galangin (Schnitzler et al., 2010).

From stingless bee *Scaptotrigona postica, the* hydromethanolic extract of geopropolis stops the entry of the virus into cell sand also *HSV* replication, this effect was ascribed to the catechin-3-O-gallate, C-glycosyl flavones, and 3,4-dicaffeoylquinic acid (Coelho et al., 2015). The replication, release within cells or inhibition of viral transcription of *Picornavirus* can be disturbed by natural and synthetic flavonoids (Tait et al., 2006).

Antiparasitic potential

Propolis shows antiparasitic activity against numerous parasites, such as against *Giardia duodenalis* trophozoites and against *S. mansoni* (Freitas et al., 2006; Issa, 2007). Portugal's propolis showed antiparasitic properties against the *Trypanosomas brucei* (Falcão et al., 2014).

The effect of European propolis showed activity against parasitic diseases; leishmaniasis, trichomoniasis, giardiasis, toxoplasmosis, Chagas disease, and malaria (Alves de Souza et al., 2013; Torres et al., 1990).

Antioxidant potential

Antioxidant capacity is one of most important properties of food products, which contributes to the prohibition of certain diseases, such as cancer, cardiovascular diseases, and diabetes (Freires et al., 2016; Halliwell et al., 1995). The free radicals stimulate oxidative damage in biomolecules, for example proteins, nucleic acids, carbohydrates, and lipids, which may reorganize the cell and promote its death. A natural product such as propolis comprises of flavonoids and phenolic compounds, which are associated with antioxidative activity even better than vitamin C and E (Pippi et al., 2015). Concisely, the antioxidant activity is useful in inhibiting the activity of some enzymes which eventually prevents the production of reactive oxygen species (Oldoni et al., 2011). Caffeic acid phenyl ester (CAPE) also plays a role in antioxidant properties of propolis (Taheri et al., 2011). Antioxidant activity plays an important role in anti-oncogenic effects of propolis as well (Pasupuleti et al., 2017; Sales et al., 2006).

Anti-inflammatory potential

Inflammation is a mechanism that generally occurs in response to the continuous exposure to endogenous, environmental stimuli and accidental damage (Chen et al., 2004). Caffeic acid phenyl ester (CAP E) showed inhibitory effects on the production of pro inflammatory interleukin-1β (IL-1β), cytokines, monocyte chemo attractant protein 1 (MCP-1) and tumor necrosis factor-α (TNF-α) from lipopolysaccharide- (LPS-) stimulated RAW264.7 macrophages (Juman et al., 2012). The water extracts of Brazilian green propolis regulated an anti-inflammatory cellular response by decreasing the quantity of neutrophils and macrophages, in the model of LPS produced pulmonary inflammation. Moreover, it induced a decrease in the secretion of TNF-αandIL-6 and an increase in IL-10 and TGF- (Machado et al., 2012). Brazilian red propolis stimulated an important reduction in renal macrophage infiltration with chronic kidney infection in rats (Teles et al., 2015). The anti-inflammatory properties of propolis are mainly due to the presence of flavonoids that prevent the development of inflammation activated by a variety of agents (Salatino et al., 2005; Mărghitaş et al., 2013; Mani et al., 2006).

Antitumor potential

When there is deficiency of glutathione synthesis, tumor cells become very sensitive to radiation effects (Pasupuleti et al., 2017; Funakoshi-Tago et al., 2015). Through the production of glutathione, propolis applies antioncogenic properties in hematopoietic tissue (Oršolić et al., 2004). Some of the beneficial radio-protective effects of propolis are increased blood cells, reduction in lipid peroxidation and enhanced hemoglobin (Franchin et al., 2013; Krylov et al., 2002). The natural product like propolis has attracted an increasing interest due to its potential to suppress malignant characteristics of cancer cells. Concisely, propolis and its products can block specific oncogene signaling pathways, which in turn leads to a decrease in tumor cell proliferation and growth (Sawicka et al., 2012; Kaidama et al., 2015). Caffeic acid phenyl ester (CAPE) in propolis has anticancer potential (Taheri et al., 2011). CAPE from poplar propolis and artepillin C from Baccharis propolis have been identified as the most potent antitumor agents (Freires et al., 2016; Ahn et al., 2007; Oršolić et al., 2005).

Nano-propolis

Nano-propolis is composed of particles of nano density (1–100 nm in diameter) that is attempted to make it more efficient without altering its characteristics. In medical physics and biology, nano-propolis can lead to stronger effectiveness (Afrouzan et al., 2012). Nano-propolis can increase the capacity to absorb a material that makes it more soluble than propolis. Nano-propolis can pass more readily through the bacteria's exterior layer so that effective antibacterial compounds can damage the walls of plant cells. Microencapsulation methods are used to obtain nano-propolis (Kim et al., 2008; Hasan et al., 2014). The micro- and nano-propolis can be used in food or health care products as antimicrobial agents or for other purposes (Sahlan et al., 2013).

Propolis applications in food

The antimicrobial, antifungal and antioxidant activities are the beneficial effects of propolis that extends its application in food industry for the formulation of functional food. (Ali et al., 2010) reported an increase in the shelf life of meat products after treatment with 0.4% of ethanolic propolis extract as compared to treatment with 0.28% of potassium sorbate. Propolis at a concentration of 1000 ppm, was reported to prevent the fungal growth in the cheese, therefore, in food industries propolis is widely used as preservative (Aly and Elewa, 2007). Due to antibacterial effect of propolis, the extract of propolis can be used as preservative in fruit juices (Koc et al., 2007).

For health benefits and diseases prevention, propolis is widely used in food formulations and dietary supplements (Ristivojević et al., 2015). Additionally, in food products propolis can be used alone or in combination with other natural products as a natural antioxidant and nutraceutical supplement (Yang et al., 2017).

CONCLUSION

Propolis has a great potential for its functional and medicinal values. The composition of propolis varies with geographical origin and that is the main factor towards the variation in bioactive potential of different varieties of propolis. Due to wide range of medicinal and functional values, propolis from different origins should be explored for the target molecules as potential drug candidate of as functional food ingredient.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

ACKNOWLEGEMENT

This work was supported by the project 6470/ Balochistan /NRPU/R&D/HEC/2016

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