

Therapeutic Effects of Propolis: Review article

Running Title: Uses of Propolis

ABSTRACT

The term apitherapy refers to the medical use of bee products, including honey, propolis, royal jelly, pollen, beeswax and, most notably, bee venom. For example, propolis is known to exhibit antiviral, immunomodulatory, anti-inflammatory and anticancer effects. Growing importance is being attached to the discovery of medications derived from natural sources. The purpose of this review is to provide a detailed analysis of the bioactive compounds in propolis and their biological effects, beneficial or adverse.

Keywords: Propolis; apitherapy; therapeutic effect

1. INTRODUCTION

The resin that bees collect from flowers and other plant tissues is mixed with wax and pollen, yielding a highly malleable substance used for hive repair and other purposes. This is known as propolis [1]. The chemical composition of this substance varies depending on its geographical and floral origins. Raw propolis may consist of more than 300 distinct compounds, notably triterpenes (50% w/w), waxes (25–30%), volatile mono- and sesquiterpenes (8–12%), responsible for its distinctive odor, and phenolics (5–10%) [2]. European and Asian propolis contains simple phenolic acids [3], while lignans represent the principal compounds in propolis from tropical regions [4]. Caffeic acid phenethyl ester (CAPE) is an important phenolic present in European, Asian and American propolis [5]. Brazilian green propolis is distinguished by its 3,5-diprenyl-4-hydroxycinnamic acid artepillin C content, in addition to other prenylated cinnamic acids and caffeic acid derivatives [6]. Organic acids, ketones, aldehydes, hydrocarbons, and minerals are among the other frequently detected constituents of propolis [7].

29 **1.1. Antioxidant Activity**

30 Propolis has the highest phenolic content of all bee products, and has therefore been the
31 subject of intensive research in terms of antioxidant and radical scavenging properties [8].
32 Various compounds contained in propolis, including pinocembrin, chrysin, and pinobanksin,
33 exhibit powerful antioxidant and antiradicalic properties [1]. DPPH and ORAC tests have
34 identified pinobanksin-3-acetate as the most potent antioxidant constituents [9].

35 **1.2. Antimicrobial Activity**

36 Propolis has been demonstrated to exhibit variable activity against numerous bacteria, fungi,
37 and viruses [10,11]. Its antibacterial activity against gram-positive and gram-negative
38 bacteria has also been investigated, and it has been shown to exhibit antibacterial activity
39 against a broad spectrum of gram-positive strains, but very little against gram-negative strains
40 [12,13]. *Salmonella* spp. and *Listeria monocytogenes* (the causative agent of listeriosis) are
41 two major food-borne pathogen bacteria. *Salmonellae*, from the family Enterobacteriaceae,
42 are gram-negative, facultative anaerobic, and non-spore forming. The most common food-
43 borne disease caused by *Salmonella* spp. and its serotypes is salmonellosis. Animal products
44 including such as meat, eggs, milk, and their derivatives are particularly responsible for
45 outbreaks of human salmonellosis [14,15]. *Salmonella enteritidis* (*Salmonella enterica* subsp.
46 *enterica* serovar Enteritidis) is one of the most commonly isolated serotypes in foods, and has
47 been particularly linked to raw, insufficiently cooked, or contaminated eggs and egg
48 products. The incidence of gastrointestinal infections due to *S. enteritidis* is believed to be
49 increasing [16,17]. *L. monocytogenes* is a gram-positive, facultative anaerobic, non-spore
50 forming bacterium, with known psychotropic properties. This bacterium is present in much of
51 the natural environment, and is therefore also found in various animal and vegetable
52 products. Common sources of *L. monocytogenes* include various thermally processed or
53 ready-to-eat foods, including raw and pasteurized dairy products (particularly milk and
54 cheese), uncooked vegetables, fermented sausages containing raw meat, cooked or uncooked
55 poultry, raw meat, and raw or smoked fish [15-18].

56 **1.3. Immunomodulatory Activity**

57 Propolis is known to exhibit immunomodulatory effects on human peripheral blood
58 mononuclear cells (PBMC). These largely derive from its effects on monocytes and on its
59 pathogen-recognizing receptors [19,20]. Toll-like receptors (TLRs) are thought to be

60 particularly responsible for the capacity of cells with innate immunity to recognize pathogen-
61 associated molecular patterns (PAMPs) and to eradicate invading microbial pathogens. These
62 receptors are expressed by various antigen presenting cells (APCs), including
63 monocytes/macrophages, dendritic cells and B cells, and also by neutrophils, T cell and
64 natural killer cells. They are also significantly involved in the development of adaptive
65 immunity. Additionally, they perform a known function in fungi recognition, specifically
66 reported in the context of *Candida albicans*, inducing the production of a number of cytokines
67 [21].

68 **1.4. Anti-inflammatory Activity**

69 Anti-inflammatory properties of propolis have been described in various studies, and are
70 probably associated with the presence of phenolic acids. CAPE is a potent anti-inflammatory
71 component, capable of specifically targeting NF- κ B signaling [22]. It has also been shown to
72 modulate ERK MAPK signaling in T cells and mastocytes [23], as well as regulating the
73 PI3K/Akt pathway in a number of human cell lines [24]. Various potential downstream
74 effects of these anti-inflammatory mechanisms have also been postulated, such as the
75 downregulation of key inflammatory enzymes, including xanthine oxidase, cyclooxygenase,
76 matrix metalloproteinases, and inducible nitric oxide synthase [22,24]. Mouthwash products
77 make especial use of the anti-inflammatory properties of propolis. Antigingivitis activity has
78 been attributed to phenolics, particularly to CAPE [24].

79 **1.5. Wound Healing and Skin Protection**

80 Animal experiments and clinical trials have reported that propolis exhibits ameliorative
81 effects on diabetic foot ulcers and other tissue injuries [25]. The wound healing activities of
82 propolis are facilitated by the immunomodulatory, antioxidant and antiseptic activities of its
83 natural ingredients [26]. In one study, the topical application to excision wounds in rats of
84 Indian propolis containing flavonoids, phenolic acids and terpenes was reported to upregulate
85 hydroxyproline, hexosamine, uronic acid, nucleic acids and protein levels in wounded tissue,
86 similarly to nitrofurazone [27].

87 **1.6. Anticancer Activity**

88 Propolis consists of polyphenols, flavonoid aglycones, phenolic acids and their esters and
89 phenolic aldehydes and ketones. Its exact composition depends on the plants sampled, and is
90 therefore also related to biogeographic and seasonal factors, and different bee species [28].

Caffeic acid, CAPE and quercetin suppress cancer cell growth [29]. One study demonstrated that the propolis-derived compound artemillin C induced cytotoxicity in carcinomas and malignant melanoma cells through apoptosis, abortive mitosis and mass necrosis. Such suppression of tumor growth may probably be attributed to propolis' own direct cytotoxicity, in addition to enhanced immunity [30] and lipid peroxidation suppression [31]. Research has also demonstrated induction of apoptosis in human melanoma cells by three distinct propolins (A-C) [32]. PM3, another propolis-based compound, has been shown to suppress the growth of MCF-7 breast cancer cells in vitro, and to induce apoptosis [33]. Propolis induces apoptosis pathways in cancer cells. CAPE and chrysin have been identified as principal agents responsible for these antiproliferative effects by modifying cancer related gene expression.

2. CONCLUSION

In contrast to various other natural remedies, propolis still enjoys considerable popularity. Its pharmacologically active molecules consist of flavonoids, phenolic acids, and their esters, which exhibit various effects on bacteria, fungi and viruses. Propolis is also known to exhibit antioxidant, antimicrobial, immunomodulatory, anti-inflammatory, and anticancer activities. However, these claims now need to be corroborated by clinical studies. In the meantime, physicians should consider the potential benefits of propolis as an adjuvant therapy for cancer patients.

3. REFERENCES

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