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Short Communication

Propolis' Potential for Drug Discovery

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Abstract

Introduction: Propolis has been popularly used for centuries for treating inflammatory diseases and wounds. This review aimed to present a short report on *in vitro* and *in vivo* assays, clinical trials using propolis, and the main outcomes obtained.

Methods: Recent research (2010-2024) conducted *in vitro* using different cell types, and *in vivo* studying laboratory animals was reviewed. Clinical trials using propolis were also analyzed.

Results: Data revealed the significant antimicrobial, anti-inflammatory, and antitumor effects of propolis in isolation or combination with medicines, indicating its efficiency and usefulness.

Conclusion: Propolis' pharmacological activities demonstrate its potential role as an adjuvant or alternative to conventional drugs, alone or in combination with drugs commonly used to treat several diseases. Since propolis composition may change according to phytogeographic conditions, a standardization of research on propolis is imperative.

Keywords: Propolis, Drug utilization, Biological products

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Introduction

Investigation into the biological effects of bee products has increased in recent years, revealing numerous pharmacological activities. Clinical trials, as well as *in vitro* and *in vivo* studies, have demonstrated that bee products can be used for treating various diseases and for maintaining health.[1] Additionally, bee products have been widely used in food, cosmetics and by the pharmaceutical industry for drug discovery.[2]

Propolis is a resinous material that honeybees make from leaf buds and tree bark, mixing salivary secretions and beeswax. The word propolis originates from the Greek and means "defense of the city," because bees use it to protect the hive against the entrance of water and intruders, and to seal holes. The pharmacological activities and chemical composition may vary among propolis samples depending on the geographical location where it was collected, due to the local flora and climatic conditions.[3,4] Several vegetal species have been reported as propolis sources all over the globe, such as alder, birch, palm, pine, poplar, willow, *Baccharis dracunculifolia,* and *Dalbergia ecastaphyllum*.[5] Its chemical composition may include phenolic acids, amino acids, aromatic aldehydes, alcohols, esters, fatty acids, lignans, minerals, terpenes, and vitamins.[6]

Propolis has been popularly used for centuries for distinct purposes. Romans and Greeks used propolis empirically to treat wounds, due to its healing properties. The Persians used propolis to treat myalgia, eczemas, and rheumatism, while the Incas used it as an anti-pyretic agent. The Egyptians used propolis to embalm corpses and prevent decomposition. During the Second World War, propolis was used to heal wounds and to treat tuberculosis.[1]

Propolis has been used in the preparation of extracts, cosmetics, beverages, health food, and by the pharmaceutical industry in the manufacture of capsules and mouthwashes.[7,8]

Given the growing interest in natural products for drug discovery, a consolidated evaluation of propolis is warranted. This review aims to present some *in vitro* and *in vivo* assays, as well as clinical trials using propolis, and the main outcomes obtained.

Propolis potential for drug discovery

In vitro evidence

Several *in vitro* assays have been conducted to verify propolis' pharmacological properties, providing clues to understand hwo it could promote human health. *In vitro*, the assays revealed its immunomodulatory, antioxidant, antibacterial, antifungal, antiviral, antitumor, and anti-inflammatory action, among others.[9] Propolis exerts anti-inflammatory effects via NF-κB inhibition.

In vivo studies

In vivo studies revealed numerous propolis activities, e.g., antidiabetic and hypolipidemic, antidepressant and anxiolytic, analgesic, antihypertensive, antinephrotoxic, antioxidant, antipsoriatic, antitumor, antiurolithiasis, hepatoprotective, immunomodulatory, neuroprotective,

Figure 1. Propolis has been investigated *in vitro*, *in vivo* and in clinical trials, presenting its potential for drug discovery.

photoprotective, wound and burn healing, and many others.

Clinical applications

Clinical trials demonstrated propolis' efficiency in dentistry,[8,10-13] and in diabetic subjects.[14-16] Propolis efficacy was also verified as an anti-inflammatory agent,[17] and to treat women with recurrent vaginal infection.[18] Veiga et al reported the antifungal activity of propolis studying patients with toenail onychomycosis.[19]

Our group investigated propolis effects on asymptomatic HIV-infected people on antiretroviral therapy, observing that propolis intake was safe, improved the immunity and reduced inflammation in these patients.[7,20]

A possible interaction between a Brazilian propolis extract with commonly used drugs (fexofenadine, losartan, metoprolol, midazolam and omeprazole) revealed that propolis did not alter the activity of enzymes involved in drug metabolism, and the magnitude of the changes in the area under the plasma concentration-time curve values were < 20%, considered safe with respect to possible interactions involving such enzymes.[21]

A recent review described propolis potential to treat COVID-19 patients, pointing out several mechanisms and perspectives.[22] Silveira et al reported the benefits of propolis as an adjuvant treatment for patients hospitalized with COVID-19. Hospital stay after the intervention was shorter in the propolis-treated groups compared to the control.[23]

Although propolis has demonstrated therapeutic effects for patients with different diseases, it has also exhibited benefits for healthy people. Diniz et al carried out a clinical trial, and the participants received two different doses of propolis for 7 days. Propolis doses decreased the levels of a marker for lipid peroxidation and increased an antioxidant enzyme. Propolis also decreased a marker for DNA oxidation, indicating its potential in attenuating oxidative stress.[24] Qu et al reported the significant effects of propolis supplementation in patients with hypertension.[25]

Overall, propolis is safe, non-toxic, and may be indicated for consumption by both healthy and sick individuals, showing rare adverse effects.[6] Notably, propolis is safer than many synthetic medications.[5] However, some cases of hypersensitivity have already been described after its topical application, mainly among beekeepers, and it is important to consult a doctor advice before using it.[6]

Clinical trials indicate that propolis is a promising product for treating several diseases showing an enormous potential for drug discovery (Figure 1). In addition, a low-cost treatment may be easily obtained. However, its efficacy as a complementary treatment for some clinical conditions still needs investigation. It is worth highlighting that its activity depends on its vegetal origin, and distinct samples should be compared observing their efficacy. Our group has been investigating the so-called "green propolis",[26] but also the red one[27] and more recently the sample produced in the Brazilian caatinga biome.[28] However, there is no consensus on the preparation of propolis extracts, concentrations and doses, intake period and other conditions to obtain the same effects using propolis samples from different geographic regions. Thus, standardization of extraction methods and large-scale clinical trials are needed to validate propolis efficacy.

Conclusion

Traditional knowledge has given clues of propolis effects for treating several diseases. *In vitro* and *in vivo* assays have demonstrated important findings related to propolis' pharmacological properties and mechanisms of action, despite the limitations of these models. Clinical trials assessing propolis showed its benefits in relation to various diseases, both internally and externally. Overall, these findings point to the potential of propolis for drug discovery in the fields of dentistry, diabetes, immunity, tumors, and others.

Competing Interests

The author have no conflicts of interest.

Ethical Approval

Not applicable.

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