APIS

Review

Propolis: Research, Apitherapy and Clinical Applications

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ABSTRACT

Background

The literature shows that propolis has been widely used in the treatment of inflammatory diseases and wound healing for centuries.

Objective

The aim of this paper is to present the key findings from in vitro and in vivo assays, as well as clinical trials, involving propolis.

Methods

Publications related to research conducted in vitro using different cell cultures, and in vivo using mice and other experimental animals, were examined. Clinical trials involving propolis were also analysed.

Results

Literature revealed the significant antimicrobial, anti-inflammatory and antitumor effects of propolis, either on its own or when combined with medicines, indicating its efficiency and usefulness. The pharmacological activities of propolis demonstrate its potential as an adjuvant or alternative to conventional drugs, either on its own or in combination with drugs commonly used to treat various diseases.

Conclusion

The in vitro and in vivo assays allowed for the conducting of clinical trials, which confirmed the benefits of propolis for human health.

Keywords: propolis; drug development; natural products

1. INTRODUCTION

Propolis has been used empirically for centuries due to its biological properties.

Ancient civilizations such as the Greeks and Romans used it to treat wounds due to its healing properties. The Incas used propolis as an antipyretic agent, the Persians used it to treat eczema, myalgia and rheumatism, and the ancient Egyptians used it for embalming the dead. During World War II, propolis was used to heal wounds and treat tuberculosis (Weis et al., 2022). These observations enabled us to confirm these pharmacological properties and explore its potential for developing new drugs, as well as its applications in the food and cosmetics industries (Berretta et al., 2020).

Propolis is produced from various parts of plants, such as leaf buds and tree bark. The bees mix these substances with their own secretions and beeswax. The word 'propolis' originates from the Greek for "defense of the city", which is fitting given that bees use it to seal holes and protect the hive from water and intruders.

The chemical composition and biological activities of propolis samples may vary depending on their geographical origin, due to local flora and climatic conditions (Burdock, 1998, Bankova et al., 2016). Propolis can be sourced from various plant species around the world, including alder, birch, palm, pine, poplar, willow, and others (Toreti et al., 2013). It may contain phenolic acids, aromatic aldehydes, terpenes, lignans, amino acids, esters, alcohols, fatty acids, vitamins and minerals (Braakhuis, 2019). Research into the biological effects of bee products

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has increased in recent years, revealing numerous pharmacological activities. In vitro and in vivo studies, as well as clinical trials, have demonstrated the efficacy of bee products in treating various diseases and maintaining health. (Weis et al., 2022) Propolis is currently used in cosmetics, health foods, beverages and extracts, as well as in pharmaceutical products such as capsules and mouthwashes (Conte et al., 2021, Santiago et al., 2018).

In light of the growing interest in propolis research, this paper aims to present in vitro and in vivo assays, as well as clinical trials and their main outcomes, which confirm on a scientific basis the effects of propolis.

2. RESEARCH ON PROPOLIS FALLS INTO DIFFERENT CATEGORIES, EACH WITH ITS OWN SPECIFIC GOALS

2.1. In vitro evidence

In vitro assays are essential for toxicity studies, allowing the control of variables, lower cost, and reduced animal use. In vitro studies have the limitation of being an isolated model, in which cells come into direct contact with propolis, allowing one aspect of its action to be observed without the influence of other factors. On the other hand, these studies provide insights into the activities of propolis, which can be further explored in other in vitro assays or even lead to the initiation of pre-clinical in vivo studies.

Several in vitro assays have been conducted to verify the pharmacological properties of propolis, shedding light on how it could promote human health. The assays revealed its anti-inflammatory, immunomodulatory, antioxidant, antibacterial, antifungal, antiviral, antitumor and anti-inflammatory properties, among others (Sforcin, 2016).

2.2. In vivo studies

In vivo assays are useful for evaluating the safety, efficacy, and toxicity of new drugs and treatments in laboratory animals. These assays expand our understanding of the effects of propolis and enable us to investigate its mechanisms of action. In vivo, the action of propolis can be observed in a broader context, involving other cells, tissues and systems, which is not the case in vitro.

In vivo studies have revealed a variety of propolis activities, including immunomodulatory, antioxidant, antitumor, antidiabetic, hypolipidemic, antidepressant, anxiolytic, analgesic, antihypertensive, antinephrotoxic, antipsoriatic, antiurolithiatic, hepatoprotective, neuroprotective, photoprotective, and wound and burn healing properties, among others.

2.3. Clinical applications

Gathering meaningful data in vitro and in vivo enables the design of clinical trials to determine whether propolis does indeed have preventive or therapeutic potential in relation to a range of conditions affecting human health.

Clinical trials have disclosed the efficacy of propolis in dentistry (Piekarz et al., 2017, Santiago et al., 2018, Askari et al., 2019, Dileep, 2019, Neto et al., 2020) and in subjects with diabetes (Henshaw et al., 2014, Oryan et al., 2018, Afsharpour et al., 2019). The efficacy of propolis as an anti-inflammatory agent has also been verified (Khayyal et al., 2003), as has its effectiveness in treating recurrent vaginal infections in women (Imhof et al., 2005). The antifungal action of propolis in patients with toenail onychomycosis has also been reported (Veiga et al., 2018). The effects of propolis on asymptomatic people infected with HIV who were being treated with antiretroviral therapy were investigated, revealing that propolis intake was safe and improved the immune response and exerted antiinflammatory effects on the patients (Conte et al., 2021, Tasca et al., 2024).

Possible interactions were investigated between a Brazilian propolis extract and commonly used drugs (fexofenadine, losartan, metoprolol, midazolam and omeprazole). It was found that propolis did not alter the activity of enzymes involved in drug metabolism, and that the magnitude of changes in the area under the plasma concentration-time curve was less than 20% for all drugs, which is considered safe with respect to possible interactions involving such enzymes (Cusinato et al., 2019).

The potential of propolis was reported to treat patients with SARS-CoV-2 infection, highlighting several mechanisms and perspectives (Ripari et al. 2021). The benefits of propolis were demonstrated as an adjunct treatment for adults hospitalized with SARS-CoV-2 infection. The propolis-treated groups had a shorter duration of hospitalization postintervention compared to the control group (Silveira et al., 2021).

Propolis has demonstrated therapeutic effects for patients with various diseases and has also been shown to benefit healthy individuals. Diniz et al. conducted a clinical trial in which participants received two different doses of propolis for seven days. Both doses decreased levels of a biomarker for lipid peroxidation and increased antioxidant enzyme activity. Propolis was also found to decrease a biomarker for DNA oxidation, indicating its potential to attenuate oxidative stress (Diniz et al. 2020). The positive effects of propolis supplementation were reported in the context of hypertension (Qu et al.).

In general, propolis is safe and non-toxic, and can be consumed both by healthy and unwell individuals, with few adverse effects (Braakhuis, 2019). Importantly, propolis is considered safer than many synthetic medicines (Toreti et al., 2013). However, cases of hypersensitivity after its topical application have already been reported mainly among beekeepers, so it is important to seek medical advice before using it (Braakhuis, 2019).

Based on clinical trials, propolis shows enormous potential for the development of new drugs in the treatment of several diseases. It is also a low-cost, easily obtainable treatment. However, its effectiveness as an adjuvant treatment for certain clinical conditions requires further investigation. It is worth highlighting that its activity depends on its botanical origin and that different samples should be compared in terms of their efficacy. Our group has been investigating so-called 'green propolis' (Sartori et al. 2024a), as well as red propolis (Ripari et al. 2025), and, more recently, a sample produced in the Brazilian caatinga biome (Sartori et al. 2024b). However, there is no consensus on how to prepare propolis extracts, what concentrations and doses to use, how long to take them for, or what other conditions are needed to obtain the same effects using propolis samples from different geographic regions. Thus, standardized extraction methods and large-scale clinical trials are required to validate its efficacy.

3. CONCLUSION

Traditional knowledge has provided insight into the effects of propolis in the treatment of various diseases. Despite the limitations of these models, in vitro and in vivo assays have revealed important findings related to its biological properties and mechanisms of action. Clinical trials assessing propolis have demonstrated its efficacy in treating various diseases, both internally and externally. Overall, these findings highlight the potential of propolis in the development of new medicines for dentistry, diabetes, immunity, tumors and other conditions.

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