Therapeutic properties of propolis for treatment of skin lesions*

Ação terapêutica da própolis em lesões cutâneas

Acción propóleos en el tratamiento de lesiones en la piel: estudio de la revisión de la literatura

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ABSTRACT

This integrative literature review aimed to analyze the findings of studies that focused on the therapeutic properties of propolis for treatment of skin lesions. Studies were obtained through literature searches using LILACS, MEDLINE, and BDENF databases. The search was limited to publications in Portuguese, English, or Spanish languages from 1980 to 2007. Initially, 1127 publications were identified. However, only 38 publications met the study inclusion criteria. Seven publications (18.42%) were clinical studies and remainder of the 31 publications (81.58%) used "in vitro" or with animal experiments. These publications were focused on the therapeutic properties of propolis in wound healing and on the antimicrobial properties of propolis. Findings suggested the effectiveness of propolis for treating skin lesions, acting as a natural healing and antimicrobial agent whose therapeutic properties depends on the form and place of extraction and concentration of the product.

Keywords: Propolis/therapeutic use; Wound healing/nursing

RESUMO

Trata-se de uma revisão integrativa da literatura que teve como objetivo analisar os estudos que abordam o uso terapêutico da própolis em lesões cutâneas. Os dados foram obtidos por meio de busca nas bases de dados LILACS, MEDLINE, e BDENF, abrangendo o período de 1980 a 2007, nos idiomas português, inglês e espanhol. Identificaram-se 1127 artigos, dos quais 38 atenderam aos critérios de inclusão deste estudo. Destes artigos, 7 (18,4%) eram estudos clínicos e 31 (81,6%) experimentais "in vitro" e em animais. Quanto à abordagem, foram classificados em dois focos temáticos: atuação terapêutica da própolis na cicatrização das lesões e ação antimicrobiana da própolis. A análise dos trabalhos destacou a eficácia da própolis no tratamento de feridas, atuando como agente cicatrizante e antimicrobiano natural, cujas propriedades dependem diretamente da forma e local de extração e concentração do produto.

Descritores: Própole/uso terapêutico; Cicatrização de feridas/enfermagem

RESUMEN

Se trata de una revisión integradora de la literatura con el objetivo de analizar los estudios que abordan el uso terapéutico del própolis en lesiones cutáneas. Los datos fueron obtenidos por medio de la búsqueda en las bases de datos LILACS, MEDLINE, y BDENF, abarcando el período de 1980 al 2007, en los idiomas portugués, inglés y español. Se identificaron 1127 artículos, de los cuales 38 atendieron a los criterios de inclusión del estudio. De estos artículos, 7 (18,4%) eran estudios clínicos y 31 (81,6%) experimentales "in vitro" y en animales. En cuanto al abordaje, fueron clasificados en dos focos temáticos: actuación terapéutica del própolis en la cicatrización de las lesiones y acción antimicrobiana del própolis. El análisis de los trabajos destacó la eficacia del própolis en el tratamiento de heridas, actuando como agente cicatrizante y antimicrobiano natural, cuyas propiedades dependen directamente de la forma y local de extracción y concentración del producto.

Descriptores: Própolis/uso terapéutico; Cicatrización de heridas/enfermería

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INTRODUCTION

In the last years, growing interest in popular medicine has been observed, with the use of natural products to control diseases. Among these products, propolis, originated from bees of the species *Apis mellifera*, has gained great acceptance due to its therapeutic properties[1-2].

Known since antiquity, propolis was already used and viewed as medication for skin diseases by certain peoples. In the late 19th century, it was employed as wound healing agent, and subsequently, in the 2nd World War, in several Soviet clinics[3-4].

Propolis is currently considered a prominent natural product, known by its diverse biological properties, and being thus used as antimicrobial, antioxidant, anti-inflammatory, immune-modulating, hypotensor, wound healing, anesthetic, anti-cancer, anti-HIV, and anti-cavity agent. These properties are found to be associated with its chemical composition, which has, until this moment, about 200 compounds already identified, of which the main groups are flavonoids, fat acids, alcohols, amino acids, vitamins and minerals[2, 4-11].

Flavonoids are considered the main compounds responsible for the beneficial effects of propolis. They are defined as phenolic compounds originating from plants, which act in different physiological processes, participating in vitamin action and absorption, and in wound healing processes as antioxidants, and also playing an antimicrobial and modulating role in the immune system[2-3, 6].

The chemical composition of propolis is viewed as complex, because the substances present in it vary according to their geographic area and genetic differences of the bees responsible for its collection. These variations result in changes of its pharmacological properties, which tend to be greater in tropical regions, due to their existing rich vegetation, and smaller in temperate regions. Collection season is another important factor to determine the chemical composition of propolis, as this occurs year-round in countries such as Brazil, causing possible seasonal variations. These factors end up interfering with the therapeutic efficacy provided by propolis[2-4,6,11].

The action of propolis in tissue regeneration and granulation is currently questioned. In this perspective, propolis is suggested as a product that favors wound healing, in addition to its natural antibiotic property, free from side effects, which does not occur with synthetic antibiotics, and its low cost in comparison with other products currently applied on wounds, thus becoming accessible to the population[1-2,4,9].

As a result, a study of integrative review of literature was performed, aiming to analyze research on the therapeutic use of propolis on skin lesions and examine its healing process efficacy.

METHODS

Integrative review preparation used the following guiding question: What are the actions of propolis in skin lesion treatment?

Data were selected through a search in three databases: *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (*LILACS*), Medical Literature Analysis and Retrieval System on-line (MEDLINE), and *Base de Dados de Enfermagem* (*BDENF*).

Criteria for inclusion in this study were articles published in Portuguese, English and Spanish, with respective abstracts available in the selected databases, between 1980 and 2007. Theses and review articles were excluded. It should be emphasized that the methodological consistency of articles was not assessed by this study, even though it deals with integrative review of literature.

Key words used were propolis, *feridas* (wounds), *cicatrização de feridas* (wound healing), wound and healing. Search was conducted online and 1,127 studies were identified. Sample was comprised by 38 studies, which met the criteria of inclusion in this study. Articles selected were analyzed and classified in two categories: therapeutic action of propolis on wound healing and microbial action.

RESULTS

Of all the 38 (100%) studies analyzed, seven (18.4%) were clinical studies in human beings and 31 (81.6%) were experimental "in vitro" studies and studies on animals. In terms of period of publication, 15 (39.5%) studies were published from 2006. As regards the authors of these studies, 28 (73.7%) did not identify their professional category, seven (18.4%) were grouped in the biological sciences area and three (7.9%) included nurses.

All the 38 studies analyzed, according to the thematic focus involved, were thus classified:

- Antimicrobial action of propolis;
- Therapeutic action of propolis on wound healing.

Chart 1 shows articles according to thematic focus identified.

DISCUSSION

Antimicrobial action of propolis

A total of 31 (81.6%) studies on the antimicrobial action of propolis were thus classified. Of these, two (6.5%) are clinical studies, and 29 (93.5%) are experimental studies.

Some of the studies identified confirmed the inhibitory action of propolis on gram-positive and gram-negative

Chart 1 - Studies on therapeutic actions of propolis, 1980-2007

Study	Type of study	Thematic focus approach
Bernardo et al[1]; Quintana[13]	Clinical	- Antimicrobial action - Therapeutic action in wound healing
Martinez Garcia et al[14];Duailibe et al[15]	Clinical	- Antimicrobial action
Azevedo et al[4];Santos et al[11]; Lofuto et al[35]	Clinical	- Therapeutic action in wound healing
Peruchi et al[2];Park et al[3];Vargas et al[5]; Fernandes Júnior et al[6]; Silva et al[7];Sforcin et al[8]; Sforcin et al[9];Oliveira et al[10]; Auricchio et al[35]; Fernandes Júnior et al[17];Machado et al[18];Longhini et al[19];Sawaya et al[20];Fernandes et al[21];Fernandes Júnior et al[22]; Muli et al[23];Gebara et al[24];Fernandes Júnior et al[25];Bianchini et al[26];Gonçales et al[27];Dantas et al[28]; Ayres et al[29];Orsi et al[30];Orsi et al[31];Sforcin et al[32];Sforcin et al[33];Orsi et al[34]; Fernandes Júnior et al[36];Fernandes et al[37]; Araújo et al[38]	Experimental	- Antimicrobial action
Rahal et al[16]	Experimental	- Therapeutic action in wound healing

bacteria, yeast and fungi, highly pathogenic for both human beings and animals. However, it should be emphasized that the inhibitory action of propolis against microorganisms is found to be associated with its chemical composition, of which flavonoids are suggested as the main compounds responsible for this property. Propolis concentration differs according to area, period in time and the way it was collected and prepared, with values reaching up to 10%, as is the case of the European propolis[5,11-38].

In a study with propolis samples produced by the *Universidade Estadual de São Paulo – UNICAMP*, its antimicrobial activity against pathogenic agents isolated from human infections was observed. Among pathogens tested, *Candida albicans* and *Candida tropicalis* showed higher susceptibility than *Candida parapsilosis* and *Candida guillermondii*. *Candida parapsilosis* strains were only inhibited by concentrations two times lower than those used with gram-negative bacteria. The mechanisms that cause this difference in susceptibility to propolis among microorganisms tested are not well known. As a result, further studies on this issue are necessary[21].

In another study, of all 161 bacterial isolates (81 gram-positive and 80 gram-negative), belonging to the *Universidade Federal de Santa Maria – RS* Bacteriology Laboratory, 92.6% of gram-positive isolates were found to be sensitive to propolis, whereas only 42.5% of gram-negative bacteria were sensitive to the propolis extract[5, 27].

By analyzing the propolis extract preparation using water and different ethanol concentrations, the aqueous extract and ethanol extracts of propolis at 10% and 20% did not show antimicrobial activity, whereas the ethanol extracts between 30% and 50% showed little activity. However, ethanol extracts of propolis between 60% and 80% assured high inhibition of microbial growth and a decrease in antimicrobial activity with higher percentages of ethanol. In this way, it could be affirmed that the ethanol concentration used to prepare propolis extracts, as well as how these were made, tend to influence flavonoid concentration and, as a result, the antimicrobial activity of propolis[3].

Other studies emphasize the influence that the chemical composition of propolis has on its antimicrobial activity, warning that flavonoid concentration changes according to the flora and seasonal conditions of the region where collection was conducted[3,7,27,35].

Therapeutic action of propolis in wound healing

In this thematic focus, four (10.5%) studies, focusing on the therapeutic use of propolis on skin lesions, were included. Of these, three were clinical studies and one was experimental.

In a study performed with ten patients of a Vascular

Surgery Outpatient Clinic, people with skin lesions, such as ischemic ulcer, stasis ulcer, venous ulcer, iatrogenic lesion and ulcer after cutting-contusion injury, showed debridement of all exudates adhered to the wound surface, with the presence of granulation tissue, in the first week of use of aqueous propolis solution with extract at 30%. After the first week of use already, improvement of wound odor and patient's sensitivity to pain was observed, as well as a decrease in the number of microorganisms *Staphilococos aureus, Pseudomonas aurigenosa, Citrobacter freundii, Proteus vulgaris, Enterobacter sp, Cândida sp* and *Klebsiella p.* in up to 60 days, according to results of secretion cultures conducted every two weeks. Authors of this study emphasized that wound healing efficacy is intimately associated with the propolis concentration in the solution[1].

Another study, which used propolis ointment on 22 chronic wounds, of which 11 were venous ulcers, seven pressure ulcers, two diabetic ulcers, and two post-trauma injuries, found that necrotic tissue was present in 14 (8.2%) during tissue assessment process. However, there was no necrotic tissue after therapeutic intervention. In terms of odor assessment, 78.8% were sui generis, the same being absent in 53.3% of cases after therapeutic treatment. As regards healing time, mean time was 13.2 weeks. Considering a 20-week follow-up, 74.1% of ulcers healed before this period. In addition, regarding pain felt by people with chronic wounds, all of them reported improvement, even though its level was not assessed by this study. Despite research limitations, authors confirmed the anti-inflammatory and analgesic efficacy of propolis, among other things[11].

By comparing subcutaneous healing induced in rats with an alcoholic solution of propolis at 10% another at 30%, both were found to stimulate tissue repair, with significant neo-vascular formation occurring, followed by rapid tissue regeneration, despite the result of lesions treated with solution at 30% being slower[2].

It should be emphasized that the majority of these studies focused on the advantages of propolis in terms of its easy handling and access, and its low cost, compared to those commonly used, even though authors have not proved the findings from their studies. In addition, propolis is a natural product, without contraindications[1,4,11-12].

Despite methodological consistency of studies having not been analyzed by this research, the use of propolis in lesions was found to decrease healing time, speed up tissue regeneration process and provide wounded tissue recovery, due to its antimicrobial and anti-inflammatory action.

FINAL CONSIDERATIONS

Studies on the therapeutic use of propolis in lesions are still scarce, even though there has been noticeable growth in research since 2002.

As regards the therapeutic action of propolis in wound healing, studies showed positive results, including antimicrobial, anti-inflammatory, analgesic and neo-angiogenic action, even though the methodological consistency of these studies was not a focus of analysis of the present research.

In view of these facts and based on the studies analyzed, it could be concluded that the therapeutic use of propolis to treat skin lesions is promising, as a result of its efficacy. However, standardization of propolis collection areas, the ways to perform this and solvents used to extract it are believed to contribute positively to guarantee better results.

Finally, it is suggested that further studies should be performed to increase scientific evidence, thus subsidizing new alternatives of treatment for people who have skin lesions and also enabling safe, high-quality care.

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