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## **From Hive to Health: Harnessing Propolis Accelerated Wound Recovery and Tissue Regeneration**

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## **Abstract**

Wound management remains a critical challenge in modern medicine, particularly concerning chronic, infected, or slow-healing lesions. Propolis, a resinous mixture collected by honeybees from various plant sources, has emerged as a potent natural therapeutic agent due to its diverse biological properties. This narrative review synthesizes evidence from the most recent studies, investigating the efficacy of propolis in various wound healing and tissue regeneration contexts, ranging from oral mucositis to diabetic ulcers and surgical site infections. The findings consistently demonstrate that propolis promotes tissue regeneration, modulates inflammatory responses, and provides significant antimicrobial activity. Furthermore, the integration of propolis into advanced delivery systems, such as nanostructured lipid carriers and thermoresponsive gels, has been shown to enhance its therapeutic index compared to traditional formulations.

### **Background**

The process of wound healing is a complex physiological sequence involving inflammation, proliferation, and tissue remodeling. Disruptions in this process, often exacerbated by bacterial biofilms or systemic conditions like diabetes, necessitate multi-targeted therapeutic interventions. Propolis has gained significant attention in recent years for its ability to address these challenges. Its rich chemical composition, primarily consisting of polyphenols, flavonoids, and phenolic acids, allows it to act as an antioxidant, anti-inflammatory, and antimicrobial agent. This review aims to provide a comprehensive overview of the current state

of research regarding the application of propolis in wound care, highlighting its mechanisms of action and clinical potential across diverse medical fields.

#### Aim

The aim of this narrative review is to provide a comprehensive overview of the current state of research regarding the application of propolis in wound care. It synthesizes evidence from the most recent studies to evaluate the efficacy of propolis across various healing contexts. Including oral mucositis, diabetic ulcers, and surgical site infections while highlighting its specific mechanisms of action and clinical potential in diverse medical fields.

#### Materials and methods

In this narrative review a non-systematic review method was implemented. Online databases (PubMed, Scopus) were searched for the following terms: “wound healing”, “propolis”. Inclusion criteria: published from 2020 onward, publication types: review, systematic review, controlled trial, clinical trials, metanalysis. To ensure the quality and credibility of our research the article selection was conducted by at least two authors independently.

#### Results:

##### Mechanisms of Action and Bioactive Components

The therapeutic potential of propolis is rooted in its ability to influence the molecular pathways of healing. Research into Brazilian red and green propolis has identified a significant polyphenolic profile that modulates skin inflammatory conditions and reduces oxidative stress [1]. These extracts have been shown to increase the production of essential growth factors such as interleukin-6 (IL-6) and vascular endothelial growth factor (VEGF), while stabilizing hypoxia-inducible factor 1-alpha (HIF-1 $\alpha$ ) to promote regeneration [1]. Specific compounds within propolis, such as Caffeic acid phenethyl ester (CAPE), have been identified as key drivers of accelerated healing [2]. Furthermore, isolated benzophenones like Guttiferone E from red propolis exhibit potent antibacterial action against Methicillin-resistant *Staphylococcus aureus* (MRSA), demonstrating a minimum inhibitory concentration similar to reference antibiotics like Ceftaroline while effectively inhibiting biofilm formation [3]. The ability of propolis to inhibit biofilms is particularly crucial in treating chronic wounds where persistent bacterial colonies often impede recovery [4].

## Introduction

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#### Clinical Applications in Oral Health and Stomatology

Propolis has demonstrated remarkable efficacy in treating various conditions of the oral cavity. Clinical studies have shown that a 10% w/w thermoresponsive, propolis-based in situ gel significantly improves healing scores following laser-assisted gingival depigmentation compared to placebos [5]. In the management of radiation-related toxicities, such as oral mucositis and candidiasis in head and neck cancer patients, a 5% aqueous extract of Brazilian organic propolis administered as a mouthwash delayed the onset of symptoms and reduced microbial counts [6]. Similarly, propolis oral films have been developed for chemotherapy-induced oral mucositis, showing therapeutic efficacy comparable to conventional doxepin or dexamethasone patches, though with shorter adhesion times [7]. For patients undergoing gingival biopsy, a 2% Thai propolis extract gel was found to reduce postoperative pain and accelerate wound contraction [8]. Beyond acute injuries, propolis paste has been successfully used in non-invasive techniques to treat gingival recession, achieving complete root coverage without the need for traditional incisions [9]. The broader utility of bee products in oral diseases is well-supported by reviews, emphasizing their role in managing various oral pathologies [10].

## Management of Chronic and Diabetic Wounds

The treatment of diabetic wounds remains one of the most significant hurdles in wound care due to impaired vascularization and prolonged inflammation. Innovative delivery systems have been developed to address this, such as hydrogel film-forming sprays containing propolis-based nanostructured lipid carriers (NLCs) loaded with alpha-mangostin, which have shown significant improvements over silver sulfadiazine cream in mice models [11, 12]. Similarly, propolis nanoparticles prepared using NLC systems have proven highly effective in treating chronic diabetic ulcers in rat models, performing comparably to povidone-iodine [13]. Clinical trials involving human subjects have further validated these findings [14]. The antioxidant and antimicrobial superiority of propolis-NLCs over crude extracts highlights the importance of advanced formulation in maximizing the regenerative potential of bee glue [15].

## Dermatological Applications and Specialized Wound Care

Propolis is equally effective in general dermatological applications and specialized surgical contexts. In the treatment of second-degree burns, a nano-emulsion combining propolis, hyaluronic acid, and vitamin K has been shown to enhance wound contraction and tissue regeneration speeds [16]. For acute excisional wounds, propolis formulations have achieved shorter average healing times than other natural products like sweetgum oil [17]. The age-related delay in wound healing can also be mitigated by propolis [18]. Furthermore, oral administration of propolis extract has been found to decrease oxidative stress and inflammation in skin graft models, supporting the systemic benefits of its bioactive compounds [19, 20]. In surgical settings, the development of surgical sutures coated with propolis and silver compounds offers a promising method for reducing postoperative wound infections [21].

## Innovative Therapies and Future Directions

The integration of propolis into multi-modal therapies has yielded impressive results. One notable example is the use of 10% propolis ointment in conjunction with photodynamic therapy (PDT) and blue LED light for lower limb ulcers, which resulted in an 80% complete healing rate compared to 0% in the control group [22]. Other specialized applications include the use of Anatolian propolis extract to improve tissue repair and reduce inflammation in urethral wounds [23]. As research continues, the exploration of potentially attractive methods for synthesizing and applying propolis extracts will likely expand its clinical footprint [24]. While systematic reviews provide a broad foundation for its use [25], ongoing studies into green propolis extracts and their effects on aged gingival irritation further refine our understanding of its targeted benefits [26]. Despite the complexity of the mixtures used in some studies, the central role of propolis in promoting recovery remains evident [27]. Future research must continue to

standardize these formulations to ensure consistent quality and efficacy across various clinical settings [28, 29].

#### Conclusions

The body of evidence presented in these studies underscores the versatility and potency of propolis as a therapeutic agent in wound healing. From its molecular impact on inflammatory cytokines and macrophages to its clinical success in treating diabetic ulcers and oral mucositis, propolis consistently outperforms or matches conventional treatments. The advancement of nanotechnology and innovative delivery systems has further enhanced its bioavailability and effectiveness. Given its natural origin and favorable safety profile, propolis is poised to become an integral component of modern wound management strategies [30].

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None to report.

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#### Key words:

Wound healing, Antimicrobial activity, Anti-inflammatory, Antioxidant, Polyphenols  
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