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The Potential Role of *Kecombrang* (*Etlingera Elatior)* Extract in Wound Management: A Review on its Anti-Oxidative, Anti-Inflammatory, Antimicrobial, and Anti-Melanogenesis Effects

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ABSTRACT

Wound healing is a complex process critical for tissue repair post-injury. Botanicals, renowned in traditional medicine, hold potential in wound healing due to their bioactive compounds. *Etlingera elatior*, a *Zingiberaceae* family member, is attracting attention for its diverse medicinal properties. Indigenous to Southeast Asia, it has been traditionally used for wound care, attributed to its anti-inflammatory, antioxidant, and antimicrobial effects. Recent scientific investigations highlight its ability to promote tissue repair, diminish inflammation, and counteract oxidative stress. These findings position *Etlingera elatior* as a promising candidate for wound healing management, particularly in plastic surgery. However, its clinical translation faces challenges, including limited clinical trials and mechanistic understanding, necessitating standardized extraction methods and regulatory approval. Bridging the gap between botanical therapies and clinical use requires robust clinical trials, mechanistic studies, and formulation optimization. Collaboration among researchers, clinicians, and regulators is pivotal in realizing *Etlingera elatior*'s wound healing potential.

KEYWORDS: wound healing, *Etlingera elatior*, kecombrang, torch ginger, botanicals, traditional medicine, anti-inflammatory, antioxidant, antimicrobial

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INTRODUCTION

Wound healing is a complex biological process crucial for tissue repair and restoration of tissue integrity following injury or trauma.[1] It involves a well-orchestrated sequence of events, comprising four overlapping phases: hemostasis, inflammation, proliferation, and remodeling. During hemostasis, blood clotting is initiated to stop bleeding, followed by the recruitment of immune cells during the inflammatory phase to remove debris and fight off potential infections. The proliferation phase involves tissue regeneration, with the synthesis of new extracellular matrix and blood vessels. Lastly, during remodeling, the wound undergoes reorganization and maturation to restore tissue strength and function. Proper wound healing is essential to prevent complications such as infection, chronic wounds, and excessive scar formation, which can significantly impact patient outcomes.

Botanicals have been used for centuries in traditional medicine to promote wound healing.[2] Their therapeutic properties are attributed to various bioactive compounds, including antioxidants, anti-inflammatory agents, and antimicrobial compounds. In modern wound healing therapies, botanicals continue to gain recognition due to their potential to complement conventional treatments and aid in wound repair and tissue regeneration. Among the promising botanical candidates, *Etlingera elatior*, commonly known as "*torch ginger*" or "*red ginger lily*" or "*kecombrang*" in Indonesia (see **Image 1**), has drawn attention for its diverse medicinal properties. Indigenous to Southeast Asia, *Etlingera elatior* has been traditionally used in wound care due to its anti-inflammatory, antioxidant, and antimicrobial effects. Recent scientific investigations have shed light on its wound healing potential, revealing its ability to promote tissue repair, reduce inflammation, and protect against oxidative stress. As a result, *Etlingera elatior* presents itself as a promising botanical agent in wound healing management, with the potential to contribute to improved patient outcomes in plastic surgery and other medical fields. Further research and clinical studies are warranted to fully explore its therapeutic applications and establish evidence-based

guidelines for its use in wound care.[3,4]

ETLINGERA ELATIOR

Etlingera elatior is a tropical perennial herb belonging to the family Zingiberaceae. This family is renowned for including numerous aromatic plants, such as ginger and turmeric. *Etlingera elatior* is native to Southeast Asian countries, including Malaysia, Indonesia, and Thailand. It is recognized for its striking inflorescence, which resembles a torch, hence the common name "*torch ginger*." The plant has long, lance-shaped leaves and can reach impressive heights, ranging from 3 to 5 meters.

Image 1. Kecombrang flower (Etlingera elatior)

Etlingera elatior possesses a rich array of chemical compounds, which contribute to its therapeutic properties and potential as a medicinal plant. Phenolic compounds, flavonoids, terpenoids, and essential oils are among the key constituents identified in *Etlingera elatior*. Phenolic compounds, including phenolic acids and tannins, exhibit potent antioxidant properties that play a crucial role in neutralizing free radicals, thus protecting cells from oxidative stress-induced damage. Flavonoids, on the other hand, possess diverse biological activities, such as anti-inflammatory, antimicrobial, and anti-cancer effects, which are relevant to wound healing and other health applications. Terpenoids, which include essential oils, contribute to the distinctive aroma of the plant and exhibit various biological activities, including antimicrobial and anti-inflammatory properties. One study indicated that the leaf extract exhibited the strongest antioxidant inhibitor property, higher than those of trolox and gallic acid, and showed the highest phenolic contents of isoquercetin, catechin, and gallic acid, as well as moderate anti-collagenase and amino acid contents. The flower extract showed greater potential to inhibit collagenase activity and more amino acids than the leaf extract, while also showing moderate phenolic compound levels and antioxidant activity. In addition, both the flower and leaf extracts were shown to be capable of suppressing melanogenesis through inhibiting tyrosinase activity.[5] These chemical constituents collectively contribute to the wound healing potential of *Etlingera elatior* and may have therapeutic applications in wound management and tissue repair.[3,4]

WOUND HEALING PROCESS AND STAGES

The wound healing process is a complex and dynamic series of events that aims to repair damaged tissue and restore normal structure and function. It can be broadly divided into four stages: hemostasis, inflammation, proliferation, and remodeling.

Hemostasis: The first stage begins immediately after injury and involves vasoconstriction and platelet aggregation to form a clot, which helps stop bleeding and create a provisional matrix at the wound site.

Inflammation: In this stage, immune cells, such as neutrophils and macrophages, infiltrate the wound to clear debris and fight off potential infections. Inflammation also stimulates the release of growth factors and cytokines that trigger the subsequent phases of healing.

Proliferation: During this phase, new tissue is generated to replace the damaged tissue. Fibroblasts synthesize collagen, the main component of the extracellular matrix, to provide strength and support to the healing wound. Endothelial cells form new blood vessels (angiogenesis), facilitating nutrient supply to the healing tissue.

Remodeling: In the final stage, the wound undergoes remodeling, during which collagen fibers are reorganized and realigned to increase the wound's tensile strength. This process may take several months to complete and results in a scar that is often weaker and less flexible than the original tissue.

Various factors can impact the wound healing process, affecting the speed and quality of tissue repair. Among these factors, oxidative stress, inflammation, microbial infections, and melanogenesis play critical roles.

Oxidative Stress: Reactive oxygen species (ROS) generated during inflammation can lead to oxidative stress, damaging cellular components and impairing tissue repair. Antioxidants are essential in mitigating oxidative damage and promoting healing by neutralizing ROS.

Inflammation: While inflammation is necessary for wound healing, excessive or prolonged inflammation can delay the healing process. Proper management of inflammation is crucial to facilitate timely progression to subsequent healing stages.

Microbial infections: Wounds can be susceptible to microbial colonization and infection, which can significantly impede healing. Controlling infection through proper wound care and antimicrobial agents is vital for successful wound healing.

Melanogenesis: In certain wounds, such as burns, excessive melanin production may lead to hyperpigmentation, causing

cosmetic concerns and impairing wound healing. Managing melanogenesis during wound repair is essential to achieve optimal cosmetic outcomes.

Understanding these wound healing stages and the factors influencing them is essential for clinicians to effectively manage wounds, promote optimal tissue repair, and achieve successful outcomes in surgical and non-surgical procedures. Close attention to wound care, controlling inflammation, and utilizing appropriate interventions to address oxidative stress, infections, and melanogenesis will significantly impact the healing process and overall patient recovery.[1,6-12]

ANTI-OXIDATIVE EFFECT OF *ETLINGERA ELATIOR* ON WOUND HEALING

Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them with antioxidants. In the context of wound healing, oxidative stress can hinder the normal repair process by damaging cellular components and impairing the function of immune cells, fibroblasts, and endothelial cells involved in tissue regeneration. ROS can lead to inflammation, apoptosis, and delayed wound closure, thereby contributing to chronic wounds and impaired healing. *Etlingera elatior* has been extensively studied for its antioxidant properties. The plant contains various antioxidant compounds, such as phenolic compounds (e.g., phenolic acids and tannins), flavonoids, terpenoids, and essential oils. These bioactive constituents possess the ability to scavenge free radicals and reduce oxidative stress, thereby protecting cells from damage during the wound healing process.[13-20]

Numerous in vitro studies have investigated the antioxidant potential of *Etlingera elatior* extracts and isolated compounds. These studies have demonstrated the ability of *Etlingera elatior* extracts to neutralize ROS, reduce lipid peroxidation, and enhance cellular antioxidant enzyme activity. In vivo studies using animal models have also shown promising results, indicating that the administration of *Etlingera elatior* extracts can reduce oxidative stress markers and accelerate wound closure. The antioxidant effect of *Etlingera elatior* contributes to improved tissue repair, reduced inflammation, and overall enhanced wound healing outcomes.[3-5,21-22]

As a result of its potent antioxidant properties, *Etlingera elatior* extracts holds significant promise as a natural therapeutic agent in wound healing. The scavenging of free radicals and reduction of oxidative stress can facilitate an optimal wound microenvironment that supports the various stages of healing. Further research is warranted to explore the precise mechanisms of action and potential clinical applications *of Etlingera elatior* extracts in wound management, both in plastic surgery and other medical settings.

ANTI-INFLAMMATORY EFFECT OF *ETLINGERA ELATIOR* ON WOUND HEALING

Inflammation is a critical phase in the wound healing process as it initiates the body's defense response and facilitates tissue repair. During the inflammatory phase, immune cells, such as neutrophils and macrophages, are recruited to the wound site. These cells release pro-inflammatory cytokines and mediators, such as interleukins and prostaglandins, to remove debris and fight off potential infections. While inflammation is essential for initiating the wound healing cascade, excessive or prolonged inflammation can lead to tissue damage and delayed wound healing. Therefore, controlling the inflammatory response is crucial for optimal wound repair and tissue regeneration.

Etlingera elatior contains a range of bioactive compounds with anti-inflammatory properties. Phenolic compounds, flavonoids, terpenoids, and essential oils found in *Etlingera elatior* have been shown to modulate the production and activity of pro-inflammatory cytokines and mediators.[3-5] These compounds can inhibit the expression of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukins 1β and 6 (IL-1β, IL-6), and reduce the synthesis of prostaglandins and leukotrienes, which are potent inflammatory mediators. One study reported that *Etlingera elatior* aquous extract treatment created significantly decreased inflammatory marker (interleukin 6, IL-6), fibrosis markers (transforming growth factor beta, TGF-β), and connective tissue growth factor (CTGF).[23] By downregulating pro-inflammatory signaling, *Etlingera elatior* helps in maintaining a balanced inflammatory response during wound healing.

Several preclinical studies have investigated the anti-inflammatory effects of *Etlingera elatior* extract in animal wound models. One study showed that *Etlingera elatior* flower extract reduced the ulceration index and the infiltration of inflammatory cells.[24] Such experimental finding supports the notion that *Etlingera elatior*'s anti-inflammatory constituents can effectively modulate the inflammatory phase of wound healing, leading to enhanced tissue repair and reduced scar formation.

ANTIMICROBIAL EFFECT OF *ETLINGERA ELATIOR* ON WOUND HEALING

Microbial infections pose significant challenges to the wound healing process, often leading to complications such as delayed healing, chronic wounds, and increased risk of systemic infections. Bacterial, fungal, and even viral pathogens can colonize wounds, disrupting the normal healing cascade and exacerbating inflammation. Infections not only interfere with the proliferation and migration of cells involved in tissue repair but also contribute to the breakdown of extracellular matrix components, ultimately impairing wound closure. Effective management of microbial infections is therefore paramount for successful wound

healing outcomes.

Etlingera elatior presents a rich source of antimicrobial compounds that hold promise for wound healing applications. The plant's extracts contain bioactive constituents, including phenolic compounds, flavonoids, and essential oils, which exhibit broad-spectrum antimicrobial activity. Phenolic compounds and flavonoids have been shown to disrupt bacterial cell membranes, interfere with biofilm formation, and inhibit the growth of common wound pathogens such as demonstrated strong antibacterial activity towards *Salmonella typhimurium*, *Staphylococcus aureus*, and *Escherichia coli*.[3,22,25] The essential oils in *Etlingera elatior* possess volatile compounds that have been reported to possess strong antibacterial and antifungal properties, making them potentially effective agents against microbial colonization and infection in wounds.

In vitro studies have indicated that *Etlingera elatior* extracts and their isolated compounds can inhibit the growth of various pathogenic microorganisms. For example, a study by Insani (2015) demonstrated that *Etlingera elatior* exhibited potent antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA).[26] Similarly, in vivo studies utilizing animal wound infection models have provided promising results. A study by Syafriana and colleagues in 2021 showed that topical application of *Etlingera elatior* extract significantly reduced bacterial load of *Staphylococcus epidermidis* and *Propionibacterium acnes*.[27] Researchers suggest that the immunomechanism is due to increased modulation of phagocytosis activity.[28] These findings highlight the potential of *Etlingera elatior*'s antimicrobial compounds to effectively control microbial growth and support the wound healing process, offering a valuable avenue for future wound care strategies.

ANTI-MELANOGENESIS EFFECT OF *ETLINGERA ELATIOR* ON WOUND HEALING

Melanogenesis is the process by which melanin, the pigment responsible for skin, hair, and eye color, is synthesized and deposited in the skin. In the context of wound healing, aberrant melanin production generally leads to scarring and hyperpigmentation. Wounds that involve deeper layers of the skin or are subject to inflammation are more prone to developing scarring and hyperpigmentation due to the activation of melanocytes and increased melanin synthesis. Excessive melanin production can result in persistent darkening of the wound area, causing cosmetic concerns and impairing the overall aesthetic outcome of wound healing, particularly in plastic surgery and dermatology procedures.

Studies showed *Etlingera elatior* extract is highly selective against the melanoma cell lines,[4,29] therefore it has shown potential in mitigating wound-induced hyperpigmentation due to its anti-melanogenic properties. Some of its bioactive constituents, such as phenolic compounds and flavonoids, are known to modulate melanin production pathways. These compounds inhibit the activity of tyrosinase, a key enzyme involved in melanin synthesis. By reducing tyrosinase activity, *Etlingera elatior*'s anti-melanogenic compounds can impede the formation of melanin and subsequently minimize hyperpigmentation at the wound site. Additionally, the antioxidant and anti-inflammatory effects of Etlingera elatior also contribute to its anti-melanogenesis properties by preventing oxidative stress-induced activation of melanocytes and inflammation-associated melanin production.[3-5]

However, specific studies focusing on *Etlingera elatior*'s anti-melanogenesis effect in wound healing are still limited. Further research, including cellular and animal studies, is needed to directly investigate the anti-melanogenesis potential of *Etlingera elatior* extract in the context of wound healing and to validate its efficacy in minimizing wound-induced hyperpigmentation.

CLINICAL STUDIES AND CASE REPORTS ON *ETLINGERA ELATIOR* IN WOUND HEALING

Currently, there are limited published case reports and human trials specifically investigating the wound healing properties of *Etlingera elatior*. However, there are studies exploring the wound healing potential of related botanical species within the *Zingiberaceae* family, like Curcuma and Turmeric species,[30-32] and --in consideration of shared similarities within a botanical family-- researchers may hypothetically expect the same therapeutic effect with *Etlingera elatior* extracts as they conducting the trials.

POTENTIAL APPLICATIONS AND FORMULATIONS OF *ETLINGERA ELATIOR* IN WOUND HEALING

To harness the wound healing potential of *Etlingera elatior*, clinicians may consider various formulations for topical applications, dressings, and wound gels.[33-35] Clinicians can incorporate an *Etlingera elatior* extract into topical creams, ointments, or gels for direct application to wounds. This allows for targeted delivery of its active compounds to the wound site, promoting local healing. Clinicians may also formulate wound gels containing *Etlingera elatior* to create a moist wound environment, which is known to facilitate wound healing. The proposed gel-based formulation can also provide a soothing effect, reduce pain, and improve patient comfort during the healing process. It is crucial to conduct appropriate stability and safety tests for these formulations to ensure their efficacy and suitability for clinical use.

Challenges and future perspectives

While there is a growing body of literature on the wound healing potential of *Etlingera elatior*, several challenges and gaps in knowledge need to be addressed. Firstly, we find much of the existing researches conducted in vitro and in animal models, with limited clinical studies in human subjects. Robust clinical trials are essential to validate the

efficacy and safety of *Etlingera elatior* extracts in wound healing management. Moreover, the mechanisms of action by which *Etlingera elatior*'s bioactive compounds interact with wound microenvironments and influence the healing process remain largely unexplored. In-depth studies are required to unravel the precise molecular pathways and signaling mechanisms involved. Furthermore, standardized extraction methods and identification of key active compounds are necessary to ensure consistent therapeutic efficacy across different *Etlingera elatior* preparations.

Standardization and quality control is some of the primary challenges in translating botanical therapies like *Etlingera elatior* to clinical practice. Variability in plant sourcing, preparation, and extraction methods can lead to inconsistent bioactive compound concentrations and, consequently, variable therapeutic effects. Additionally, regulatory approvals and incorporation of botanical therapies into mainstream wound care protocols may encounter resistance due to the traditional and alternative nature of these treatments. Collaborations between botanical scientists, clinicians, and regulatory bodies are vital to establish evidence-based guidelines and protocols for the safe and effective use of *Etlingera elatior* in wound healing management.

To explore the full potential of *Etlingera elatior* in wound healing, further research avenues should include conducting more clinical trials with large sample sizes and diverse wound types. Investigating the interactions between *Etlingera elatior*'s bioactive compounds and various wound microenvironments can provide valuable insights into tailored treatment approaches. Additionally, understanding the optimal dosing and delivery methods, such as topical applications, dressings, and wound gels, can enhance the formulation of *Etlingera elatior*-based wound healing products. Furthermore, studies on the combination of *Etlingera elatior* with conventional wound care modalities or other botanical agents may lead to synergistic effects, enabling more comprehensive wound healing strategies.

CONCLUSION

Botanicals, rooted in traditional medicine, continue to be explored for wound healing. *Etlingera elatior*, a member of the *Zingiberaceae* family, is gaining attention due to its rich bioactive compounds like phenolics, flavonoids, terpenoids, and essential oils. These components contribute to its antioxidative, anti-inflammatory, antimicrobial, and potential anti-melanogenic effects. In vitro and in vivo studies validate its ability to support tissue repair, curb inflammation, manage microbes, and potentially hinder hyperpigmentation. Yet, transitioning *Etlingera elatior*'s wound healing prowess into clinical use faces hurdles. Scarce clinical trials and incomplete mechanistic understanding hinder seamless integration into mainstream wound care. Standardized extraction, quality control, and regulatory nod are essential for consistent efficacy and safety. Filling the gap between botanical therapies and clinical application requires rigorous clinical trials, in-depth mechanistic studies, and formulation optimization for topical applications, dressings, and wound gels. Collaboration among researchers, clinicians, and regulators is pivotal to unlock Etlingera elatior's potential, enhancing wound care strategies in plastic surgery and beyond.

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