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Cinnamon as a Potential Biomaterial for Treating Methicillin-Resistant Staphylococcus Aureus (MRSA) in Wound Healing

Abstract

Methicillin-resistant Staphylococcus aureus (MRSA) is a gram-positive bacterial strain resistant to numerous antibiotics, posing significant challenges in treating infections and increasing the risk of complications in wound healing (Centers for Disease Control and Prevention, 2019; Siddiqui & Koirala, 2022). MRSA infections are often associated with healthcare settings, such as hospitals and long-term care facilities, but community-acquired infections are also rising (Chambers & Deleo, 2009). When MRSA infects a wound, it can delay healing and heighten the risk of complications, including sepsis and necrotizing fasciitis (Forbes & Cooper, 2013, p. 141). Consequently, exploring alternative treatments, such as cinnamon, for MRSA-infected wounds is crucial to enhance wound healing and minimize complications. Cinnamon has been shown to positively impact the inflammation and proliferation stages of wound healing (Jayaprakasha & Rao, 2011; Rao & Gan, 2014). Research indicates that engineered cinnamon-based biomaterials have potential health benefits as anti-inflammatory, antioxidant, and antimicrobial agents (Rao & Gan, 2014; Saini et al., 2021). Furthermore, cinnamon promotes the proliferation and migration of skin cells, assisting in new tissue formation and wound closure (Seyed Ahmadi et al., 2019). This review investigates the potential advantages, challenges, and limitations of cinnamon as a biomaterial for treating MRSA in wound healing and the studies supporting its effectiveness against MRSA and in promoting wound healing.

Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) is a gram-positive type of bacteria resistant to several common antibiotics, complicating treatment and presenting challenges in wound healing (Centers for Disease Control and Prevention, 2019; Seyed et al., 2019; Siddiqui & Koirala, 2022). Infections caused by MRSA, i.e., staph infections, can lead to severe complications, particularly in individuals with weakened immune systems or chronic conditions like diabetes (Forbes & Cooper, 2013, p. 141). Given the growing concern of antibiotic resistance, there is an urgent need for alternative biomaterials to address these challenges and promote effective wound healing. Cinnamon, a natural plant-based material commonly used as a spice or flavoring agent, has emerged as a potential biomaterial, i.e., engineered natural material, due to its antimicrobial properties (Elgayyar et al., 2001; Prestwich & Atzet, 2013). This review investigates the potential advantages and limitations of cinnamon as a biomaterial for treating MRSA-infected wounds, with a focus on its composition, properties, and applications supported by studies such as those by Elgayyar et al. (2001), Ranasinghe et al. (2017), Saini et al. (2021), Anandhi et al. (2022), and Panjaitan et al. (2022).

Engineered Cinnamon-Based Biomaterials: Composition and Properties

Cinnamon has been used for medicinal purposes since 3000 BC, and there are more than 250 species known around the world, the most common among them is *Cinnamomum verum/zeylanicum, Cinnamomum cassia, Cinnamomum burmannii,* and *Cinnamomum loureiroi* (Banu & Lunghar, 2022, p. 257; Thomas et al., 2012, p. 182-183). Cinnamon, derived from the bark of trees in the Cinnamomum genus, can be considered an engineered natural material when modified to improve its properties or functionalities for specific biomedical applications (Prestwich & Atzet, 2013). Engineered natural materials are advantageous because the host can successfully clear and metabolize the implanted substance through enzymatic or hydrolytic degradation (Prestwich & Atzet, 2013). Cinnamon contains various bioactive components, like cinnamaldehyde and eugenol, which contribute to its properties and potential applications as a biomaterial (Rahman, 2015).

Cinnamaldehyde, a primary compound in cinnamon, is responsible for cinnamon's distinct flavor and aroma. It has robust antimicrobial properties, effective against various microorganisms, including bacteria and fungi (Jayaprakasha & Rao, 2011; Elgayyar et al., 2001; Anandhi et al., 2022; Panjaitan et al., 2022; Saini et al., 2021). Eugenol, another critical component of cinnamon, is a phenolic compound that exhibits a broad range of biological activities, including antimicrobial, anti-inflammatory, and antioxidant properties (Rao & Gan, 2014; Mbaveng & Kuete, 2017; Nayik et al., 2023).

Engineered natural materials, such as alginate, chitosan, silk, collagen, gelatin, and chondroitin sulfate, have been used directly on wounds (Prestwich & Atzet, 2013). Researchers have explored the antimicrobial properties of cinnamon, primarily due to cinnamaldehyde and eugenol, for applications in food preservation, wound healing, and infection prevention (Rao & Gan, 2014; Elgayyar et al., 2001; Anandhi et al., 2022; Panjaitan et al., 2022; Saini et al., 2021). These compounds have proven effective in inhibiting the growth of numerous pathogenic bacteria, including MRSA (Seyed Ahmadi et al., 2019).

Cinnamon essential oil also possesses anti-inflammatory and antioxidant properties (Rao & Gan, 2014; Ranasinghe et al., 2017; Banu & Lunghar, 2022). Cinnamon's anti-inflammatory effects can help modulate the inflammatory response in various contexts, such as wound healing, potentially promoting tissue repair and regeneration (Forbes & Cooper, 2013; Seyed Ahmadi et al., 2019). Antioxidants, primarily due to eugenol, assist in neutralizing harmful free radicals, safeguarding cells and tissues from oxidative stress and damage (Rao & Gan, 2014).

In summary, engineered cinnamon-based biomaterials, enriched with bioactive components like cinnamaldehyde and eugenol, exhibit various biological properties, including antimicrobial, anti-inflammatory, and antioxidant effects. These properties make them promising candidates for various applications, especially in wound healing and infection prevention.

Cinnamon Essential Oil Antibacterial Effects Against Staphylococcus aureus (Staph)

Seyed Ahmadi et al. (2019) and Banu & Lunghar (2022) described how cinnamon, particularly its essential oil, has shown antibacterial effects against Staphylococcus aureus (Staph). The primary compound responsible for the antibacterial activity is trans-cinnamaldehyde, which is present in cinnamon oil. One of the potential mechanisms of cinnamon's antibacterial action against S. aureus is the <u>degradation of the bacterial cell wall.</u> Cinnamon oil can weaken and damage the cell wall of S. aureus, resulting in the compromised structural integrity of the bacterial cells. Another mechanism is <u>increased membrane permeability</u>. Cinnamon oil can increase the permeability of the bacterial cell membrane, leading to the leakage of cytoplasmic materials, which disrupts the normal functioning of the bacterial cells. In addition, the compounds present in cinnamon can <u>cause shrinkage and distortion of bacterial cells</u>, further inhibiting their growth and reproduction. Lastly, cinnamon oil can <u>denature bacterial proteins</u>, affecting their structure and function and disrupting the essential processes within the bacterial cells. These mechanisms contribute to the antibacterial activity of cinnamon oil against S. aureus. It is important to note that further research is needed to determine the specific concentrations and effectiveness of cinnamon oil against different strains of S. aureus, including MRSA.

Cinnamon-Based Biomaterials and MRSA

Cinnamon has gained attention for its potential to combat methicillin-resistant Staphylococcus aureus (MRSA) infections and be integrated into wound dressings or other medical materials. Several studies have demonstrated the antimicrobial properties of cinnamon extracts against MRSA.

Elgayyar et al. (2001) conducted a study evaluating the antimicrobial activity of essential oils derived from various herbs and plants against several foodborne pathogens. They highlighted cinnamon's antimicrobial activity and essential oils' role as "antimicrobial inhibition zones for essential oils against foodborne pathogens, spoilage bacteria, yeasts, and molds." The study found that some oils, including oregano and thyme, had potent antimicrobial effects against several bacteria and fungi. In contrast, others, such as angelica and carrot, exhibited little to no inhibitory effect. The study suggests that further research is needed to explore the potential use of essential oils in food formulations as natural preservatives. However, their effectiveness may be limited by the evaporation of antimicrobial compounds during heat treatment.

Ranasinghe et al. (2017) reported the results of a Phase I clinical trial evaluating the safety and efficacy of Cinnamomum zeylanicum (CZ) in healthy adults. The study aimed to determine CZ's appropriate dosage and formulation for future clinical trials. Participants were given CZ as an aqueous extract, ethanolic extract, or essential oil. The researchers found that all forms of CZ were safe and well-tolerated, with no significant adverse effects. The essential oil demonstrated the greatest antimicrobial activity against gram-positive and gram-negative bacteria, including MRSA. The study concluded that CZ has the potential as a natural antimicrobial agent, and further clinical trials are warranted to assess its effectiveness in treating infections.

Seyed Ahmadi et al. (2019) explored the wound healing properties of Cinnamon verum essential oil in an infected wound model using mice. The mice had circular excisional wounds infected with Staphylococcus aureus and Pseudomonas aeruginosa and were treated topically with control and ointments containing 2% and 4% Cinnamon verum essential oil. The results indicated that Cinnamon verum essential oil accelerated wound healing by shortening the inflammatory phase, increasing fibroblast distribution and collagen deposition, and enhancing cellular proliferation, reepithelialization, and keratin synthesis. Additionally, the mRNA levels of insulin-like growth factor I (IGF-1), fibroblast growth factor-2 (FGF-2), and vascular endothelial growth factor (VEGF) were higher in the Cinnamon verum-treated groups. The study suggests that Cinnamon verum could be a potential natural remedy for wound healing, with its essential oil proving effective in combating infections such as MRSA.

Saini et al. (2021) discussed the preparation of nanocellulose-based aerogel architectures impregnated with cinnamon extract for improved antibacterial properties. They found that incorporating cinnamaldehyde, the primary compound in cinnamon bark, resulted in excellent and long-term antimicrobial activity against gram-positive, e.g., MRSA, and gram-negative bacteria. The antibacterial action mechanism of cinnamaldehyde was attributed to its ability to disrupt the bacterial membrane structure. The resulting flexible and durable architectures can be used as scaffolds in tissue engineering applications or biomedical materials such as wound dressings and medicine band-aids.

Anandhi et al. (2022) investigated the antibacterial activity of cinnamon and clove oil against various wound pathogens, including Pseudomonas aeruginosa, Escherichia coli, and Klebsiella pneumoniae. The results revealed that cinnamon oil was more effective in killing wound pathogens than clove oil. Cinnamon and clove oils are shown to be effective antibacterial agents due to their ability to reduce the virulence and pathogenicity of drug-resistant bacteria. The study suggests these oils could be used in various food and sanitizing products as antibacterial agents.

Panjaitan et al. (2022) investigated the antibiofilm activity of a cinnamon ethanol extract against two periodontal pathogens, Porphyromonas gingivalis, and Aggregatibacter actinomycetemcomitans. The study found that the cinnamon ethanol extract contained active compounds such as flavonoids, alkaloids, saponins, tannins, quinones, and terpenoids that were effective against the bacteria. The extract exhibited antibiofilm effects against both bacteria and was as effective as 0.2% chlorhexidine, a "gold standard" antibacterial mouthwash. The study also found that the cinnamon ethanol extract demonstrated non-toxicity to fibroblasts at high concentrations. The authors suggest that the cinnamon ethanol extract might be useful as an alternative therapy for periodontal diseases. However, further in vivo studies are needed to confirm its efficacy as a mouthwash.

In summary, cinnamon and its derivatives have shown promising results in combating MRSA and other bacterial infections. Research has demonstrated the antimicrobial properties of cinnamon extracts against various pathogens, and studies have explored the potential application of cinnamon-based biomaterials in wound dressings and tissue engineering. Although further research is needed to confirm the efficacy of cinnamon and its extracts in clinical settings, these studies suggest that cinnamon could be an effective, natural alternative for treating infections and preventing the spread of drug-resistant bacteria.

Cinnamon-Based Biomaterials for Wound Healing Applications

Cinnamon-based biomaterials have demonstrated significant potential in wound healing applications due to their bioactive components, such as cinnamaldehyde and eugenol (Nayik & Ansari, 2023). The advantages of incorporating cinnamon into wound dressings or other medical materials include promoting skin cell proliferation and migration, leading to faster tissue formation and wound closure (Seyed Ahmadi et al., 2019). Additionally, cinnamon's anti-inflammatory and antioxidant properties can support healing by reducing inflammation and mitigating oxidative stress. Studies have also shown that cinnamon-based biomaterials can effectively combat MRSA infections in wounds. However, further research is needed to explore the underlying mechanisms and evaluate their potential for clinical use.

Challenges and Limitations

The utilization of cinnamon-based biomaterials in wound healing presents certain challenges and limitations. Ensuring safety and biocompatibility is a primary concern, as cinnamon or its components can cause irritation or cytotoxicity if applied at high concentrations or misused (Ranasinghe et al., 2017). Determining the optimal concentration and application method is essential for maximizing the benefits while minimizing potential harm (Panjaitan et al., 2022).

Another challenge is devising effective techniques for incorporating cinnamon into wound dressings or medical materials (Saini et al., 2021). Researchers must investigate different formulations and delivery systems, such as hydrogels, films, or nanoparticles, to optimize cinnamon's antimicrobial properties and minimize cytotoxicity.

Discussion and Conclusions

Cinnamon-based biomaterials show promising therapeutic benefits for wound healing due to their antimicrobial, anti-inflammatory, and antioxidant properties. These properties can promote skin cell proliferation, alleviate inflammation, and protect against oxidative stress, making them particularly beneficial for treating MRSA-infected wounds. However, addressing safety, biocompatibility, and effective delivery challenges is critical for harnessing cinnamon's potential in clinical applications.

Further research is essential to better understand the mechanisms behind cinnamon's wound healing effects and optimize its use as a biomaterial. In vivo studies and clinical trials can provide valuable information on the safety, efficacy, and overall impact of cinnamon-based treatments in wound care. Despite the challenges and limitations, the potential benefits of cinnamon in wound healing warrant continued investigation.

In conclusion, ongoing research efforts are necessary to identify optimal application methods, concentrations, and delivery systems that maximize the therapeutic potential of cinnamon in wound care, ultimately leading to improved patient outcomes. Studies and clinical trials are needed to evaluate the safety, efficacy, and optimal concentrations of cinnamon-based biomaterials for wound healing applications. Moreover, research should explore different formulations and delivery systems to maximize the therapeutic benefits of cinnamon while minimizing potential harm. Ultimately, integrating cinnamon-based biomaterials into wound dressings and medical materials may offer an effective, natural alternative for treating MRSA infections and enhancing wound healing outcomes.

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