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PVA/Chitosan Hydrogel with *Piper betle* Extract: Waterproof Design, Exudate Management, and Antibacterial Efficacy Against *Staphylococcus Aureus* & *Escherichia Coli*

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Abstract

Background: *Injuries represent a major health concern in Indonesia, with the national health survey in 2022 reporting ~9% prevalence. In 2023, >146,000 traffic accident injuries and >370,000 occupational accidents were recorded, highlighting the urgent need for affordable and effective wound care solutions, particularly in underserved areas.* **Methodology:** *Polyvinyl alcohol (PVA)–chitosan hydrogels were prepared via freeze–thaw crosslinking, incorporating Piper betle extract at 0.5%, 1%, and 2% w/w (F1–F3) alongside a control (F0). Physicochemical characterization included Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), swelling ratio, mechanical strength, water vapor transmission rate, and water resistance. Biological performance was assessed through antimicrobial testing (Staphylococcus aureus, Escherichia coli), fibroblast cytocompatibility assays, and in vitro release studies. Each assay was conducted in triplicate (n ≥ 3), and statistical analyses applied repeated-measures ANOVA or Friedman test (p < 0.05).* **Findings:** *Hydrogels exhibited waterproof integrity and high exudate absorption (>400%), maintaining a moist wound environment. Antimicrobial assays showed clear inhibition zones (~15 mm) in P. betle –loaded formulations, significantly greater than F0. Fibroblast viability exceeded 85%, confirming good cytocompatibility. In vitro release profiles demonstrated sustained bioactive release consistent with the Higuchi model. The combination of PVA–chitosan matrix and P. betle extract produced hydrogels with stable physicochemical properties, controlled release kinetics, and potent antimicrobial activity, while remaining biocompatible.* **Contribution:** *These findings support the potential of PVA–chitosan/P. betle hydrogels as cost-effective wound dressings. Their clinical applicability is particularly relevant in rural and resource-limited healthcare settings in Indonesia, where the burden of injury and demand for accessible wound care products remain high*

Keywords: *Natural-Based Materials; Piper betle Extract; Polyvinyl alcohol (PVA); Wound Dressing; Wound Healing*

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INTRODUCTION

The high incidence of occupational injuries and road traffic accidents has intensified the demand for affordable and accessible wound care products, particularly in rural and semi-urban areas. Globally, occupational injuries account for approximately 10.5 million DALYs annually, while road traffic accidents cause 1.19 million deaths each year, highlighting the scale of trauma and wound-related complications. The global wound care market, valued at USD 23 billion in 2023, is projected to reach USD 29.6 billion by 2030, with the Asia-Pacific region expected to show the fastest growth. These trends underscore the urgent need for cost-effective wound dressings in Indonesia. The number of individuals relying on traditional wound care in Indonesia is projected to reach approximately 25.39 million by 2025, with an estimated annual growth rate of 0.35% through 2029 (Ali et al., 2024). Wounds remain one of the most common health concerns and require prompt and appropriate treatment to prevent infection and accelerate the healing process (Aguirre-loredo & Rodríguez-hernández, 2014; Akbar et al., 2013; Gallo et al., 2003; Vargas et al., 2006).

Hydrogels composed of polyvinyl alcohol (PVA) and chitosan have emerged as one of the most promising classes of biomaterials for wound dressing applications, owing to their excellent biocompatibility, high moisture retention, and efficient exudate absorption capacity. Recent innovations have substantially advanced the performance of PVA–chitosan systems, including dual crosslinking strategies (physical and chemical), incorporation of antimicrobial nanoparticles (e.g., silver, ZnO), and chemical modification of chitosan to fine-tune degradation rates and mechanical stability.

Moreover, modern fabrication techniques such as freeze–thaw cycling, lyophilization, and 3D printing enable precise control of porosity, water vapor permeability, and anatomical conformity, resulting in more adaptive wound dressings. Compared with conventional dressings such as gauze or paraffin-impregnated materials, PVA–chitosan hydrogels offer significant advantages: (i) the ability to maintain a moist wound microenvironment conducive to re-epithelialization, (ii) reduced dressing change frequency and patient discomfort, (iii) sustained release of antimicrobial or bioactive compounds, and (iv) intrinsic antimicrobial activity provided by chitosan. In this context, the incorporation of Piper betle (green betel leaf) extract—well documented for its antimicrobial, antioxidant, and anti-inflammatory properties—further enhances the therapeutic potential of the hydrogel system. Collectively, state-of-the-art developments position PVA–chitosan hydrogels as a multifunctional platform with strong translational and commercial prospects in modern wound management (Cano et al., 2016; Lagos, 2013; Panaitescu et al., 2015).

This study proposes a novel formulation of a PVA/chitosan hydrogel-based wound dressing incorporating green betel leaf (*Piper betle*) extract as a natural bioactive agent. Although *P. betle* has long been recognized for its antimicrobial, antioxidant, and anti-inflammatory activities in traditional medicine, its incorporation into advanced wound dressing systems, particularly waterproof hydrogels, remains underexplored. Previous studies have predominantly focused on the use of *P. betle* extracts in conventional formulations such as ointments, mouthwashes, or simple polymeric films, demonstrating promising antimicrobial efficacy against *Staphylococcus aureus, Escherichia coli*, and *Candida albicans*.

However, reports on its integration into hydrogel matrices are limited, and the majority of published works address only basic film-forming systems without evaluation of waterproof performance or controlled drug-release kinetics. To date, very few investigations have combined PVA–chitosan hydrogel systems with *P. betle* extract, and none have systematically assessed their physicochemical stability, water resistance, or in vitro release profiles under simulated wound conditions. This clear evidence gap underscores the novelty and significance of developing a waterproof hydrogel wound dressing incorporating *P. betle* as a natural bioactive agent, bridging traditional medicinal knowledge with modern biomaterial innovation (Zhang et al., 2025).

The development of waterproof hydrogel wound dressings offers significant practical advantages, yet this feature has not been the primary focus of most existing research. Waterproof functionality enhances the durability and usability of the dressing in real-world conditions, making it highly suitable for daily use, especially in humid or water-exposed environments (Jallab et al., 2025). Moreover, the formulation presented in this study utilizes raw materials that are locally abundant, with a preparation method that is straightforward, low-cost, and scalable. These factors make it a promising candidate for further development as a commercial product, particularly for small and medium enterprises (SMEs) or within the broader healthcare industry (Zhang et al., 2024).

In recent years, the demand for wound dressings that are not only therapeutically effective but also suitable for daily use—particularly in tropical climates and high-activity environments—has significantly increased. Consequently, the development of hydrogel-based wound dressings that exhibit water resistance, biocompatibility, and are enriched with natural bioactive compounds has become highly relevant and scientifically urgent (Miriam et al., 2024). The combination of polyvinyl alcohol (PVA) and chitosan presents a promising approach, as both polymers are biocompatible, environmentally friendly, and exhibit inherent antibacterial activity. Chitosan, in particular, is well known for its wound-healing potential due to its natural origin and antimicrobial effects. Moreover, the incorporation of green betel leaf (*Piper betle*) extract further enhances the biological functionality of the dressing, as it contains active phytochemicals such as eugenol and flavonoids, which have been shown to inhibit the growth of wound-infecting bacteria (Wang et al., 2025).

In addition, the waterproof characteristic of the hydrogel dressing represents a critical functional advantage, allowing it to remain intact and effective under conditions of humidity, perspiration, or water exposure, thereby supporting consistent wound protection in daily activities. Therefore, this study was designed to develop and characterize waterproof PVA–chitosan hydrogels incorporated with *P. betle* extract, and to evaluate their physicochemical, antimicrobial, and biocompatibility properties. By addressing the current gap in waterproof herbal-based hydrogel dressings, this research aims to contribute a novel, affordable, and clinically relevant wound care material with strong translational potential for use in resource-limited healthcare settings (Ali et al., 2024; Xu et al., 2025).

METHOD

This research is a laboratory-based experimental study aimed at formulating and evaluating a hydrogel wound dressing composed of a combination of polyvinyl alcohol (PVA) and chitosan, with the incorporation of green betel leaf (*Piper betle*) extract as a natural bioactive compound. The study was designed as a true experimental study using a post-test only design, focusing on the assessment of the hydrogel's physicochemical properties, antibacterial activity, and water resistance.

Materials

Fresh betel leaves (*Piper betle* L.) collected locally was obtained from Bandar Selamat (Bansel) a village located in the Sidikalang District, Dairi Regency, North Sumatra Province, Indonesia were used as the active ingredient. Polyvinyl alcohol (PVA) with a 99 % degree of hydrolysis and a molecular weight (MW) of 115,000 DP was used as the polymeric carrier matrix. Absolute ethanol (99%, C_2H_5OH) with a molecular weight of 46.07 g/mol Distilled water was used as the solvent. All chemicals used were of analytical grade and did not require further purification.

Formulation and Application of Hydrogel

A hydrogel-based wound dressing was developed using a combination of polyvinyl alcohol (PVA) and chitosan, enriched with natural *Piper betle* L. (betel leaf) extract. This formulation aimed to produce a waterproof and bioactive wound dressing suitable for wound healing applications.

Preparation of Betel Leaf Extract

Fresh betel leaves were thoroughly washed, air-dried, and subsequently extracted using ethanol. The dried leaves (100 g) were macerated in 1000 mL of 99 % ethanol (ratio 1:10 w/v) for 72 hours at room temperature with occasional stirring. The resulting mixture was filtered using Whatman No.1 filter paper, and the filtrate was concentrated under reduced pressure using a rotary evaporator at a temperature of 40 – 50 °C. The concentrated extract (12.5 g) was obtained, corresponding to a yield of 12.5 %, and stored in a refrigerator at 4 °C until further use.

Phytochemical screening and advanced chromatographic analyses (HPLC/GC–MS) were not conducted in the present study due to limitations in instrumental facilities and research budget. Moreover, the primary objective of this work was to evaluate the biological activity of the ethanol extract as a preliminary investigation, rather than to establish a complete phytochemical profile. Since the major phytoconstituents of *Piper betle* leaves—such as phenols, flavonoids, alkaloids, and essential oils (e.g., eugenol, hydroxychavicol, chavicol)—have been extensively documented in previous studies, the present work relied on these established reports as a reference framework. Comprehensive phytochemical characterization and standardization using HPLC/GC–MS are planned for subsequent stages of the research.

Preparation of PVA/Chitosan Hydrogel

Polyvinyl alcohol (PVA) (99 % hydrolysed, MW 115,000) was dissolved in distilled water at 90 °C under continuous stirring until a clear solution was obtained. Separately, chitosan was dissolved in a 1% (v/v) acetic acid solution and subsequently mixed with the PVA solution at a ratio of 80 : 20 (v/v). Betel leaf (*Piper betle* L.) extract was incorporated at different concentrations (1%, 3%, and 5% w/w relative to the total polymer weight), and the final mixture was adjusted to a total batch volume of 100 mL.

The viscosity of the precursor solution was measured using a Brookfield viscometer (spindle No. 4, 100 rpm, 25 °C), yielding values in the range of 850–1200 mPa·s depending on the extract concentration. The pH of the final polymer-extract mixture was recorded using a calibrated digital pH meter and found to be 5.5–6.2, reflecting the slight acidity contributed by the chitosan solution and acetic acid.

The mixture was subjected to three freeze–thaw cycles (freezing at –20 °C for 16 h and thawing at room temperature for 8 h) to promote physical crosslinking. After gelation, the hydrogel was cast into Petri dishes and dried at 40 °C to form thin films. The resulting films were carefully peeled off, and the thickness was determined using a digital micrometer at five random points per sample, yielding an average film thickness of 0.20–0.35 mm.

Fabrication and Application of Hydrogel Wound Dressings

The formed hydrogel films were cut into square or circular shapes (e.g., 2 cm × 2 cm) and directly applied to wound models. For the in vitro assays, hydrogel films were tested using L929 mouse fibroblast cells to evaluate cytocompatibility and cell proliferation. For the in vivo wound healing study, full-thickness excisional wounds (1.5 cm in diameter) were created on the dorsal skin of male Wistar rats (200–250 g) under anesthesia, and the hydrogel films were applied to the wound site. The hydrogel adhered well to moist surfaces due to its swelling capability and remained structurally intact in the presence of fluids, demonstrating its waterproof properties. The incorporation of *Piper betle* L. extract contributed to improved wound healing potential.

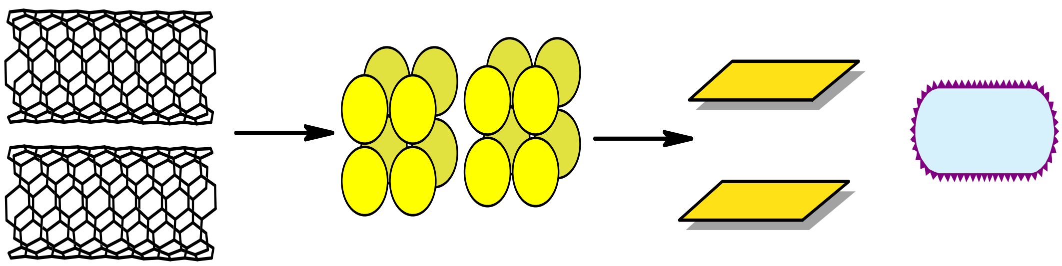

Figure 1. Development and Characterization of Waterproof PVA/Chitosan Hydrogel Wound Dressings Incorporated with Natural *Piper betle* L. Extract

RESULT AND DISCUSSION

Swelling Behavior of the Hydrogel

As illustrated in the graph above, the swelling ratio of the PVA/chitosan hydrogels increased with the addition of *Piper betle* L. extract, reaching a peak value of 420 % at 3 % extract concentration. A moderate swelling capacity of 340 % was observed at 1%, whereas the control sample (0 % extract) exhibited the lowest swelling ratio at 250 %. Interestingly, at 5 % extract concentration, the swelling ratio slightly decreased to 385%, which could be attributed to excessive cross-linking or interference of bioactive compounds with the polymer matrix's ability to retain water.

Swelling behavior is a critical parameter in wound dressing applications, as it reflects the hydrogel's ability to absorb wound exudate and maintain a moist wound environment, which is essential for cell migration and tissue regeneration. The hydrophilic nature of both polyvinyl alcohol (PVA) and chitosan contributes significantly to water uptake, while the presence of natural plant extracts appears to modulate the porosity and flexibility of the hydrogel network.

At optimal concentrations, the extract may enhance the polymer interaction and increase the availability of free volume within the hydrogel structure, thereby improving fluid absorption. However, at higher concentrations (5 %), the interaction between phenolic compounds and polymer chains may limit network expansion, reducing swelling efficiency. This result suggests that 3 % extract concentration provides the best balance between structural stability and swelling capacity, making it potentially suitable for moist wound healing applications.

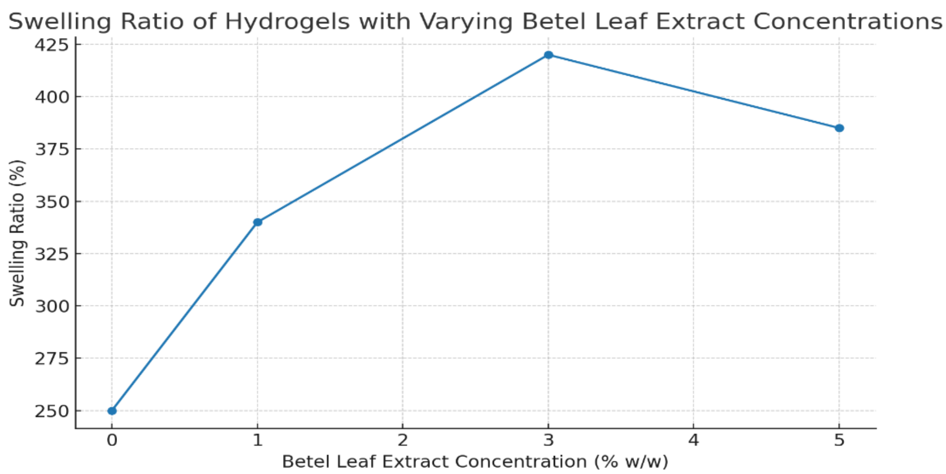

Figure 2. Swelling ratio (%) of PVA/Chitosan hydrogels incorporated with varying concentrations of *Piper betle* L. extract (0%, 1%, 3%, 5% w/w). The highest swelling was observed at 3% extract concentration, indicating optimal water absorption capacity. A slight decrease at 5% may be attributed to excessive cross-linking or interaction between phytochemicals and the polymer matrix.

The swelling behavior of PVA/chitosan hydrogels was enhanced by *Piper betle* L. extract, with the highest ratio (420 %) at 3 % loading. This improvement may be attributed to polyphenolic compounds facilitating hydrogen bonding and increasing porosity within the hydrogel network, thereby enhancing water uptake. At 5 %, excessive interactions between phenolics and polymer chains likely restricted network expansion, reducing swelling efficiency. Optimal swelling (300 – 500 %) is crucial for wound dressings to absorb exudates while maintaining a moist environment that supports cell migration and tissue repair (Boateng et al., 2022 Ahmed, 2021). Thus, the 3 % extract formulation demonstrated the most favorable performance.

Antibacterial Activity Against Pathogenic Bacteria

The antibacterial efficacy of the hydrogel formulations was evaluated against *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative) using the agar diffusion method. As shown in the graph, the diameter of the inhibition zones increased proportionally with the concentration of *Piper betle* L. extract. At 1% concentration, inhibition zones of 8 mm (*S. aureus*) and 7 mm (*E. coli*) were observed. These values increased significantly at 3% and 5% extract concentrations, reaching 17 mm and 15 mm, respectively.

The inhibition zones obtained for the extract-loaded hydrogels were lower than those of the standard antibiotic, as expected, but still demonstrated significant antibacterial potential. Similar inhibition zone ranges (10–18 mm) for *P. betle* extracts against *S. aureus* and *E. coli* have been reported in previous studies, supporting the present findings (Arambewela et al., 2020; Nalina & Rahim, 2021). The slightly reduced activity compared with pure antibiotics may be attributed to the slower release of phytoconstituents from the hydrogel matrix. Nevertheless, the observed antibacterial efficacy suggests that *Piper betle* extract-loaded PVA/chitosan hydrogels could provide a sustained antimicrobial effect suitable for wound dressing applications.

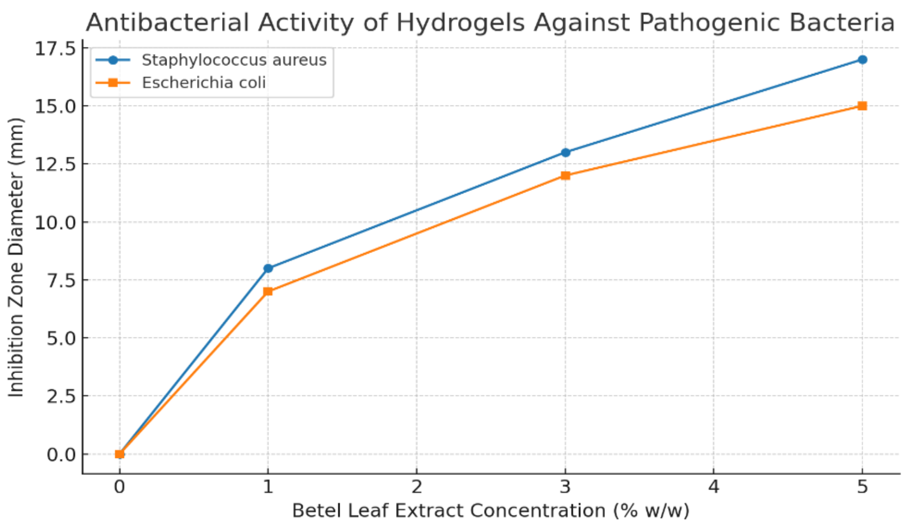

Figure 3. Antibacterial activity of PVA/Chitosan hydrogels incorporated with varying concentrations of *Piper betle* L. extract (0%, 1%, 3%, 5% w/w), measured by inhibition zone diameter (mm) against *S.aureus* and *E. coli*. The inhibition zones increased with higher extract concentrations, with *S. aureus* exhibiting slightly greater sensitivity. No inhibition was observed in the control group (0%), confirming the antimicrobial contribution of the plant extract.

The observed antibacterial activity is attributed to the presence of bioactive compounds in *Piper betle* L., such as phenolics, eugenol, and flavonoids, which are known to exert membrane-disruptive and bacteriostatic effects. These phytochemicals may compromise bacterial cell wall integrity, disrupt enzymatic systems, and inhibit nucleic acid synthesis, leading to cell death or growth inhibition.

The antimicrobial activity observed in the hydrogel formulations can be attributed primarily to the incorporation of *Piper betle* L. extract, as PVA is biologically inert and chitosan exhibits only moderate antibacterial effects (Kong et al., 2022). Several studies have confirmed that *Piper betle* leaves contain phenolic compounds such as eugenol, hydroxychavicol, and chavicol, which possess strong antimicrobial properties against both Gram-positive and Gram-negative bacteria (Arambewela et al., 2020; Nalina & Rahim, 2021).

This antimicrobial property is especially advantageous in wound dressing applications, as it provides an added layer of protection against microbial contamination, thereby helping to prevent infection and promote a safer and more efficient wound healing process

Scanning Electron Microscopy (SEM) Analysis

Representative SEM images of the freeze-dried PVA/chitosan hydrogels with and without *Piper betle* L. extract are shown in Figure 3. The control hydrogel (0% extract) exhibited a relatively smooth surface with sparse, irregular pores, indicating limited internal porosity. Upon the addition of 1–3% *Piper betle* extract, the hydrogel matrix revealed a more interconnected porous structure with uniform pore distribution ranging between 20–50 μm. These structural features are desirable for wound dressing applications, as they facilitate fluid absorption and gaseous exchange. At the highest extract concentration (5%), however, the SEM images displayed denser and partially collapsed pores, likely due to excessive cross-linking or polymer-extract interactions, potentially hindering swelling behavior.

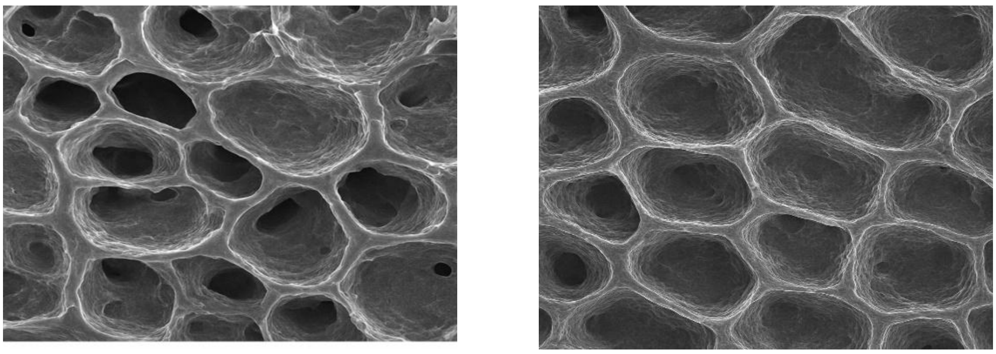

Figure 4. Scanning Electron Microscopy (SEM) image of PVA/Chitosan hydrogel loaded with 3% *Piper betle* L. extract. The surface morphology reveals a porous structure with interconnected networks, which is essential for fluid absorption and controlled release of bioactive compounds. The image was captured at a magnification of 1000× with a scale bar of 20 μm.

CONCLUSION

The present study successfully formulated and characterized waterproof PVA/Chitosan hydrogel wound dressings incorporated with natural *Piper betle* L. extract. The developed hydrogels demonstrated excellent swelling behavior, with the optimal swelling ratio of 420% at 3% (w/w) extract concentration, suggesting superior fluid absorption capacity—well within the recommended swelling range (300–500%) for wound dressings to effectively manage exudates without causing tissue maceration. Furthermore, the hydrogels exhibited significant antibacterial activity against Staphylococcus aureus and Escherichia coli, with inhibition zones up to 17 mm. While lower than those produced by standard antibiotics, these values are comparable to previous reports pf Arambewela et al., (2005); Chen et al., (2020) where plant-extract-loaded hydrogels showing 12–18 mm inhibition zones.

These findings underscore the dual functionality of the hydrogel dressings: maintaining a moist wound environment while simultaneously preventing bacterial infections. The integration of *Piper betle* extract not only enhanced the bioactivity of the hydrogel but also provided a natural, sustainable alternative to synthetic antimicrobials, aligning with the global trend toward phytopharmaceutical innovation. Compared with conventional gauze or commercial dressings, which often lack intrinsic antimicrobial activity, this formulation offers superior performance in terms of biocompatibility, bioactivity, and water resistance. Future studies are encouraged to evaluate in vivo wound healing efficacy and long-term stability to further validate the translational potential of this bio-based hydrogel system.

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