MS.ID-IJPBS-3265
International Journal of Pharmacy and Biological Sciences-IJPBS™ (2026) 16 (2): 76-83
Online ISSN: 2230-7605, Print ISSN: 2321-3272
Review Article | Biological Sciences | OA Journal | MCI Approved | Index Copernicus

# Mineral-Herbal Functionalized Collagen Composites for Scar-Reduced Superficial Wound Healing: A Comparative Review of Polymer Systems and Bioactive Additives

**Geetha Balasubramani[1*], K. Muthukumaran[1], Deekshashree I. P[2], Nithya Neha. G[3] and Priyadharshini. V[4]**

[1*]Co-Founder & CRO, Medcuore Medical Solutions Private Limited, India.

[1]Associate Professor Biomedical Engineering, Dhanalakshmi Srinivasan College of Engineering and Technology, India.

[2, 3, 4]Final year student, B.E Biomedical Engineering, Dhanalakshmi Srinivasan College of Engineering and Technology, India.

Received: 16 Feb 2026 / Accepted: 17 Mar 2026/ Published online: 01 April 2026
*Corresponding Author Email: geethapriya1728@gmail.com

## Abstract

Superficial wound healing is a tightly regulated physiological process involving coordinated cellular proliferation, extracellular matrix remodeling, angiogenesis, and controlled inflammation to achieve rapid tissue closure with minimal scar formation. Conventional dressings such as gauze and synthetic films primarily function as passive barriers and lack the ability to actively promote regeneration, prevent infection, or modulate fibrosis. Growing interest in bioactive wound dressings has therefore shifted toward natural biopolymer-based systems integrated with functional additives. While single-polymer dressings offer biocompatibility, they often exhibit limited mechanical strength, poor stability, and suboptimal biological performance. In contrast, composite polymer systems such as collagen, gelatin, or chitosan-based blends provide enhanced structural integrity, controlled degradation, and improved cellular interactions by more closely mimicking the native extracellular matrix. The incorporation of bioactive fillers further improves therapeutic efficacy: mineral-based fillers like β-tricalcium phosphate enhance mechanical reinforcement and calcium-mediated tissue regeneration; metallic agents such as silver nanoparticles provide strong antimicrobial effects but may pose cytotoxicity concerns; and herbal bioactives, particularly *Centella asiatica*, offer multifunctional wound-healing, anti-inflammatory, antioxidant, and scar-modulating properties with superior biocompatibility. Overall, composite, herbal-loaded wound patches represent a promising multifunctional strategy for advanced superficial wound management, although further optimization and clinical validation remain essential. This review systematically discusses and compares mineral, metallic, and herbal fillers in single and composite polymer systems to highlight their respective advantages, limitations, and future potential in advanced wound care applications

**Keywords**

Superficial wound healing, Composite polymer systems, β-Tricalcium phosphate (β-TCP), Centella asiatica, Bioactive wound dressings

*****

## 1. INTRODUCTION

Superficial wound healing is a complex and precisely regulated biological event characterized by four interconnected stages: haemostasis, inflammation, proliferation, and tissue remodelling. These sequential yet overlapping phases involve coordinated interactions between keratinocytes, fibroblasts, endothelial cells, inflammatory mediators, and extracellular matrix (ECM) components to restore the structural and functional integrity of the skin. Efficient repair of superficial wounds is critical not only to prevent infection and excessive fluid loss but also to achieve optimal cosmetic outcomes with minimal scar formation. However, when this tightly controlled cascade is disrupted due to prolonged inflammation, microbial contamination, oxidative stress, or inadequate matrix support re-epithelialization may be delayed, increasing the risk of hypertrophic or fibrotic scar development. Such impairments affect both functional recovery and aesthetic quality, underscoring the need for advanced therapeutic approaches that actively regulate tissue regeneration and ECM remodeling. Traditional wound dressings, including gauze, cotton pads, and synthetic polymeric films, remain commonly used because of their low cost and simplicity. Despite their widespread application, these materials primarily serve as protective coverings that provide mechanical shielding and basic moisture retention. They do not intrinsically support cellular signalling, angiogenesis, or regulated collagen synthesis, which are essential for effective healing and scar control. Moreover, their limited antimicrobial performance and inability to counteract oxidative stress reduce their clinical effectiveness, particularly in wounds susceptible to infection or delayed healing (Zhong et al., 2024). Consequently, passive dressings are increasingly being replaced by bioactive systems capable of interacting with the wound microenvironment. Recent advancements in wound care have focused on natural biopolymer-based materials and multifunctional composite scaffolds designed to emulate the architecture and function of the native ECM. Biopolymers such as collagen, gelatin, and chitosan are especially attractive due to their biocompatibility, biodegradability, and capacity to support cell adhesion and proliferation. Collagen, in particular, provides structural cues that facilitate fibroblast migration and matrix deposition. Nevertheless, formulations based on a single polymer often lack sufficient mechanical robustness, exhibit rapid degradation, and show limited long-term stability. To overcome these shortcomings, mineral reinforcements such as β-tricalcium phosphate (β-TCP) have been incorporated to enhance structural strength and introduce bioactive calcium ion release, which plays a role in cellular signalling and tissue remodeling. In parallel, the incorporation of plant-derived bioactives has emerged as a promising strategy to enhance therapeutic efficacy while maintaining safety. Centella asiatica, widely recognized in traditional medicine, contains triterpenoid compounds including asiaticoside and madecassoside that promote collagen synthesis, stimulate fibroblast activity, enhance angiogenesis, and modulate inflammatory responses. Its antioxidant and scar-modulating properties further contribute to improved wound resolution. The combination of collagen with β-TCP and Centella asiatica therefore represents a synergistic design strategy that integrates mechanical reinforcement with biological regulation. Such multifunctional composite systems offer the potential to accelerate wound closure, optimize ECM remodeling, and reduce excessive scar formation (Farjaminejad et al., 2024). This review examines the mechanistic rationale, material design considerations, and therapeutic potential of collagen–β-TCP composite systems enriched with herbal bioactives, with particular emphasis on Centella asiatica, and highlights their advantages over conventional and single-polymer wound dressings.

## 2. Single-Polymer vs Composite Polymer Systems

Polymeric biomaterials have become indispensable in modern wound healing, tissue engineering, and drug delivery applications due to their versatility, biocompatibility, and tunable physicochemical properties. Early research predominantly focused on single-polymer systems because of their simplicity, ease of fabrication, and well-established biological compatibility. However, as the complexity of wound environments and regenerative requirements became better understood, it became evident that single polymers often fail to meet the multifunctional demands of advanced biomedical applications figure 1. Consequently, composite polymer systems—formed by blending natural or synthetic polymers have gained increasing attention for their ability to provide synergistic enhancements in mechanical strength, biological activity, and degradation control.

### 2.1. Limitations of Single Polymer Systems in Biomedical Applications

Although single-polymer matrices have been extensively investigated for wound healing and tissue engineering applications, their standalone use is often constrained by intrinsic material limitations. Natural polymers such as collagen, gelatin, and alginate are highly valued for their biocompatibility, biodegradability, and ability to support cellular attachment and proliferation (Table 1). Despite these advantages, they frequently exhibit insufficient mechanical robustness, rapid enzymatic breakdown, high swelling behavior, and poor structural stability under physiological conditions (Xu et al., 2023; Oliveira et al., 2023). Such characteristics may compromise scaffold integrity, particularly in wounds subjected to mechanical stress or prolonged exposure to exudate. On the other hand, synthetic polymers including polylactic acid (PLA) and polycaprolactone (PCL) offer improved mechanical strength and more predictable, slower degradation profiles. However, these materials inherently lack biological recognition sites, hydrophilic surfaces, and intrinsic bioactivity necessary to facilitate effective cell adhesion and tissue integration (Oliveira et al., 2023). Consequently, synthetic polymers often require additional surface modification, blending, or biofunctionalization to improve their biological compatibility. Another critical drawback of single-polymer systems lies in their limited capacity for controlled therapeutic delivery. Many polymer matrices demonstrate rapid initial drug release, commonly referred to as burst release, followed by inconsistent degradation behavior, which reduces their suitability for sustained and regulated drug delivery applications (Choi et al., 2024). Moreover, individual polymers rarely provide multifunctional performance such as simultaneous mechanical reinforcement, antimicrobial protection, hemostatic action, and controlled biodegradation within a unified scaffold design (Krishnan & Sampath, 2025). These cumulative limitations have encouraged the advancement of composite polymer systems, where synergistic material combinations are employed to enhance mechanical, biological, and therapeutic functionality in a single integrated platform.

## 2.2. Advantages of Gelatin–Chitosan Composite Systems in Biomedical Applications

Gelatin–chitosan composites have gained considerable attention in wound healing and tissue engineering because of the complementary advantages offered by both polymers. Gelatin, which is derived from collagen, closely resembles the natural extracellular matrix and supports cell attachment and proliferation due to the presence of RGD sequences. These features make gelatin highly favorable for tissue regeneration. However, when used alone, gelatin tends to degrade rapidly in moist environments and lacks sufficient mechanical strength, limiting its practical application in wound dressings.

Chitosan, a natural polysaccharide obtained from chitin, offers different but equally valuable properties. It possesses inherent antimicrobial activity, hemostatic capability, and good film-forming potential. Its positively charged amino groups enable interaction with negatively charged bacterial cell membranes, contributing to its antibacterial effects. Despite these advantages, chitosan alone has limited flexibility and does not always provide optimal cell-interactive properties for tissue regeneration. When gelatin and chitosan are combined, their individual limitations are significantly reduced, resulting in a more balanced and functional composite material (Liu et al., 2023). The electrostatic attraction between the positively charged amino groups of chitosan and the negatively charged carboxyl groups of gelatin forms a stronger and more stable polymer network. This interaction enhances tensile strength, elasticity, and overall structural stability compared to single-polymer systems (Zhang et al., 2022). Such improvements are particularly important in wound dressings that must withstand movement and mechanical stress while maintaining a supportive environment for healing.

Another key benefit is tunable biodegradation. By adjusting the gelatin-to-chitosan ratio and incorporating crosslinking agents such as genipin or EDC/NHS, researchers can regulate degradation rates to align with tissue regeneration timelines. This controlled degradation addresses the rapid enzymatic breakdown observed in gelatin-only systems while preserving the composite's biocompatibility (Hosseini et al., 2024). Biologically, gelatin–chitosan composites demonstrate enhanced wound healing performance. Gelatin supports fibroblast adhesion and proliferation through RGD-mediated interactions, while chitosan provides antimicrobial protection and promotes hemostasis. Studies have reported accelerated re-epithelialization, increased collagen deposition, improved angiogenesis, and faster wound closure rates in composite systems compared to single polymer constructs (Singh et al., 2023). Additionally, these composites exhibit improved drug loading efficiency and sustained release profiles. The formation of a polyelectrolyte complex within the blended matrix reduces burst release and enables prolonged therapeutic delivery, which is particularly advantageous for chronic wound management (Zhang et al., 2022). Such systems can incorporate antibiotics, growth factors, antioxidants, and plant-derived bioactives for multifunctional therapeutic action.

**Table 1: Comparative analysis of single-polymer and composite polymer systems in biomedical wound healing applications.**

| Parameter | Single Polymer System | Composite Polymer System |
|---|---|---|
| Material Composition | Consists of a single natural (e.g., gelatin, chitosan) or synthetic (e.g., PCL, PLA) polymer | Combination of two or more polymers (natural–natural or natural–synthetic) forming blended or interpenetrating networks |
| Mechanical Properties | Often exhibits limited tensile strength and poor load-bearing capacity, especially for natural polymers | Improved tensile strength, elasticity, and compressive modulus due to synergistic intermolecular interactions and crosslinking |
| Structural Stability | Higher swelling ratio and rapid degradation under physiological conditions | Reduced swelling, enhanced structural integrity, and tunable degradation rate |
| Degradation Behavior | Difficult to control; may degrade too rapidly or too slowly depending on polymer type | Degradation kinetics can be tailored through polymer ratio and crosslinking density |
| Biological Activity | Natural polymers offer good biocompatibility but may lack durability; synthetic polymers lack intrinsic bioactivity | Combines bioactivity (e.g., cell adhesion from gelatin) with antimicrobial or hemostatic properties (e.g., chitosan) |
| Clinical Potential | Suitable for simple wound coverage applications | More suitable for advanced wound healing, chronic wounds, and tissue engineering |

### 2.3. Improved Mechanical Strength, Stability, and Biological Performance

Composite polymer systems significantly enhance the overall functional performance of wound healing materials through polymer blending and crosslinking strategies.

#### 2.3.1. Improved Mechanical Strength

Single natural polymers such as gelatin or chitosan often exhibit inadequate tensile strength and susceptibility to deformation under physiological conditions. The formation of gelatin–chitosan composites improve mechanical resilience through electrostatic interactions and hydrogen bonding. Crosslinking agents such as genipin or EDC/NHS further strengthen the polymer network by forming stable covalent bonds, enhancing structural integrity and resistance to mechanical stress (Zhang et al., 2021; Wang et al., 2022). This reinforcement ensures scaffold durability during handling, application, and in vivo wound environments.

#### 2.3.2. Improved Stability and Controlled Degradation

Composite hydrogels typically demonstrate lower swelling ratios and slower enzymatic degradation compared to single polymer matrices. The denser network architecture reduces excessive water uptake and enhances structural stability. By modulating polymer ratios and crosslinking density, degradation kinetics can be precisely controlled to match tissue regeneration rates (Li et al., 2023; Chen et al., 2020). This balance is essential for maintaining scaffold integrity throughout the healing process while allowing gradual bio-resorption.

#### 2.3.3. Enhanced Biological Performance

The biological synergy of gelatin and chitosan contributes to superior wound healing outcomes. Gelatin promotes cellular attachment and proliferation via RGD sequences, while chitosan provides intrinsic antimicrobial and hemostatic activity. Together, they enhance fibroblast proliferation, collagen synthesis, angiogenesis, and accelerate wound contraction (Liu et al., 2022; Huang et al., 2021). The composite microenvironment thus supports both structural repair and infection control, which are critical for effective superficial wound management.

## 3. Bioactive Fillers: Mineral-Based vs Metallic vs Herbal Additives

Bioactive fillers play a pivotal role in enhancing the therapeutic functionality of polymeric wound dressings. Beyond providing structural reinforcement, these fillers actively modulate cellular behavior, inflammatory responses, and extracellular matrix (ECM) remodeling. Mineral-based compounds, metallic nanoparticles, and plant-derived bioactives represent three major categories of fillers extensively explored for wound healing applications. Each class offers distinct biological mechanisms, influencing fibroblast proliferation, angiogenesis, antimicrobial defense, and scar modulation. Understanding their comparative advantages is essential for designing multifunctional wound management systems.

### 3.1. Mineral-Based Fillers (β-Tricalcium Phosphate and Hydroxyapatite)

Calcium phosphate–based biomaterials, particularly β-tricalcium phosphate (β-TCP) and hydroxyapatite (HA), have been increasingly explored as mineral reinforcements in advanced wound healing systems. Owing to their compositional similarity to the inorganic phase of bone and certain extracellular matrix components, these materials create a biologically favorable microenvironment that supports cellular attachment, proliferation, and differentiation (Table 2). Their bioactive nature makes them attractive candidates for incorporation into polymer-based wound dressings. One of the major advantages of β-TCP and HA is their predictable and controlled degradation profile. As these materials gradually resorb, they release calcium and phosphate ions into the surrounding tissue. These ions act as secondary messengers in multiple cellular pathways involved in angiogenesis, fibroblast function, and extracellular matrix deposition (Han et al., 2021). Calcium ions, in particular, are essential regulators of keratinocyte migration, collagen production, and wound contraction, all of which are critical for efficient tissue repair. Through these mechanisms, calcium phosphate fillers can actively contribute to enhanced regeneration rather than serving solely as structural additives. In the context of superficial wound applications, β-TCP is often preferred due to its comparatively higher resorption rate. Its gradual degradation enables dynamic participation in tissue remodeling without prolonged material persistence at the wound site. In contrast, hydroxyapatite demonstrates greater physicochemical stability and slower degradation, providing sustained structural reinforcement when longer scaffold integrity is required. Importantly, the ionic dissolution products generated from these materials have been associated with improved collagen alignment, increased tensile strength of newly formed tissue, and modulation of fibroblast activity. By supporting balanced ECM remodeling and influencing inflammatory signaling pathways, β-TCP and HA may help limit excessive fibrotic responses and reduce the risk of hypertrophic scar formation, thereby contributing to improved structural and functional restoration of the skin (Lu et al., 2021).

### Metallic Agents (Silver Nanoparticles and Zinc Oxide)

Metallic nanoparticles, particularly silver nanoparticles (AgNPs) and zinc oxide (ZnO), have been widely explored in wound healing applications due to their strong antimicrobial and immunomodulatory properties. Since infection is a major contributor to delayed wound healing and excessive scar formation, effective microbial control plays a central role in modern wound management strategies. AgNPs are known for their broad-spectrum antibacterial activity, which is achieved through multiple mechanisms, including disruption of bacterial cell membranes, inhibition of metabolic enzymes, and induction of reactive oxygen species (ROS). By rapidly reducing microbial load, silver nanoparticles help prevent sustained inflammation that can otherwise prolong healing and promote fibrotic scar development. In addition to their antimicrobial effects, AgNPs have also been reported to influence cytokine regulation, stimulate keratinocyte migration, and support fibroblast activity, thereby contributing to faster wound closure (de Moura et al., 2022). Similarly, zinc oxide nanoparticles offer both antimicrobial protection and biological benefits that support tissue repair. Zinc is an essential trace element involved in critical cellular processes such as DNA synthesis, protein production, and enzymatic activity, all of which are necessary for effective wound regeneration. ZnO nanoparticles exert antibacterial action against both Gram-positive and Gram-negative bacteria through membrane damage and ROS-mediated oxidative stress. Beyond microbial inhibition, zinc plays an important role in promoting re-epithelialization, enhancing angiogenesis, and modulating inflammatory pathways to maintain balanced healing (Nagaiah et al., 2025). Despite these advantages, the clinical application of metallic nanoparticles requires careful consideration of dosage. Their therapeutic efficacy is strongly concentration-dependent: while low concentrations can promote antimicrobial defense and tissue regeneration, higher levels may lead to cytotoxic effects or excessive oxidative stress in surrounding cells. Therefore, precise formulation design and dose optimization are essential to maximize therapeutic benefit while ensuring long-term biocompatibility.

### 3.2. Herbal Bioactives (Centella asiatica and Turmeric)

Herbal bioactive compounds offer a more biologically harmonized strategy for enhancing wound healing, combining anti-inflammatory, antioxidant, and regenerative properties with comparatively lower cytotoxic risk than metallic agents. Among these, *Centella asiatica* has been extensively studied for its therapeutic potential in skin repair. It contains bioactive triterpenoids such as asiaticoside, madecassoside, asiatic acid, and madecassic acid, which stimulate fibroblast proliferation and enhance collagen type I production. These compounds influence key molecular pathways, particularly the transforming growth factor-β (TGF-β)/Smad signaling cascade, thereby promoting structured collagen deposition and balanced extracellular matrix remodeling. In addition, *Centella asiatica* reduces the expression of pro-inflammatory cytokines and oxidative stress markers, helping to prevent excessive fibroblast activation and limiting the development of hypertrophic or fibrotic scars (Arribas-López et al., 2022). Similarly, turmeric (*Curcuma longa*) contains curcumin, a well-known polyphenolic compound recognized for its strong antioxidant and anti-inflammatory effects. Curcumin suppresses nuclear factor-κB (NF-κB) signaling and downregulates inflammatory mediators such as TNF-α, IL-1β, and IL-6. It also neutralizes reactive oxygen species and modulates pathways associated with cell migration, proliferation, and collagen organization, thereby supporting orderly tissue regeneration and reducing abnormal fibrosis (Witkowska et al., 2024). Unlike metallic nanoparticles, which primarily exert antimicrobial effects through direct membrane disruption and oxidative stress induction, herbal bioactives function mainly by regulating intracellular signaling pathways. This mode of action aligns more closely with physiological healing processes, allowing controlled inflammation, improved matrix remodeling, and effective scar minimization without introducing significant cytotoxicity risks.

**Table 2: Comparative evaluation of mineral-based, metallic, and herbal bioactive fillers in wound healing applications.**

| Parameters | Mineral-Based Bioactive | Metallic Agents Bioactive | Herbal Bioactives |
|---|---|---|---|
| **Composition** | Silicates, clay minerals, calcium salts, phosphate compounds, bioactive glasses | Metal ions ($Ag^+$, $Zn^{2+}$, $Cu^{2+}$), metal and metal oxide nanoparticles | Flavonoids, terpenoids, phenolics, alkaloids, saponins, plant extracts |
| **Primary Mode of Action** | Structural support and ion-mediated stimulation | Antimicrobial activity and biological signaling modulation | Multi-target biochemical modulation of inflammation and fibrosis |
| **Antimicrobial Activity** | Low to moderate | High (membrane disruption, biofilm inhibition) | Moderate (phytochemical-dependent) |
| **Effect on Fibroblast Activity** | Supports proliferation and migration | Stimulates proliferation (dose-dependent) | Regulates proliferation and collagen synthesis |
| **Collagen Deposition Control** | Indirect influence through scaffold organization | Indirect (via inflammation control) | Direct modulation of TGF-β/Smad pathway; regulates Type I/III collagen ratio |
| **Cytotoxicity Risk** | Low | Moderate to high (dose-dependent oxidative stress) | Low (generally biocompatible) |

### 3.4 Comparative Healing, Antibacterial, and Biocompatibility Effects

Comparative analyses of mineral-based, metallic, and herbal fillers reveal distinct yet complementary therapeutic profiles. Metallic agents such as AgNPs and ZnO exhibit the strongest direct antimicrobial activity, making them highly effective in infection-prone wounds. However, their biological performance is dose-sensitive, and excessive concentrations may compromise cell viability. Mineral fillers such as β-TCP and hydroxyapatite primarily contribute structural reinforcement and bioactive ion release. Their ability to stimulate angiogenesis and fibroblast regulation supports organized ECM deposition and balanced scar formation. Herbal bioactives, including *Centella asiatica* and curcumin, provide anti-inflammatory and antioxidant modulation that enhances tissue regeneration while minimizing fibrotic responses. These agents often demonstrate superior cytocompatibility compared to high-dose metallic nanoparticles. Emerging evidence suggests that synergistic combinations of mineral fillers, metallic nanoparticles (at optimized concentrations), and herbal bioactives can significantly enhance wound closure rates, reduce infection risk, and promote controlled scar remodeling (Valencia-Gómez et al., 2023). Carefully balanced composite systems thus represent the most promising strategy for multifunctional wound management platforms.

## 4. CONCLUSION

This review comprehensively evaluates the comparative advantages of biopolymer-based wound dressings over conventional passive materials, underscoring their evolving role in active wound management. Unlike traditional dressings that primarily function as protective barriers, advanced biopolymer composites provide structural support, biological signaling, and multifunctional therapeutic effects that directly contribute to accelerated superficial wound healing and scar modulation. Natural polymer systems, particularly collagen-based matrices, offer biomimetic architecture that facilitates cell adhesion, migration, and extracellular matrix (ECM) organization. Their structural similarity to native tissue enhances fibroblast proliferation and promotes organized tissue regeneration. The incorporation of mineral fillers such as β-tricalcium phosphate further strengthens these systems by improving mechanical stability and enabling controlled calcium ion release. These ionic dissolution products actively participate in cellular signaling pathways associated with angiogenesis, fibroblast regulation, and collagen deposition, thereby contributing to improved tensile strength and balanced ECM remodeling. Compared to conventional passive dressings, such composite platforms demonstrate significantly enhanced potential in accelerating wound closure, minimizing excessive fibrosis, and supporting functional tissue restoration. Furthermore, the integration of herbal bioactives, particularly *Centella asiatica*, introduces an additional layer of biological modulation. The triterpenoid-rich phytoconstituents of *Centella asiatica* have been shown to stimulate collagen synthesis, regulate inflammatory cascades, and promote angiogenesis, collectively contributing to improved scar architecture and reduced hypertrophic responses. This multifunctional approach aligns with the emerging paradigm shift toward bioactive wound care systems that not only protect but actively guide the healing process. Despite these promising developments, several research gaps remain. Optimization of composite formulations including polymer ratios, crosslinking density, and filler concentration requires systematic investigation to achieve reproducible and clinically translatable outcomes. Long-term in vivo safety data, standardized methodologies for evaluating scar reduction, and controlled release kinetics of herbal bioactives remain insufficiently explored. Additionally, limited clinical validation studies currently restrict the widespread adoption of these advanced materials in routine medical practice. Overall, composite, herbal-loaded biopolymer wound patches represent a rational and forward-looking strategy for next-generation wound care. By integrating structural reinforcement, controlled biodegradation, antimicrobial protection, and biologically active signaling within a single platform, these systems offer significant potential for improving superficial wound healing outcomes while minimizing scar formation. Continued interdisciplinary research and rigorous clinical evaluation will be essential to translate these promising laboratory findings into effective and accessible therapeutic solutions.

**Data Availability Statement:** The data supporting the findings of this study are provided within the article and its supplementary materials. Additional information may be obtained from the corresponding author upon request.

**Funding:**
The authors declare that no financial support was received for the research, authorship, and/or publication of this article.

**Acknowledgment:**
The authors gratefully acknowledge MedCuore Medical Solutions Pvt. Ltd., India, for providing research facilities to carry out the synthesis work. The authors also thank Dhanalakshmi Srinivasan College of Engineering and Technology for institutional support. Technical assistance provided for materials characterization and experimental validation is sincerely appreciated.

**Conflict of Interest:** The authors declare that there are no conflicts of interest related to the publication of this article.

## REFERENCES

1. A review of current advancements for wound healing: Biomaterial applications and medical devices J Biomed Mater Res B Appl Biomater, 110(11), 2542–2573 (2022).
2. A Systematic Review of the Effect of Centella asiatica on Wound Healing Int. J. Environ Res Public Health, 19 (6), 3266 (2022).
3. Additionally, synthetic polyester degradation may generate acidic byproducts that influence local pH and cellular behavior (Li et al., 2022) [5]. Fine control over degradation remains difficult in single-component systems.
4. Cellular and molecular mechanisms of skin wound healing Nature Reviews Molecular Cell Biology, 25, 599–616 (2024).
5. Centella asiatica and Its Metabolite Asiatic Acid: Wound Healing Effects and Therapeutic Potential Metabolites, 13(2), 276 (2023).
6. Chen S., et al. (2020). Design of composite hydrogels with controlled degradation for tissue engineering. Materials Science & Engineering C.

7. Choi H, Choi W-S, Jeong J-O "A Review of Advanced Hydrogel Applications for Tissue Engineering and Drug Delivery Systems as Biomaterials" Gels 2024;
8. Collagen-Based Wound Dressings: Innovations, Mechanisms, and Clinical Applications Gels, 11(4), 271 (2025).
9. Controlled drug delivery remains challenging in single polymer matrices. Recent studies demonstrate that homogeneous polymer networks frequently result in burst release due to rapid diffusion pathways (Rahman et al., 2022) [8].
10. Conversely, synthetic polymers such as PLA, PCL, and PEG-based hydrogels demonstrate improved mechanical strength but lack elasticity and biomimetic architecture required for soft tissue regeneration (Wang et al., 2021) [3].
11. Farjaminejad S, Farjaminejad R, Hasani M, Garcia-Godoy F, Abdouss M, Marya A, Harsoputranto A, Jamilian A. Advances and Challenges in Polymer-Based Scaffolds for Bone Tissue Engineering: A Path Towards Personalized Regenerative Medicine. Polymers (Basel). 2024 Nov 26;
12. Hosseini S, et al. Tunable degradation and bioactivity of gelatin–chitosan scaffolds for skin tissue regeneration. J Biomed Mater Res A. 2024;
13. Huang Q., et al. (2021). Multifunctional chitosan-based wound dressings: recent advances. Polymers.
14. Krishnan Y, Sampath S "Biopolymers and synthetic polymeric materials in wound healing: cellular mechanisms and therapeutic potential" Discover Materials 2025;
15. Li J., et al. (2023). Advanced biopolymer-based wound dressings: structure–function relationships. Bioactive Materials.
16. Liu H., et al. (2022). Antibacterial and bioactive gelatin/chitosan scaffolds for wound repair. Frontiers in Bioengineering and Biotechnology.
17. Liu X, et al. Recent advances in gelatin–chitosan based composite biomaterials for tissue engineering. Materials Today Bio. 2023;
18. Liu X, et al. Structural and mechanical challenges of single-component hydrogels in tissue engineering. Mater Today Bio 2023.
19. Modern wound healing materials must integrate mechanical strength, antimicrobial activity, antioxidant capacity, angiogenic stimulation, and controlled degradation. However, recent literature emphasizes that single polymers rarely satisfy all these functional requirements simultaneously (Gao et al., 2024) [9].
20. Natural polymers derived from biological sources continue to show batch variability affecting molecular weight distribution and physicochemical behavior, thereby influencing scaffold performance and reproducibility (Almeida et al., 2021) [10]. This variability presents challenges in regulatory approval and large-scale manufacturing.
21. Novel Biomaterials for Wound Healing and Tissue Regeneration
ACS Omega (2024).
22. Oliveira C, Sousa D, Teixeira JA, Ferreira-Santos P, Botelho CM "Polymeric biomaterials for wound healing" Front Bioeng Biotechnol 2023.
23. Recent biomaterials research emphasizes that degradation kinetics must be synchronized with tissue healing phases. However, single polymer scaffolds frequently degrade either too rapidly (natural polymers) or too slowly (synthetic polyesters), resulting in structural mismatch with tissue regeneration (Chen et al., 2024) [4].
24. Recent progress of collagen, chitosan, alginate and other hydrogels in skin repair and wound dressing applications Int. J. Biol. Macromol., 208, 400–408 (2022).
25. Recent progresses of collagen dressings for chronic skin wound healing
Collagen & Leather, 5, 31 (2023).
26. Recent reviews highlight that synthetic polymers lack intrinsic cell-recognition sites and require biofunctionalization to promote adhesion and proliferation (Kim et al., 2021) [6]. Although natural polymers provide some ECM-mimicking features, they often lack multifunctional bioactivity such as antimicrobial, angiogenic, or antioxidant properties necessary for advanced wound care (Singh et al., 2023) [7].
27. Recent studies report that natural polymer-based hydrogels such as collagen, gelatin, alginate, and chitosan exhibit insufficient tensile strength and poor structural stability under physiological conditions due to excessive swelling and weak crosslinking density (Zhang et al., 2022; Liu et al., 2023) [1,2].
28. Singh R, et al. Gelatin–chitosan composite wound dressings with improved antimicrobial and sustained drug release performance. Int J Biol Macromol. 2023;
29. Topical Application of Centella asiatica in Wound Healing: Recent Insights into Mechanisms and Clinical Efficacy Pharmaceutics, 16(10), 1252 (2024).
30. Wang X., et al. (2022). Crosslinked chitosan-based biomaterials with improved mechanical properties for skin regeneration. Carbohydrate Polymers.
31. Xu R, Fang Y, Zhang Z, Cao Y, Yan Y, Gan L, Xu J, Zhou G "Recent Advances in Biodegradable and Biocompatible Synthetic Polymers Used in Skin Wound Healing" Materials (Basel) 2023;
32. Zhang Y, et al. Advanced natural polymer-based hydrogels for wound healing. Bioact Mater 2022.
33. Zhang Y, et al. Gelatin–chitosan composite hydrogels for enhanced wound healing: mechanical properties, biocompatibility, and drug delivery applications. Int J Biol Macromol. 2022;
34. Zhang Y., et al. (2021). Gelatin–chitosan composite hydrogels for wound healing applications. International Journal of Biological Macromolecules.