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THERAPEUTIC POTENTIAL OF SNAIL MUCUS IN WOUND HEALING : A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Introduction: Wound healing is a fundamental biological process comprising four sequential and overlapping phases: hemostasis, inflammation, proliferation, and remodeling. The successful restoration of tissue integrity requires that these phases proceed in the correct order and within an appropriate temporal framework. Proteins are indispensable to this process, as they mediate tissue growth, cellular renewal, and reparative mechanisms. Snail mucins, a class of large glycosylated proteins, have been reported to facilitate wound healing by stabilizing protein structures, modulating solubility and viscosity, and enhancing cell–cell recognition. In light of these properties, we conducted a meta-analysis of randomized controlled trials (RCTs) to assess the therapeutic efficacy of snail mucus extract in promoting wound repair.
Method: RCTs on snail mucus extract for wound healing were identified through searches of PubMed, ProQuest, Web of Science, ScienceDirect, Scopus, EBSCOHost, and ClinicalTrials.gov. The review adhered to PRISMA guidelines, applied the PICO framework, and assessed study quality using the JADAD scale.
Result: A total of 60 rats from three RCTs conducted between 2021 and 2023 were included in the meta-analysis. The findings demonstrated that the snail mucus group exhibited a significantly improved wound healing rate compared to the control group (MD = -3.21%, 95% CI: -3.72 to -2.69%, P < 0.00001).
Conclusion: Snail mucus extract has been shown to significantly accelerate wound healing in animal models; however, further clinical studies are required to confirm its therapeutic efficacy in humans.

Highlights:

1. Snail mucus extract significantly improves wound healing rates compared to standard treatments.
2. A meta-analysis of randomized controlled trials (RCTs) showed a statistically significant effect (MD = -3.21%, P < 0.00001).
3. The bioactive compounds in snail mucus promote collagen production and reduce inflammation.

INTRODUCTION

Globally, it is estimated that over 11 million people sustain burn injuries each year, resulting in more than 180,000 deaths most of which occur in low- and middle-income countries.[1] Burn injuries occur more frequently in developing countries, in Indonesia reporting approximately 195,000 burn related deaths annually and this number is expected to grow.[2] The extensive tissue damage and immunosuppressive effects caused by wounds necessitate rigorous diagnostic protocols and specialized therapeutic approaches.[2, 3]

Wound healing is a critical physiological process that restores the integrity of injured tissues. It is essential for preventing infections, reducing complications, and improving overall patient outcomes.[4] With the increasing prevalence of non-healing wounds, researchers have continuously explored innovative treatments to enhance wound closure and tissue regeneration. In recent years, natural bioactive compounds have emerged as promising alternatives, with snail mucus extract gaining attention for its potential in wound care.[5]

Snail mucus, commonly derived from species such as *Achatina fulica* and *Cornu aspersum*, is rich in bioactive compounds. These components contribute to various aspects of wound healing, including reducing inflammation, promoting fibroblast proliferation, and enhancing extracellular matrix remodeling.[4,6] Conventional treatments such as topical antimicrobials and occlusive dressings primarily aim to prevent infection and maintain a moist environment. However, these therapies often fall short in promoting effective tissue regeneration, which can lead to prolonged healing, increased risk of secondary infections, and greater healthcare expenditure.[7,8] While traditional wound care treatments focus on hydration, infection control, and mechanical protection, snail mucus extract offers a unique combination of regenerative and antimicrobial properties.[9]

Although several preclinical studies have investigated the wound healing potential of snail mucus extract, the findings remain inconsistent and fragmented across various models. To date, no meta-analysis has systematically synthesized the evidence from randomized controlled trials to quantitatively assess its efficacy in wound healing. Given the growing interest in natural regenerative agents, such an analysis is essential to guide further preclinical and clinical applications.

Snail mucus is a bioactive secretion containing glycoproteins, hyaluronic acid, glycolic acid, allantoin, and antimicrobial peptides that provide hydrating, regenerative, and protective effects. In dermatology, it has been applied to enhance skin hydration, repair damage, promote wound healing, reduce scars and wrinkles, protect against oxidative stress, and delay aging by stimulating fibroblast proliferation and collagen synthesis.[10-16] In addition to aesthetic purposes, its strong adhesiveness to moist tissues and ability to support regeneration highlight its potential as a biomaterial for surgical sealants, wound closure, and drug delivery applications.[17,18] The diverse biological activities of snail mucus support its exploration in wound management, where standardized extraction, controlled formulations, and clinical validation could establish it as a safe, biocompatible, and affordable therapy for both acute and chronic wounds. This has further encouraged interest in its potential use for minor injuries, burns, and skin disorders including eczema and rosacea.[19] Nevertheless, despite abundant anecdotal support, high-quality clinical evidence for these uses remains scarce.[20]

Despite promising bioactivity, evidence supporting the use of snail mucus in wound care remains scattered and largely preclinical, this study aims to systematically evaluate the effectiveness of snail mucus extract in wound healing by conducting a meta-analysis of randomized controlled trials. By synthesizing data from recent animal studies, we seek to determine whether snail mucus extract significantly enhances wound closure rates compared to conventional treatments.

METHODS

Literature selection

This study was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines[21], as illustrated in Figure 1. The PICO (patients, interventions, comparisons, and outcomes) framework was utilized to define the research questions and selection criteria. Relevant keywords included "wound care," "infection," "snail mucus extract," "snail slime," and "snail excretion." These terms were combined using Boolean operators to maximize search effectiveness. The detailed search strategy is outlined in Figure 1. Searches were conducted across multiple scientific databases, including PubMed, Scopus, ScienceDirect, Cochrane, EBSCO, Web of Science, ClinicalTrials.gov, and ProQuest, up to March 2024.

Statistical Analysis

Statistical analysis was performed using RevMan (version 5.4). A random-effects model was applied to account for potential heterogeneity among the included studies. Heterogeneity was assessed using the I^2 statistic, and a p-value of < 0.05 was considered statistically significant. Hypothesis testing involved comparisons of mean wound healing percentages between treatment and control groups. Effect sizes were reported with 95% confidence intervals (CIs), and publication bias was evaluated using Egger's test.

Data extraction

Only randomized controlled trials (RCTs) that reported outcomes related to the effects of snail mucus on wound healing were included in this study. Full-text articles published in English and conducted on animal models were selected and analyzed. Studies that did not meet these criteria were excluded. Two authors independently extracted data, including publication details, study characteristics, variables measured, and outcomes such as wound healing rate. If any relevant data were missing, the corresponding authors were contacted for clarification.

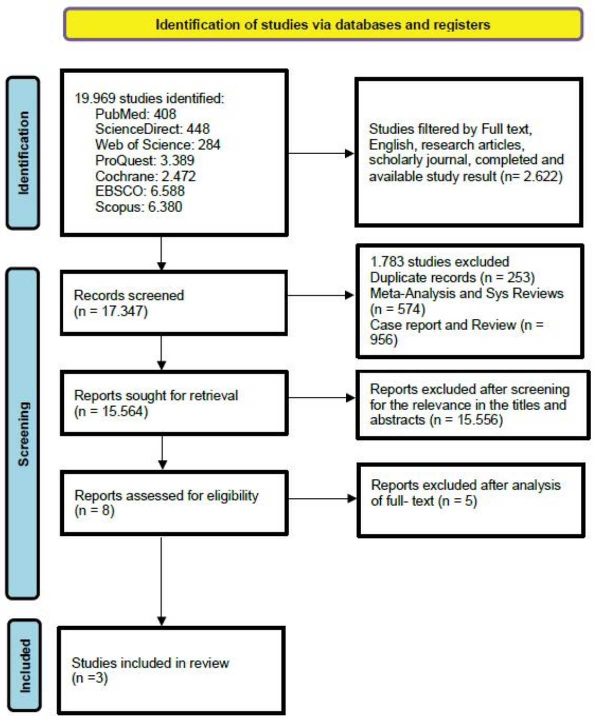

Figure 1. PRISMA flowchart

Risk of bias and quality assessment

Two independent authors assessed the methodological quality of the included studies using the JADAD scale. This scale evaluates clinical trial quality based on three key domains: randomization, blinding, and the documentation of withdrawals or dropouts. Each study could achieve a maximum score of 3 points: 1 point for randomization (with an additional point if the method was appropriate), 1 point for blinding, and 1 point for clearly reporting participant withdrawals. Studies scoring 3 points were considered high quality, while those scoring 1–2 points were categorized as low quality.[22] All included studies were assessed as having a low risk of bias (Table 1).[23-25]

Table 1. Quality Assessment of Included Studies with JADAD Scale

Study	Items	Max point	Description	Score	Interpretation
Zhou et al., 2023 [7]	Randomization	2	1 point if randomization is mentioned	1	Low risk
			1 additional point if the method of randomization is appropriate	1	
			Deduct 1 point if the method of randomization is inappropriate (minimum 0)	0	
	Blinding	2	1 point if blinding is mentioned	0	
			1 additional point if the method of blinding is appropriate	0	
			Deduct 1 point if the method of blinding is inappropriate (minimum 0)	0	
	Patient Accountability	1	All participants are accounted for, or reasons for missing data are explained	1	
Shoviantari et al., 2021 [8]	Randomization	2	1 point if randomization is mentioned	1	Low risk
			1 additional point if the method of randomization is appropriate	1	
			Deduct 1 point if the method of randomization is inappropriate (minimum 0)	0	
	Blinding	2	1 point if blinding is mentioned	0	
			1 additional point if the method of blinding is appropriate	0	
			Deduct 1 point if the method of blinding is inappropriate (minimum 0)	0	
	Patient Accountability	1	All participants are accounted for, or reasons for missing data are explained	1	
Putra et al., 2021 [9]	Randomization	2	1 point if randomization is mentioned	1	Low risk
			1 additional point if the method of randomization is appropriate	1	
			Deduct 1 point if the method of randomization is inappropriate (minimum 0)	0	
	Blinding	2	1 point if blinding is mentioned	1	
			1 additional point if the method of blinding is appropriate	1	
			Deduct 1 point if the method of blinding is inappropriate (minimum 0)	0	
	Patient Accountability	1	All participants are accounted for, or reasons for missing data are explained	1	

RESULTS

Study Selection

Following the PRISMA methodology, a total of 19,969 studies were initially identified through comprehensive searches across multiple electronic databases. After the initial screening for full-text availability, English language, and completion of study results, 2,622 studies remained. In the second phase of screening, studies that did not meet the inclusion criteria, such as meta-analyses, systematic reviews, case reports, case series, and case–control studies were excluded, reducing the number to 1,783 studies.

At this stage, many articles were removed due to being duplicates or irrelevant to the scope of this review. Some studies primarily focused on cosmetic or dermatological applications of snail mucus rather than wound healing outcomes, and were therefore excluded. In addition, several experimental studies that investigated other natural products without including snail mucus as an intervention were also discarded.

Title and abstract screening further narrowed the selection to eight potentially eligible studies. Upon full-text review, however, five studies were excluded because they did not provide the necessary quantitative data, particularly mean values and standard deviations (SD), or lacked relevant outcomes related to wound healing rates. In addition, one study was excluded as it was a non-randomized controlled trial (non-RCT) and therefore not comparable with RCT standards. Ultimately, three studies (7–9) fulfilled all the inclusion criteria and were incorporated into the final analysis, as summarized in Table 2.

Table 2. Excluded Studies and Reason for Exclusion

Study	Reason for exclusion
Song et al., 2021 [26]	No information about the mean and SD were found
Gugliandolo et al., 2021 [27]	No information about the mean and SD were found
Andrade et al., 2018 [28]	No information about the wound healing rate
Santana et al., 2012 [29]	No information about the mean and SD were found
Adikwu et al., 2007 [30]	The only included non-RCT study (no comparison)

Table 3. Baseline Characteristics of Included Studies

Study	Setting	Total sample	Study groups	Outcome
Zhou et al., 2023[23]	Kunming Institute of Botany, Hunan, China	40 rats with acute and chronic/diabetic wound	Intervention group: Snail mucus of A. fulica (dried-snail mucus glue, snail glycosaminoglycan) Control group: Normal saline	1. Outcomes were assessed in 5 days, 7 days and 11 days. 2. The wound healing rate in snail mucus group showed significantly higher healing ratio than that of the control/saline group
Shoviantari et al., 2021[24]	Indonesia	4 rats with acute/laceration wound	Intervention group: 10%, 15%, 20%, 100% extract of snail mucus Control group: no treatment	1. Outcomes were assessed after 7 days 2. It showed that 10% extract of snail mucus had the best percentage of wound healing rate than control group. The wounds in 10% extract of snail mucus already showed favorable trajectory in 5 days.
Putra et al., 2021 [25]	Universitas Gajah Mada, Yogyakarta, Indonesia	6 rats with acute punched wound	Intervention group: 24%, 48%, 96% snail mucus gel Control group: CMC-Na gel	1. All treatment groups had significantly higher wound closure rates than the control group, wound closure rates between treatment groups, and it already showed significant progression in day 7. 2. Significant differences were found between the control group and the snail mucus gel group of 24% (p = 0.022), 48% (p = 0.001), and 96% (p = 0.000).

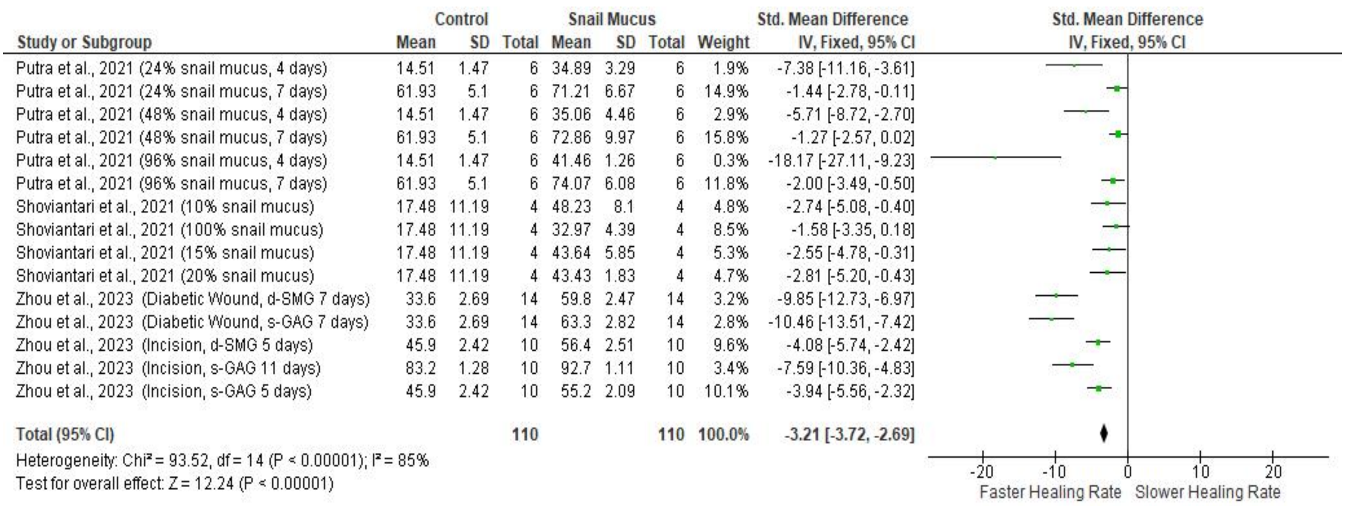

Figure 2. Forrest Plot of Pooled Outcomes from Included Studies

Baseline Characteristics

A total of 50 rats were included in the meta-analysis, based on the three selected RCTs conducted between 2021 and 2023. [23-25] These studies evaluated the wound healing effects of snail mucus extract on both acute and chronic wounds, comparing it to control treatments such as normal saline, no treatment, or CMC-Na gel (Table 3).

Synthesis of Results

The pooled meta-analysis of these three studies aimed to quantify the effectiveness of snail mucus extract on wound healing rates. The forest plot (Figure 2) visually represents the impact of snail mucus extract, consistently favoring the intervention group over the controls. Additionally, Egger's test (Figure 3) was conducted to assess the presence of publication bias, ensuring that the observed effects were not skewed by selective reporting.

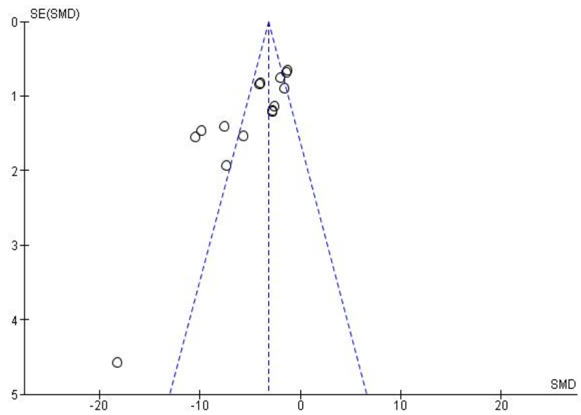

Figure 3. Egger's Test Result of Included Studies

A total of 50 rats from the three included RCTs[23-25] were analyzed to determine the effectiveness of snail mucus extract in accelerating wound healing. Snail mucus was typically obtained by gently stimulating the foot region of the gastropod using a sterile glass rod to induce mucus secretion. The collected mucus was then centrifuged to remove impurities before being incorporated into gel formulations. The results of this meta-analysis revealed that the snail mucus group exhibited a significantly higher wound healing rate compared to the control group, with a mean difference (MD) of –3.21% (95% CI: –3.72 to –2.69%, $P < 0.00001$). This statistically significant difference underscores the beneficial role of snail mucus extract in promoting wound closure.

Rate of Wound Healing

Among the various concentrations tested, the 10% snail mucus extract demonstrated the most effective healing rate, indicating an optimal balance of bioactive compounds and physiological compatibility. Higher concentrations (24%–96%) also showed dose-dependent improvements in wound healing, further supporting the therapeutic potential of snail mucus extract. Putra et al. (2021)[25] specifically demonstrated that snail mucus gel significantly increased collagen density and wound closure rates in Wistar rats. The findings indicated that higher concentrations (24%, 48%, and 96%) led to greater collagen deposition. However, the differences in wound closure rates among these concentrations were not statistically significant, suggesting that the minimum effective concentration may be lower than 96%.

Shoviantari et al. (2021)24 provided further evidence of the wound-healing efficacy of snail mucus extract through a systematic evaluation of its physical properties, bioactivity, and therapeutic effects. Using an experimental model with Wistar rats (*Rattus norvegicus*), the study demonstrated that a 10% formulation achieved the greatest wound-healing activity compared with lower concentrations. Wound repair was assessed by serial measurements of wound size reduction, with the 10% extract exhibiting a significantly faster healing rate.

These findings reinforce the notion that snail mucus extract not only accelerates wound closure but also enhances tissue regeneration, reduces inflammation, and promotes overall wound recovery.

Consequently, snail mucus extract emerges as a promising natural therapeutic option for wound management, warranting further preclinical and clinical trials to validate its applicability in human wound care.

DISCUSSION

This review employed a structured systematic review process, adhering to the PRISMA and PICO frameworks to ensure transparency and reproducibility. Evidence indicates that snail mucus enhances all phases of wound healing. Specifically, snail mucus extract has been reported to accelerate fibroblast proliferation, attenuate inflammation, increase collagen deposition, and promote extracellular matrix remodeling. Its therapeutic effects are attributed to bioactive compounds such as allantoin, glycoproteins, glycosaminoglycans, and antimicrobial peptides. Allantoin facilitates fibroblast migration and tissue regeneration, while glycosaminoglycans support extracellular matrix formation and maintain moisture balance.[23–26] Furthermore, the antimicrobial activity of snail mucus contributes to infection prevention, thereby further promoting wound healing.[25,27–29]

In the included studies, snail mucus was typically obtained by gently stimulating the foot of *Achatina fulica*, followed by centrifugation to purify the secretion prior to formulation. This straightforward yet effective extraction method preserves the high bioactivity of the secretion, which is subsequently incorporated into gel preparations with added gelling agents.Recent studies, including the work of Zhou et al. (2023)[23], have demonstrated that snail glycosaminoglycan-infused biomimetic hydrogels accelerate wound healing, particularly in diabetic models, by modulating macrophage polarization. By shifting macrophages from a pro-inflammatory M1 phenotype to an anti-inflammatory M2 phenotype, snail mucus helps regulate inflammation and promotes tissue repair.[15,30] This transition is critical, as prolonged inflammation is a major factor contributing to impaired wound healing, especially in chronic wounds such as diabetic ulcers.[31] Furthermore, snail mucus has been shown to inhibit NF-κB signaling a key regulator of inflammation which facilitates a smoother transition from the inflammatory to the proliferative phase of wound healing.[32-34] These findings suggest that snail mucus has strong potential for managing chronic wounds and may serve as a natural alternative to conventional anti-inflammatory and regenerative therapies.[35,36]

Compared with conventional treatments such as normal saline and CMC-Na gel, snail mucus extract demonstrated superior wound healing efficacy. Several studies have indicated that higher concentrations of snail mucus (24%–96%) led to increased collagen deposition, although no statistically significant differences in wound closure rates were observed beyond concentrations of 10%–15%.[25,37] This suggests that even at lower concentrations, snail mucus retains its effectiveness. Given its natural origin and low toxicity profile, snail mucus extract may offer an accessible and cost-effective adjunctive therapy, particularly valuable in low-resource settings. Shoviantari et al. (2021)[24] found that a 10% snail mucus formulation provided the most effective wound healing, supporting the idea that lower concentrations may offer optimal benefits while minimizing potential risks or resource wastage.[38-40] The ability of snail mucus to accelerate healing even at reduced concentrations highlights its potential for widespread clinical application.[34,41]

The clinical implications of these findings are significant, as they suggest that snail mucus extract could be integrated into modern wound management strategies. An acceleration of wound healing by 3.21% may have a substantial impact on treatment duration and infection risk, making it clinically meaningful in real-world settings. Given its bioactive properties, snail mucus extract may be particularly beneficial for patients with chronic wounds, burns, surgical incisions, and pressure ulcers.[36,42] Furthermore, its ability to be formulated into hydrogels, creams, and other bioactive dressings broadens its potential applications in dermatology and regenerative medicine.[43] The study by Zhou et al. (2023)[23] specifically demonstrated that snail-derived glycosaminoglycan-infused hydrogel maintained prolonged bioactivity and moisture retention two critical factors for optimal wound healing.

Compared with established wound-healing agents such as silver sulfadiazine (SSD), MEBO, and medical-grade honey, snail mucus extract demonstrates comparable or, in some cases, superior efficacy in promoting wound closure, enhancing collagen deposition, and modulating inflammation.[44] While SSD remains the gold standard for infection prevention, it has been associated with delayed re-epithelialization and cytotoxicity toward keratinocytes and fibroblasts. MEBO, a β-sitosterol–based herbal ointment, supports epithelial repair and reduces inflammation, although its effectiveness may vary depending on wound type and patient-specific factors.[11,12,45,46] In contrast, snail mucus provides a broad spectrum of bioactive compounds, including glycosaminoglycans, allantoin, and antimicrobial peptides, which act synergistically to accelerate healing with minimal adverse effects.[20]

While the current preclinical findings are promising, further validation is warranted to confirm and refine the mechanistic insights. In vitro and ex vivo studies should be conducted to delineate the molecular pathways involved such as fibroblast proliferation, NF-κB inhibition, and extracellular matrix remodeling.[12,45] Additionally, head-to-head comparisons with standard clinical treatments (e.g., SSD, MEBO, hydrocolloid dressings) are crucial to establish snail mucus as a competitive or adjunctive therapeutic option. [2,7]

Importantly, the translational relevance of animal models, such as Wistar rats, is well-documented. These models effectively simulate key phases of human wound healing hemostasis, inflammation, proliferation, and remodeling and allow detailed evaluation of histological and biochemical outcomes, including collagen density and macrophage polarization. Although human skin exhibits greater complexity, many rodent-tested treatments, including SSD and growth factor therapies, have achieved successful clinical translation.[7] Therefore, the consistent and statistically significant benefits observed in animal models provide a strong rationale for advancing snail mucus extract to human clinical trials.

Well-designed randomized controlled trials (RCTs) with standardized formulations and dosing protocols are essential to determine efficacy, safety, and cost-effectiveness in real world clinical settings. [32] Such efforts will bridge the gap between experimental and clinical application, paving the way for snail mucus-based therapies to be integrated into evidence based wound care and regenerative dermatology.

Future research should focus on refining extraction methods, determining optimal dosages, and conducting large-scale clinical trials to evaluate its safety, efficacy, and long-term effects in human subjects.[47,,48] Despite promising preclinical results, evidence in human subjects remains limited. Randomized controlled trials involving large sample sizes and standardized extraction and formulation protocols are essential to confirm its clinical efficacy and safety.

One of the major strengths of this study lies in its systematic approach to synthesizing evidence from RCTs, which enhances the reliability of the findings. The included studies employed quantitative wound healing assessments, minimizing subjective bias. Additionally, the use of multiple concentrations of snail mucus extract provided valuable insights into the optimal dosage for effective healing.

However, a key limitation is the reliance on animal models, which, although informative, do not fully replicate the complexity of human skin physiology. Another limitation is the small sample size in some included studies, which may reduce the statistical power of the conclusions.

CONCLUSION

This systematic review and meta-analysis indicate that snail mucus extract significantly enhances wound healing by stimulating fibroblast proliferation, reducing inflammation, and accelerating tissue regeneration. These findings support its potential as a promising natural alternative to conventional wound care therapies, particularly for chronic and non-healing wounds. Nonetheless, further research, especially well-designed human clinical trials is required to validate its broader therapeutic applications.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

FUNDING DISCLOSURE

Not applicable.

AUTHOR CONTRIBUTION

FAW, IDS, ARA, FCS, PF, and IBM jointly conceptualized the study, designed the methodology, and collected the data. They also conducted the background literature review and performed the statistical analyses. IDS supervised the interpretation of results and guided the discussion. FAW, ARA, FCS, PF, and IBM contributed to drafting the manuscript, conducted grammar and consistency checks, and ensured adherence to publication standards. FAW, IDS, and ARA were primarily involved in revising and finalizing the manuscript. FAW and IDS provided overall supervision, critical revisions, and final approval. All authors read and approved the final version of the manuscript.

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