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Letters to Editor

Antimicrobial peptide-infused hydrogels: Bridging infection defense and wound regeneration

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Chronic wounds represent a growing global health burden, particularly in the context of diabetes, aging populations, and the rise of multidrug-resistant (MDR) infections. One of the principal challenges in chronic wound management is the simultaneous need to eradicate microbial colonization and stimulate tissue regeneration. While systemic antibiotics are often administered, their efficacy is limited by poor tissue penetration and the risk of resistance development. In this light, antimicrobial peptides (AMPs) have emerged as promising candidates due to their dual functionality broad-spectrum antimicrobial activity and pro-regenerative properties [1].

AMPs such as LL-37, human β-defensins, and temporins are evolutionarily conserved molecules that disrupt microbial membranes through electrostatic interactions. Beyond their antimicrobial role, AMPs modulate inflammatory responses, promote keratinocyte migration, and enhance angiogenesis and collagen deposition, positioning them as attractive agents for wound healing applications. However, their clinical use is hampered by issues such as enzymatic degradation, cytotoxicity at high concentrations, and short half-lives *in vivo* [1, 2].

To address these limitations, hydrogels have gained attention as biocompatible carriers capable of encapsulating and delivering AMPs in a sustained and localized manner. Hydrogels, composed of natural or synthetic polymers such as gelatin, polyethylene glycol (PEG), or chitosan, provide a moist environment conducive to healing while offering protection against proteolytic degradation [3]. For example, LL-37-loaded chitosan-based and PEG-based hydrogels have demonstrated improved wound closure, reduced bacterial burden, and increased granulation tissue in murine models [4, 5]. Similarly, self-assembling AMP hydrogels have shown both bactericidal and antioxidant effects, enhancing the repair of infected skin wounds [6]. These AMP-infused hydrogel systems not only reduce systemic side effects but also allow for targeted action at the wound site. Moreover, their modular design enables co-delivery of growth factors, stem cells, or immunomodulators, further amplifying their therapeutic potential. Despite these advantages, several translational barriers remain.

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Peptide synthesis costs, batch-to-batch variability, and the complex interaction between peptides and polymer matrices must be systematically addressed. Furthermore, the immunogenic potential of AMPs, especially when delivered in supraphysiological doses, warrants thorough *in vivo* evaluation.

Emerging studies support the notion that AMP-functionalized hydrogels may serve as next-generation wound care therapies [7]. However, the transition from preclinical models to clinical application requires multidisciplinary collaboration and standardized testing protocols. Regulatory pathways must also evolve to accommodate the hybrid nature of such bioactive materials.

In conclusion, antimicrobial peptide-infused hydrogels offer a promising dual-action platform to combat infection and promote tissue regeneration in chronic wounds. With ongoing innovations in peptide engineering and biomaterial science, these systems are well-positioned to bridge current therapeutic gaps. We encourage future research efforts that focus on optimizing delivery systems, evaluating long-term biocompatibility, and initiating early-phase clinical trials.

Authors' contributions

Project Administration, Conceptualization, and Methodology: SMH; Investigation, Writing – Original Draft and Editing: HA, SMH. All authors read and approved the final manuscript.

Conflict of interest

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Ethical declarations

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