Hydrogel-Forming Microneedles for Vancomycin Delivery: A Novel Approach to Combat Antimicrobial Resistance

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Introduction

- Antimicrobial resistance (AMR) is a critical global health issue, worsened by antibiotic misuse and challenges in treating multidrug-resistant infections like MRSA [1]. Vancomycin, a first-line therapy, faces limitations in resource-limited settings due to its intravenous administration and storage needs [2]. Factors like needle phobia and poor adherence further exacerbate AMR. This study develops hydrogel-forming microarray patches (HF-MAPs) to optimize vancomycin delivery, enhance adherence, and combat AMR effectively.

Aims

- To develop and optimize hydrogel-forming microneedle formulations for the transdermal delivery of vancomycin, targeting effective mechanical performance and drug-loading capacity.
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- To assess the effectiveness of hydrogel-forming microneedles in improving vancomycin bioavailability and patient compliance, thereby contributing to the reduction of antimicrobial resistance.

Methods

- As shown in **Figure 1,** hydrogel-forming microneedles (HF-MNs) were cast using three formulations: super-swelling (poly(methyl vinyl ether-co-maleic acid), polyethylene glycol, sodium carbonate), standard swelling (poly(methyl vinyl ether-co-maleic acid), polyethylene glycol), and a third formulation (poly(vinyl alcohol) (PVA), poly(vinylpyrrolidone)(PVP), citric acid (CA). Next, their swelling properties and mechanical characteristics were evaluated [3].
- A direct-compressed tablet was then formulated as a reservoir, and the optimal HF-MAP formulation was tested for vancomycin delivery via solute diffusion studies using side-by-side cells.
- Finally, ex vivo skin permeation and deposition studies of HF-MAP combined with vancomycin-loaded direct compressed tablets reservoir were conducted using Franz diffusion cells.

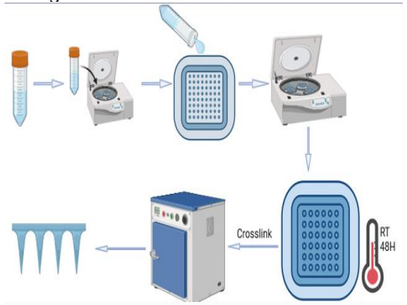
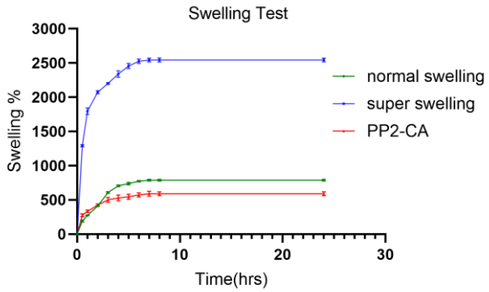
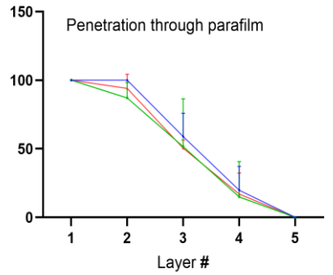


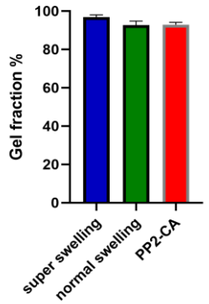
Figure 1: Hydrogel-forming microneedles (HF-MNs) casting process using various polymer formulations. The procedure involves preparing polymer solutions in falcon tubes, initial centrifugation, filling silicone moulds, second centrifugation, drying at room temperature for 24 hours, and crosslink in an oven—either at 80°C for 24 hours (super-swelling and standard formulations) or at 130°C for 3 hours (PVA/PVP-CA formulation).

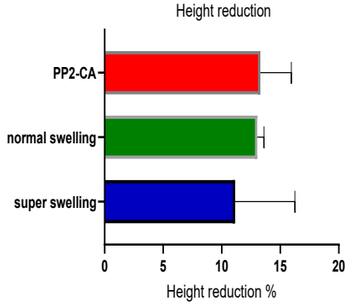
Results

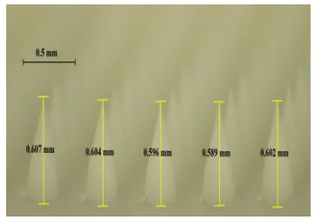
Swelling studies revealed that the super-swelling formulation had the highest swelling percentage, approximately 2400%. In contrast, the normal-swelling and PVA/PVP-CA formulations showed similar swelling but significantly less than the super-swelling formulation. Gel fraction analysis indicated over 98% for all three formulations with no significant differences. Height reduction after insertion was consistent across formulations at less than 15%, demonstrating microneedle strength and no residuals upon removal. Penetration tests confirmed that all formulations could effectively bypass the epidermis and reach the dermis, reaching blood capillaries. Vancomycin exhibited a release profile consistent with first-order kinetics across excised neonatal porcine skin in vitro, with a cumulative permeation of approximately 6 mg over 24 hours for the super-swelling HF-MAP.

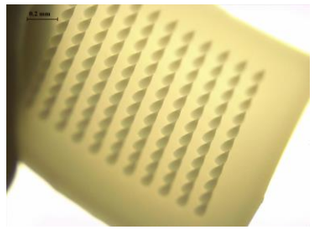


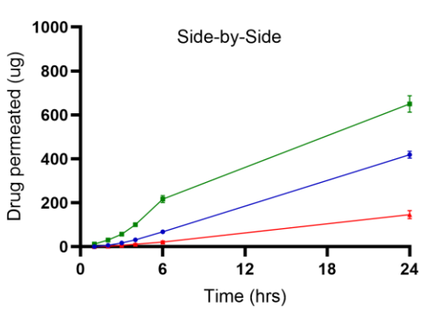


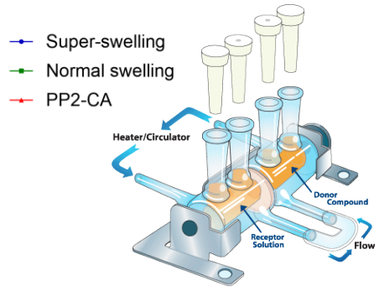


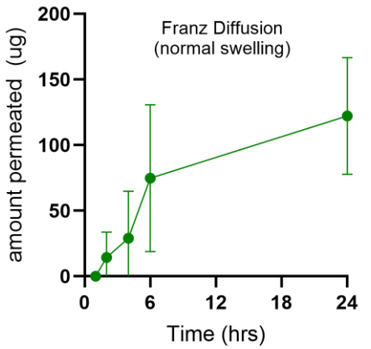


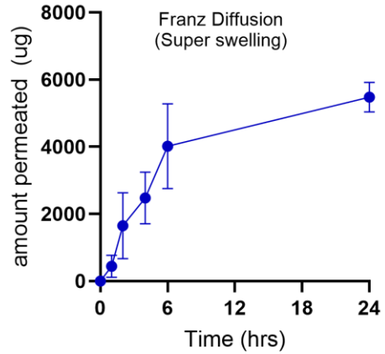












Conclusions

- Hydrogel-forming microneedles show great promise for vancomycin delivery, addressing key challenges in patient comfort and treatment adherence. By offering a minimally invasive and user-friendly alternative, this approach has the potential to enhance therapeutic outcomes and reduce the progression of antimicrobial resistance.

References

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