Targeted Release of Phage and Antibiotics from Enzyme-Responsive Microparticles to Mitigate Battlefield Wound Sepsis

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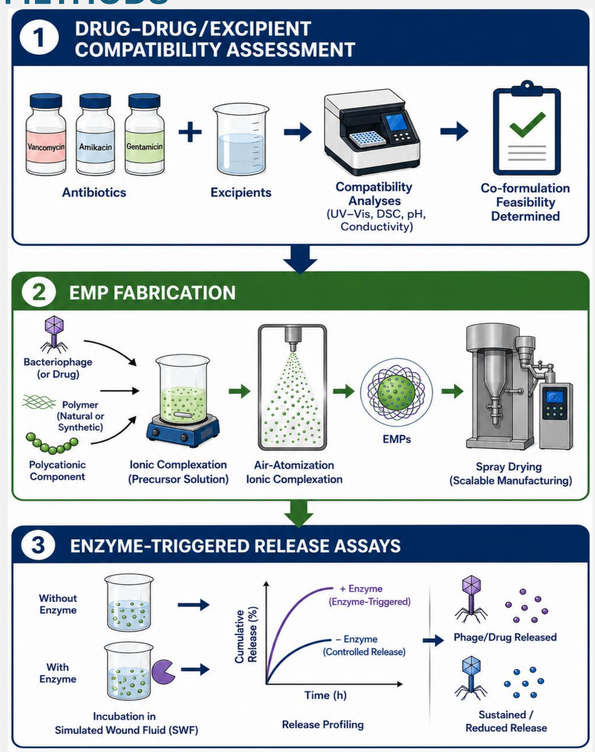
BACKGROUND

Battlefield care often occurs in austere, resource-limited environments, where delayed evacuation and limited capability increase the likelihood that wound contamination will progress toward infection without early countermeasures. Battlefield wound sepsis can be avoided with the timely use of antibacterial agents. To address this dual challenge, we developed a Enzyme-responsive microparticle (EMP) system designed for rapid, selective payload release in wound microenvironments, and evaluated its use as a multifunctional antimicrobial delivery platform capable of integrating bacteriophages and small-molecule antibiotics.

Objective

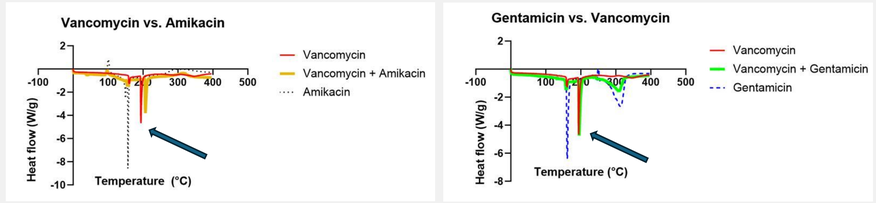
To develop a microparticle system with capability to release antibiotics and Bacteriophage in wound bed

METHODS



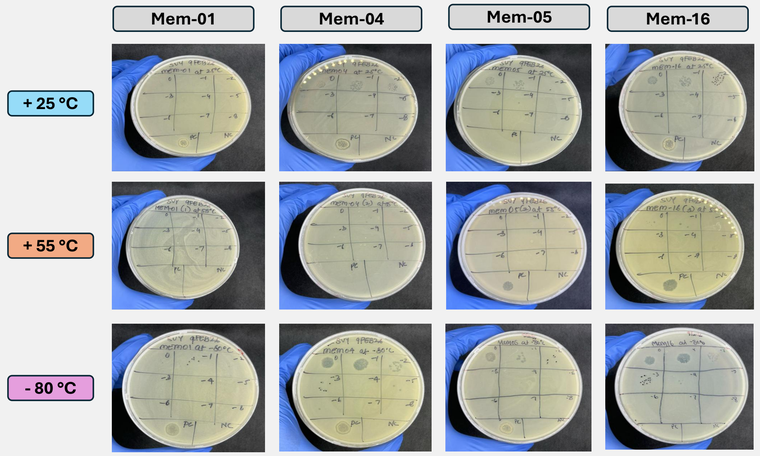
RESULTS

Amikacin was not compatible with Vancomycin



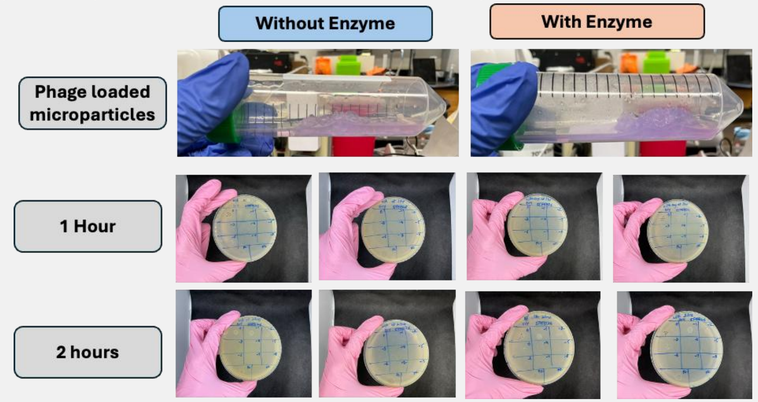
Vancomycin and amikacin combination produced a new peak, indicating clearly that a chemical modifaction was happening. This was not observed with Gentamicin and Vancomycin mixture

Microparticles show ability to release



Representative bacterial spot assay plates demonstrating the effect of formulation composition and storage temperature on bacteriophage viability, with Mem-16 exhibiting the greatest preservation of phage infectivity, particularly under refrigerated and frozen storage conditions.

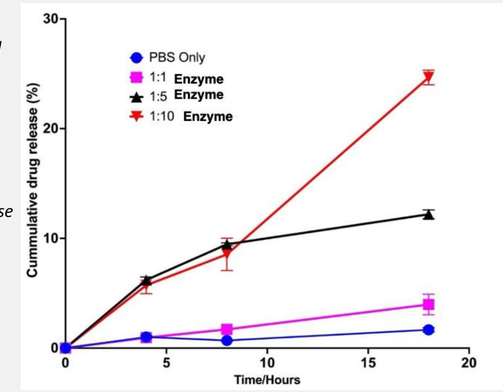
Enzyme responsive microparticles show enzyme responsive behaviour



Enzyme-mediated degradation of EMPs enhanced bacteriophage release compared with untreated controls, resulting in increased phage recovery over time.

Enzyme responsive microparticles release Vancomycin in response to enzyme activity

Cumulative Vancomycin release from hydrogel microparticles (HMPs) in phosphate-buffered saline (PBS) containing increasing concentrations of Enzyme. Drug release increased in an enzyme concentration-dependent manner, with the 1:10 hyaluronidase condition producing the highest cumulative release, demonstrating enzyme-responsive degradation of the HMP matrix. Error bars represent mean ± standard deviation.



FUNDING AND GRANT INSTITUTIONS

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- Domestic Preparedness Support Initiative
- Defense Health Agency (DHA),
- Medical Technology Enterprise Consortium
- Walter Reed Army Institute of Research,
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- US Army Medical Research Acquisition Activity (USAMRAA)

CONCLUSION

- Gentamicin was identified as the preferred antibiotic for co-formulation, demonstrating compatibility with vancomycin.
- The optimized HMP formulation was successfully manufactured by spray drying while preserving bacteriophage viability.
- HMPs exhibited hyaluronidase-responsive degradation, enabling controlled, on-demand release of both antibiotics and viable bacteriophages under simulated wound conditions.