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## Curcumin-loaded Hydrogels as Phototherapeutics against Antibiotic-resistant Pathogens

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The rise of antibiotic-resistant microbial infections has emerged as an urgent health problem. Multidrug-resistant bacteria can easily spread especially in healthcare settings such as hospitals and post-surgical care. Consequently, there is a growing need for innovative therapeutic strategies and antimicrobial biomaterials to effectively combat pathogens in periprosthetic joint infections, thereby accelerating postoperative recovery.<sup>1</sup> In ongoing research on supramolecular photosensitizing systems,<sup>2</sup> we present the development of rapidly resorbable hydrogels based on DAC® (HA-PLA) loaded with curcumin (Cur). These hydrogels improve the water solubility and bioavailability of curcumin, leading to controlled release at the site of infection. Curcumin has broad-spectrum antibacterial properties, effective against both Gram-positive and Gram-negative bacteria.<sup>3</sup> In parallel, we developed another hydrogel composed of Cur-loaded DAC® and Vancomycin (VAN). Vancomycin is an antibiotic used to treat various bacterial infections, although it has limitations. The combination of Cur and VAN in a hydrogel may help solve antimicrobial resistance problems and allow reduced dosages of antibiotics with minimal side effects. Hydrogels were prepared by hydrating a Cur-based organic film obtained by solvent evaporation and DAC® powder with Cur or Cur/VAN dispersion. The interaction between Cur and DAC in the DAC/Cur complex was studied using various techniques, including UV/Vis spectroscopy, fluorescence, Dynamic Light Scattering (DLS) and  $\zeta$ -potential measurements. We also evaluated the stability and erosion kinetics of these hydrogels in media mimicking physiological conditions to ensure controlled and effective performance over time. We evaluated the antimicrobial efficacy of hydrogels by determining the bacterial load

reduction of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), and *Pseudomonas aeruginosa* under light conditions compared with dark conditions.

### References

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