Local antibiotic therapy: in situ time-resolved powder diffraction studies on drug carrier systems

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Local antibiotic therapy offers targeted treatment of bone and joint infections while limiting systemic toxicity. [1,2] Calcium sulfate ($CaSO_4$) is widely used as a resorbable carrier and is compatible with multiple antibiotics, including vancomycin [2], ceftriaxone [3], and tobramycin [4]. The present study investigates the molecular interactions and controlled uptake mechanisms of antibiotic-loaded $CaSO_4$ carriers.

In-situ kinetic studies of drug-carrier interactions were conducted via time-resolved powder X-ray diffraction (PXRD), which tracked a real-time hemihydrate-to-dihydrate phase transition, directly linked to the interactions of the respective antibiotics with the $CaSO_4$ carriers (Figure 1). The final matrix microstructure and drug distribution were characterized by X-ray micro-CT and SEM-EDX.

Kinetic analysis revealed antibiotic-specific transformation rates with ceftriaxone and vancomycin, showing faster phase transition, with maximum rate constants of 4.5 and 4.0 $\%\cdot min^{-1}$ and complete transformation within 100 min, comparable to unloaded $CaSO_4$. Tobramycin reduced the maximum rate constant to 0.2 $\%\cdot min^{-1}$ within the longest transformation time of 2800 min. XCT revealed that ceftriaxone has the strongest impact on pellet-scale morphology with a highly inhomogeneous pore distribution. SEM-EDX confirmed antibiotic-dependent crystal morphologies and localized drug distribution within high-density regions.

These findings demonstrate antibiotic-specific drug-carrier interactions: vancomycin primarily through extended hydrogen-bonding networks, ceftriaxone through Ca^{2+} complexation, and tobramycin through electrostatic adsorption complemented by H-bonding. This molecular-level understanding of drug-carrier interactions supports the advancement of local antibiotic delivery systems, improving infection management in orthopedic and trauma surgery.

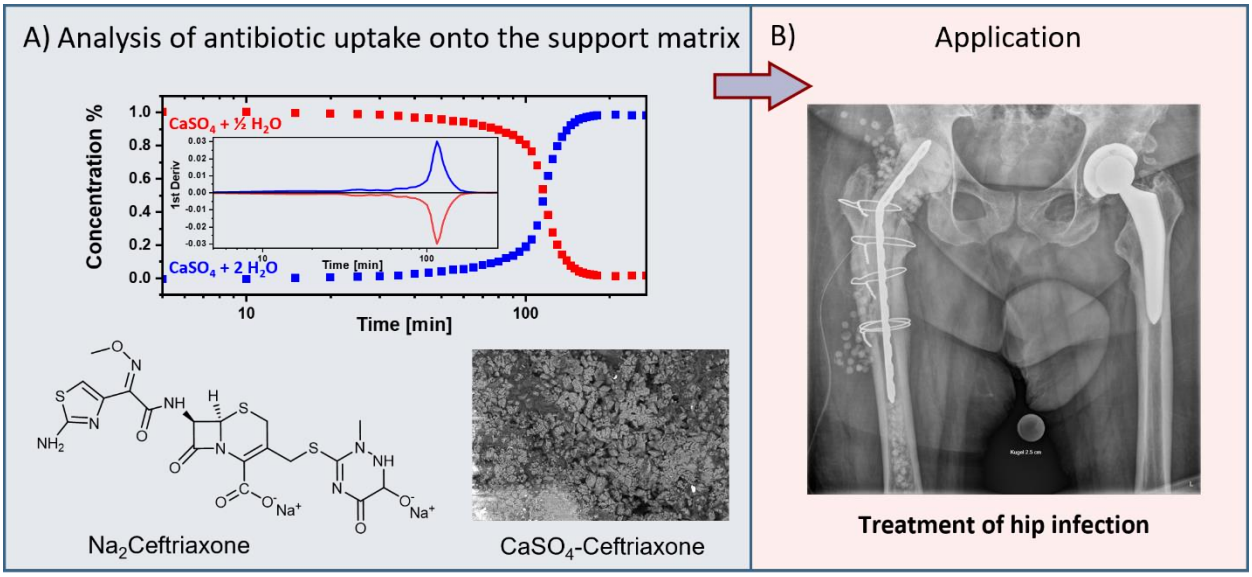


Figure 1. Summary of A) the in-situ PXRD kinetics of Ceftriaxone uptake into the $CaSO_4$ matrix with the chemical structure of the Ceftriaxone and the resulting morphology of the system, and B) its application.

References:

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