Evaluation of antimicrobial-loaded calcium sulfate composites for the management of resistant Gram-negative diabetic foot osteomyelitis

Antibiotic-loaded calcium inhibit bacterial growth over 10 weeks, suggesting utility for AMR diabetic foot osteomyelitis.

Usman Arshad[1] & Ryan A Hamilton[1,2]
1. School of Pharmacy, De Montfort University, Leicester, UK
2. Pharmacy Department, Kettering General Hospital NHS Foundation Trust, Kettering, UK

Background
One of the most serious complications of diabetes is diabetic foot osteomyelitis (DFO) which can lead to limb amputation, reduced quality of life, and early mortality (International Diabetes Federation, 2020). Antimicrobial resistance (AMR) is a leading cause of death globally and is an increasing problem within DFO.

Aim
To investigate the antimicrobial and pharmaceutical properties of antimicrobial-loaded calcium sulfate composites for the targeted treatment of DFO.

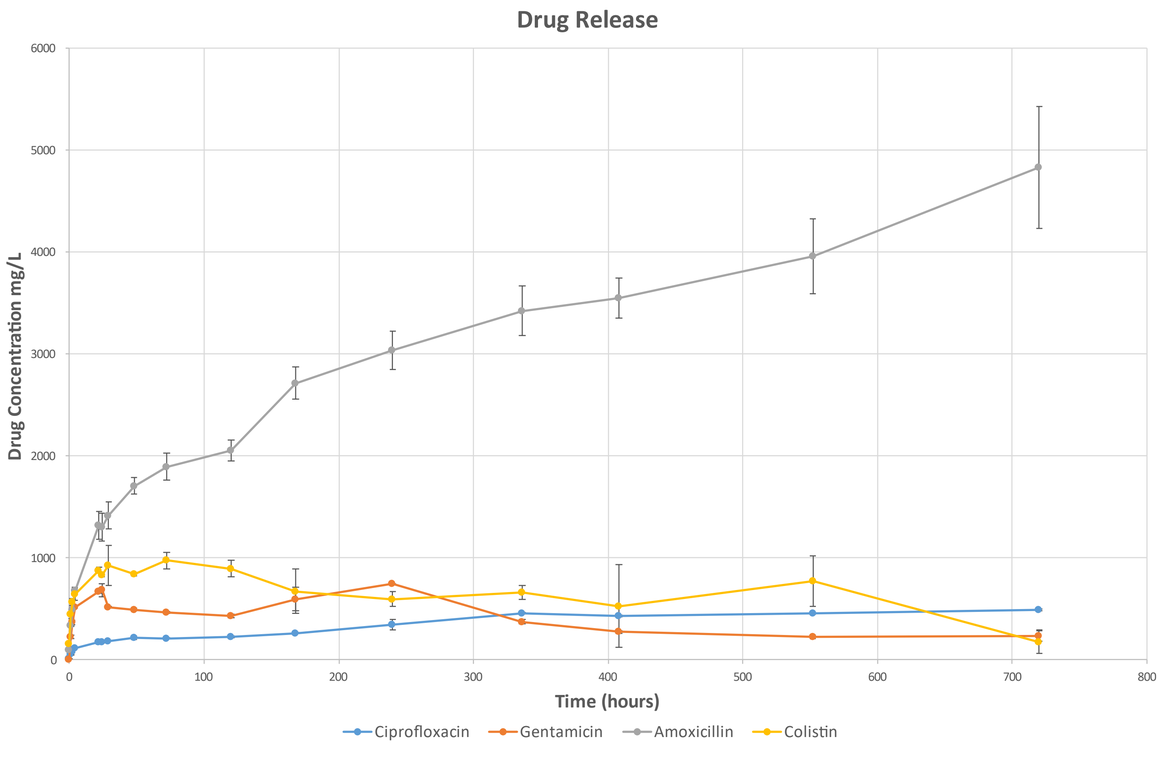
Methods
Calcium sulphate (Stimulan® Rapid Cure) beads containing 120 mg gentamicin, 500 mg ciprofloxacin, 500 mg amoxicillin or 200 mg (2.5 MU) colistin were tested against *Staphylococcus aureus* (NCTC6571), *Pseudomonas aeruginosa* (NCTC6750 and an extensively drug-resistant clinical isolate from DFO) and *Escherichia coli* (NCTC8196) over time using an adapted EUCAST disk-diffusion methodology. Synergy testing, drug-release studies, dose uniformity and hygroscopicity testing were undertaken to further characterise these composites.

Results

Drug Release & Antimicrobial Effects

- Amoxicillin and ciprofloxacin released continuously, and zones of inhibition (ZOI) remained constant.
- Gentamicin and colistin underwent burst-release, with ongoing release and ZOI decreasing over time.
- Calcium sulfate had no antimicrobial effect.
- No synergy was observed between the antimicrobials.

Research is needed on pellets containing multiple drugs, and to search for synergistic combinations



Dose Uniformity

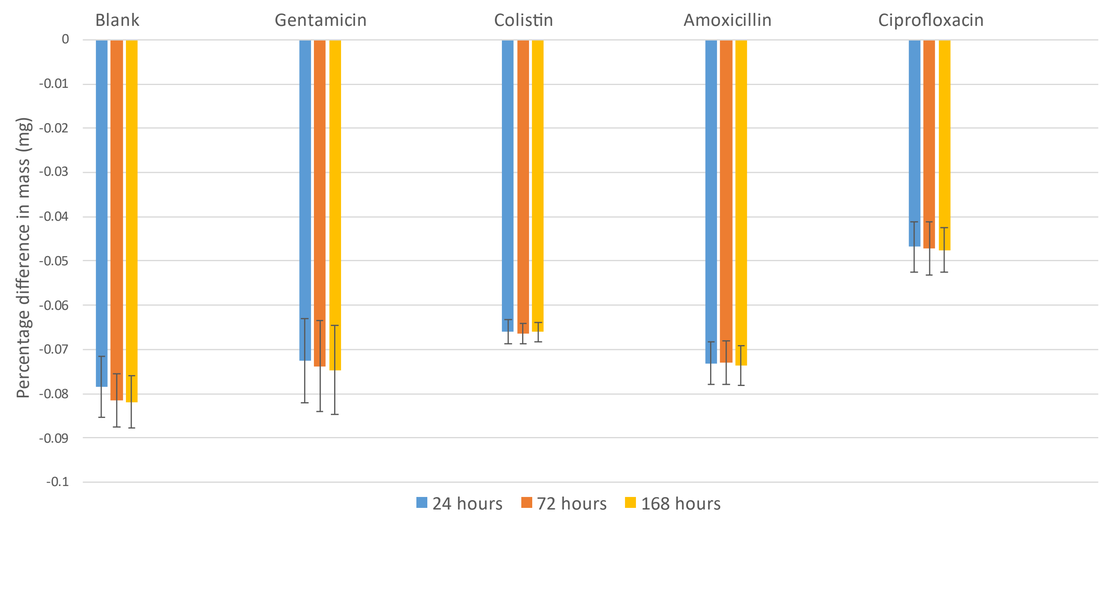
- Amoxicillin and ciprofloxacin had acceptable dose variation
- Gentamicin and colistin content was highly variable and may impact on clinical concentrations.

Research is needed to determine the effect of drug and mixing method on dose uniformity

	Amoxicillin	Ciprofloxacin	Gentamicin	Colistin
Percentage coefficient variant (%)	4.0	10.7	48.0	113.6

Hygroscopicity Testing

Pellets lost mass over the study time period



References
ARMSTRONG, D.G. and LIPSKY, B.A. (2004) Diabetic foot infections: Stepwise medical and surgical management. International Wound Journal, 1(2), Available from: doi.org/10.1111/j.1742-4801.2004.00035.x.

Acknowledgements
Biocomposites for providing Stimulan® 5cc packs. Dr Raymond Allan, Claire West, Jasira Patel, Richard Smith, Dr Michael Pierides and Paul Bird for their advice and support during the projects.

DE MONTFORT UNIVERSITY LEICESTER

NHS Kettering General Hospital NHS Foundation Trust