Biodegradable injectable polymer/calcium phosphate bone paste with antibacterial properties

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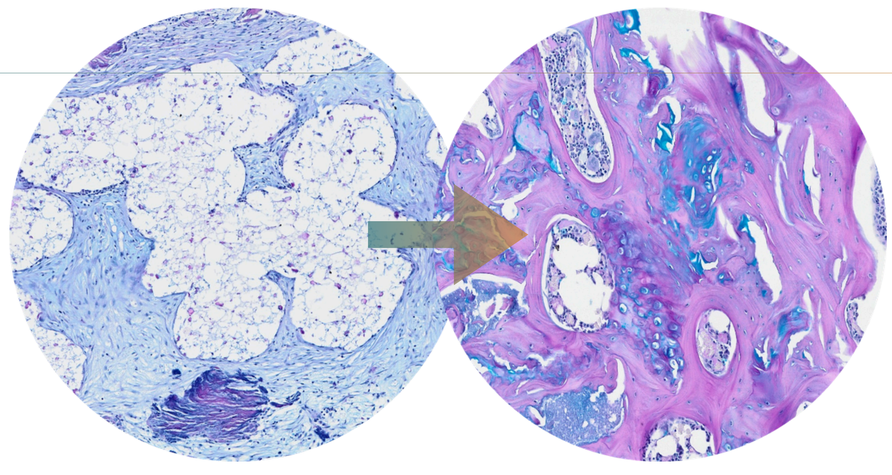
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BIOMEDICAL CENTER

Introduction

Osteomyelitis (bone tissue infection) remains a significant clinical challenge in orthopedics. The most common causative agents are gram-positive staphylococci, particularly Staphylococcus aureus. Other relevant pathogens include methicillin-resistant S. aureus, Staphylococcus epidermidis, and gram-negative bacteria such as Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae. Orthopedic clinicians are actively seeking easily injectable resorbable bone defect fillers that stimulate new bone formation, prevent infection, and provide mechanical support.

BONE PASTE DEGRADATION & NEW BONE FORMATION



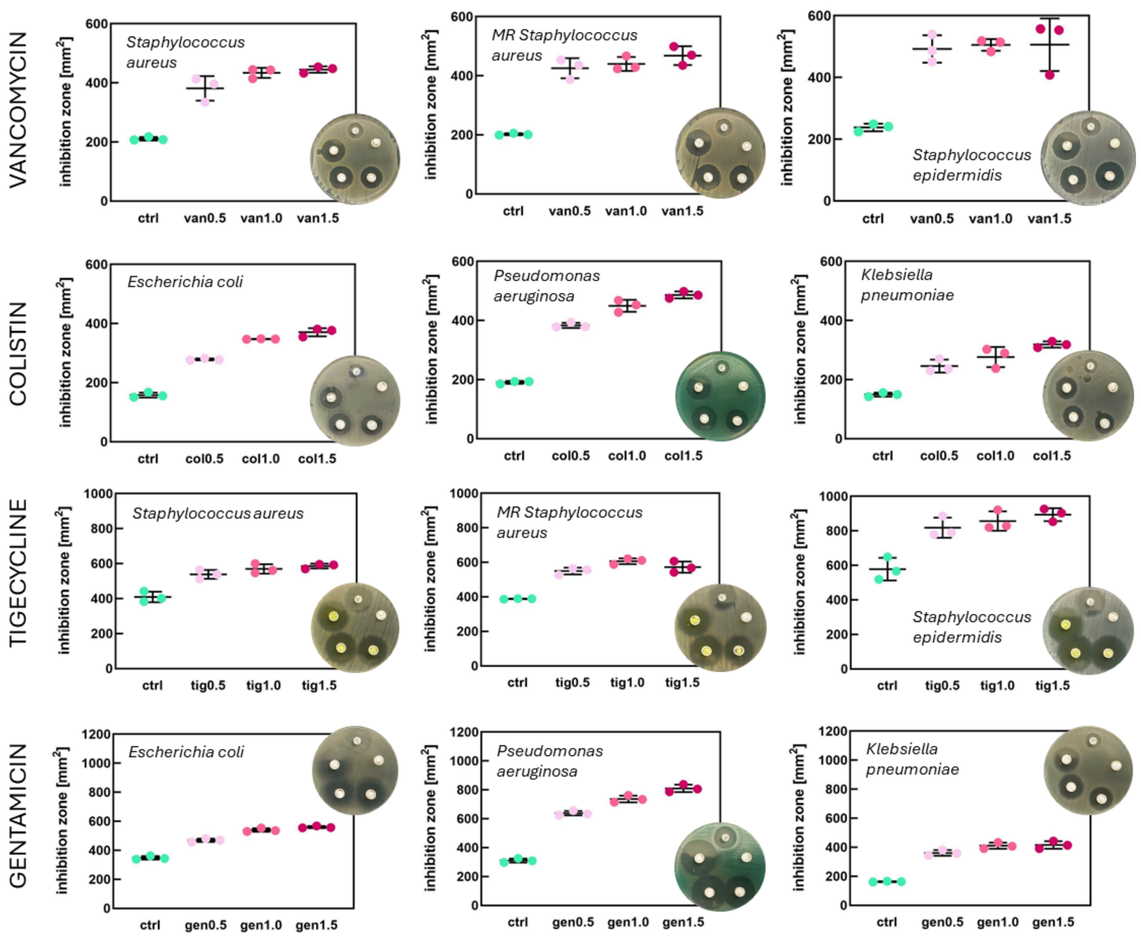
Aims of the study

1. To verify the in vitro antibacterial efficacy of a newly developed biodegradable polymer/calcium phosphate bone paste with prolonged injectability enriched with selected antibiotics (vancomycin, gentamicin, tigecycline, colistin) effective against the common bone pathogens (S. aureus, S. epidermidis, MRSA, E. coli, P. aeruginosa, K. pneumoniae).
2. To establish a functional animal model of bone infection for subsequent evaluation of the bone paste's antibacterial effects in relevant pre-clinical conditions.

BONE PASTE: novel thermosensitive thixotropic copolymer based on hydrophobic poly(lactide) and poly(glycolide) (PLGA) and hydrophilic poly(ethylene glycol) (PEG) developed by **Vojtova et al. (Int. J. Mol. Sci. (2019), 20(2), 391).**



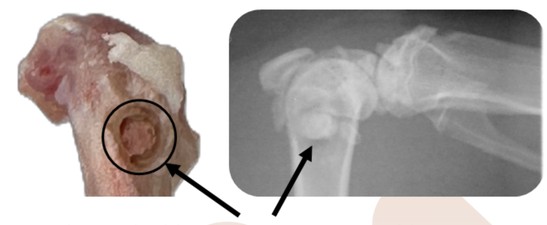
In vitro antibacterial efficacy - diffusion method



Animal model of early bone infection

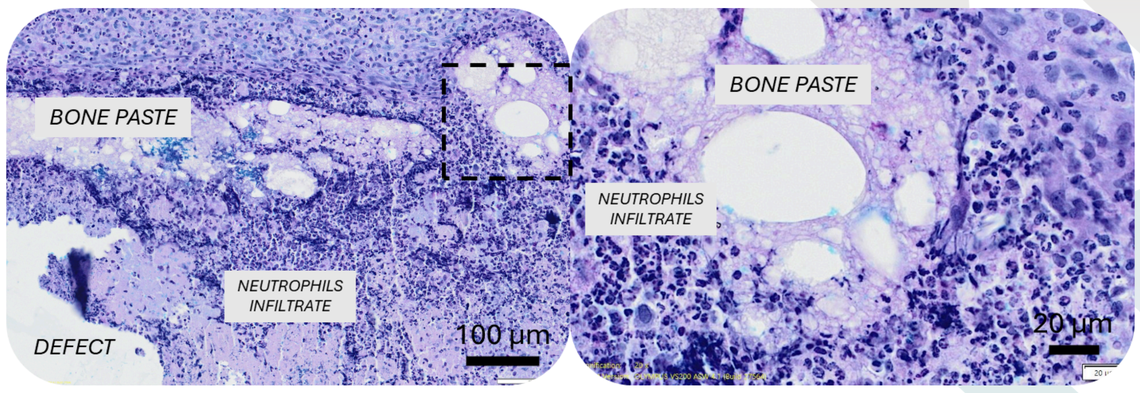
Four concentrations of Staphylococcus aureus (strain ATCC 25923; 10^2, 10^4, 10^6, 10^8 CFU/ml) were tested, delivered in 1% agar blocks applied into 2 x 5 mm defects induced in femur of experimental rats. Defects were sealed with bone paste without antibiotics to prevent the leakage of bacteria. Analyses were performed at day 4, 11, and 42 post implantation to determine the bacterial presence in defects and to evaluate the bone tissue damage.

IN: 10^4 CFU/mL S. aureus
42 DAYS = clinically expected time of bacterial elimination when ATB are applied as the treatment of bone infection



degraded bone matrix around bone paste
OUT: 8 x 10^5 CFU/mL S. aureus

HISTOLOGICAL EVALUATION OF BONE INFECTION



Results and Discussion

- Diffusion microbiological tests confirmed the effective release of all four tested ATBs from the bone paste. The antibiotics demonstrated the formation of concentration-dependent growth inhibition zones against all tested bacterial strains.
- The highest SA concentration (10^8 CFU/ml) induced painful animal movement and was excluded from further study. 10^4 and 10^6 CFU/ml resulted in stable S. aureus positivity without causing distress, establishing them as suitable baseline concentrations for subsequent pre-clinical bone paste antibacterial efficacy evaluations.

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