Vancomycin Adsorption and Desorption to 3D Printed Calcium Phosphate Ceramics

U. Gbureck[1], E. Vorndran[1], F. A. Müller[2], J.E: Barralet[2]
[1]Department for Functional Materials in Medicine and Dentistry, University of Würzburg, Germany
[2] Department for Materials Science III - Biomaterials, University of Erlangen-Nürnberg, Germany
[3]Faculty of Dentistry, McGill University, Montreal, Quebec, Canada

Statement of Purpose

Currently used antibiotic delivery systems for the treatment of infected bone are based on non-resorbable poly(methyl-methacrylate) (PMMA) beads or self setting PMMA bone cement. Drug delivery systems based on calcium phosphate chemistry could have the advantage of being resorbed after release such that a second surgery to remove the implant could be avoided. In this work we investigated the adsorption and desorption behavior of vancomycin hydrochloride to microporous calcium phosphate (CaP) ceramics, which were fabricated using 3D powder printing as rapid prototyping technology.

Materials and Methods

Cylindrical samples (10mm diameter x 5mm height) consisting predominantly of either brushite ($CaHPO_4 \cdot 2H_2O$), monetite ($CaHPO_4$) or hydroxyapatite ($Ca_5(PO_4)_3OH$) were manufactured from tricalcium phosphate (d_{50}=19.4µm) or tetracalcium phosphate (d_{50}=15µm) powder using 3D printing technology[1]. Samples were printed with an acidic phosphate solution as liquid on a 3D-powder printing system (Z-Corporation, USA) following by immersion of the samples in the same solution for 3x60s to increase the degree of conversion to brushite and a hydrothermal treatment of the hydroxyapatite samples in 2.5% Na_2HPO_4 solution (2h, 100°C). Loading of the samples with vancomycin hydrochloride was performed by immersing the printed samples in solutions with 0.1-10mg/ml drug concentration for time periods of 1h - 7d. The drug release was measured photometrically at 251nm after immersion of the samples in PBS solution for up to 5d. An additional polymer impregnation was performed by immersion the drug loaded samples in 10-50wt% solutions of PLA/PGA (Resomer 504H, Boehringer, Ingelheim, Germany) polymer following drying in air.

Results

The adsorption of vancomycin to microporous CaP samples from various concentrated solutions showed a linear relationship between the drug concentration in solution and the adsorbed vancomycin (Figure 1A) whereas a square root of time relationship between the immersion time and the amount of adsorbed drug was found (Figure1B). Differences in the total amount of adsorbed drugs were correlated to the specific surface areas of the matrices, which varied between 2.3 - 12.1m^2/g. Drug release followed for all structures a square root of time kinetic with a quantitative drug release after approx. 2 days, whereas the hydroxyapatite samples released the drug comparatively slower than the brushite and monetite matrices (Figure 2A). A retarded release profile was obtained by polymer impregnation of the drug loaded brushite matrices (Figure 2B).

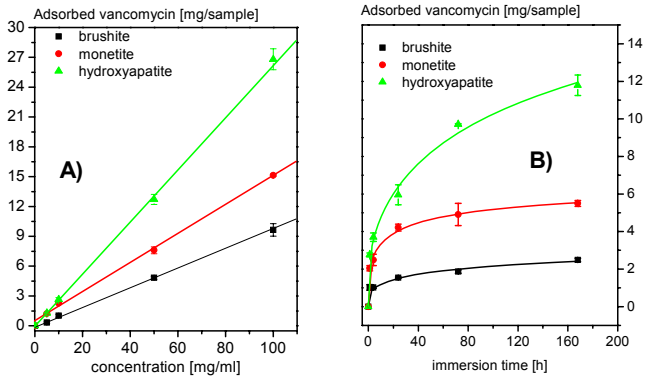

Figure 1: Vancomycine adsorption to CaP structures A) from solutions with 5 - 100mg/ml drug concentration (immersion time = 1h) and B) immersed in a 10mg/ml drug solution for various times

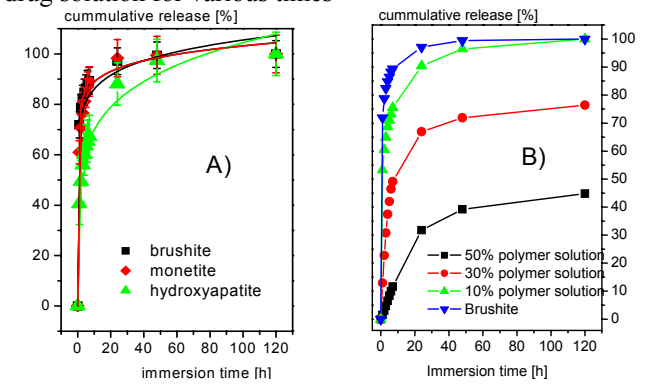

Figure 2: Vancomycin release from different CaP matrices after immersion in PBS buffer for up to 5d (A) and from brushite after additional polymer impregnation (B)

Discussion

Acute and chronic bacterial osteomyelitis remains an important clinical problem in orthopedic surgery. Conventional treatment includes surgical removal of necrotic bone tissue and the application of local drug delivery systems. In this work we present a drug delivery system based upon microporous brushite / monetite structures. The manufacturing of the structures via rapid prototyping technology enables the preparation of patient specific custom implants and the fast release rate of this system compared to PMMA based materials could minimise the risk of bacterial resistance. At the same time, these osteoconductive matrices may be resorbable such that a second surgery to remove the devices would be avoided.

References

[1] U. Gbureck et al. Direct printing of bioceramic implants with spatially localised angiogenic factors Advanced Materials, In Press 2006.