Application of α-Cristobalite and β-Rhenanite as Drug Delivery Systems

Pacheco, H., Vedantham, K., El-Ghannam, A.
University of North Carolina at Charlotte, Charlotte, NC 28223.

Introduction: The efficacy of the systemic treatment of osteomyelitis is limited due to the poor accessibility of antibiotics to the infection site. Alternative approach is to use biomaterials for local drug delivery of antibiotics. Earlier work has shown the capability of a silica-calcium phosphate nanocomposite (SCPC75) to provide a sustained release of therapeutic dose of antibiotics to treat infections.[1,2] In the present preliminary study, we synthesized and characterized α-Cristobalite (Cris) and β-rhenanite (Rh), then investigated the ability of both materials to bind and release vancomycin (Vanc) in a controlled fashion. Long term release studies up to 288 hrs confirmed the sustained release of therapeutic dose of Vanc from Rh and Cris.

Methods: Rh (β-$NaCaPO_4$) was synthesized by heating a homogeneous mixture of $CaHPO_4.2H_2O$ and Na_2CO_3 (2:1 molar ratio) at 1100°C for 16hrs. Cris was synthesized by heat treatment of α-quartz (SiO_2) powder at 1500 °C for 15 hours. SCPC powder (SCPC75) containing a molar composition of 22.8% CaO, 11.4% P_2O_5, 32.9% SiO_2 and 32.9% NaO_2 was prepared as reported earlier.[1] The structure and morphology of Rh, Cris, and SCPC75 was analyzed using XRD and SEM. The surface chemistry of the material loaded with and without antibiotic was characterized by FTIR in the diffuse reflectance mode. 1.5g of each ceramic powder was immersed separately in 15ml of 8 mg Vanc /ml PBS for 24 hrs. The total amount of Vanc adsorbed onto each powder was determined by calculating the difference in the concentration of the drug solution before and after immersion using UV-vis spectrophotometer (λ_{abs} at 280nm). To study release kinetics, 0.2 g of each drug-ceramic hybrid was immersed in 5 ml of PBS on an orbital shaker (120 rpm) at 37 °C. 1 ml of the solution was withdrawn at 4, 12, 24, 48, 96, 144 and 288 hrs for concentration measurements. The solution was refreshed with 1 ml of PBS at every sampling time point to maintain a constant volume of the media. Five replications were measured (n=5) per each sample and the data are presented as mean ± SD.

Results: XRD (Figure 1) and FTIR analyses confirmed the crystalline structure of Rh and Cris. SEM analysis showed the particles to be porous with porosity in the size range 10nm- 2 μm. Quantitative analyses of the porosity and the surface area, are currently underway. The amount of Vanc loaded per gram of ceramic was 64.9, 39.85 and 40.0 mg for Rh, Cris, and SCPC75 respectively. Initial Vanc burst release of 43.2±29.0, 84.2±40.5 and 36.7±15.7 μg/ml/h from Rh, Cris and SCPC75 respectively was measured in the first 4 hrs. After 12 hrs, a steady rate of release of 14.05±1.54, 16.96±2.41 and 11.88±1.89 μg/ml/h was observed for Rh, Cris and SCPC75 hybrids, respectively (Figure 2). After 288 hrs the percentages of drug released from Rh, Cris and SCPC75 were 25.33%, 16.42% and 15.81% respectively.

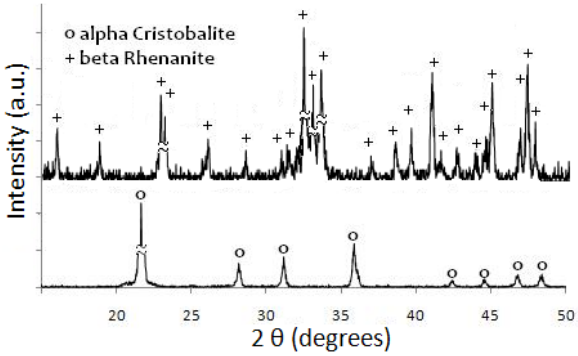

Figure 1. XRD patterns measured for Rh and Cris.

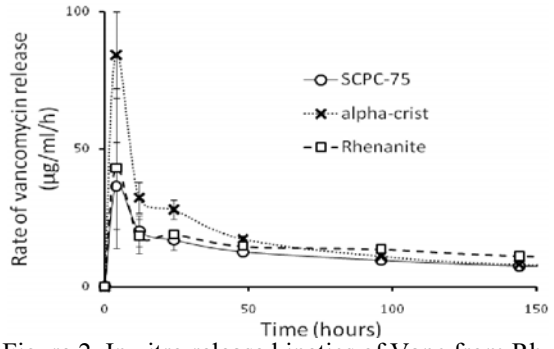

Figure 2. In vitro release kinetics of Vanc from Rh, Cris and SCPC75

Conclusions: Results of the preliminary study indicated that Rh and Cris have the ability to provide a sustained release of therapeutic doses of Vanc until 288 hrs. The average concentration of the released drug falls within the therapeutic dose range of Vanc (5 μg/ml – 80 μg/ml). The retaining of 75 and 84 % of the initial loaded drug after 288 hrs on the surfaces of Rh and Cris respectively indicates the possibility of using these materials for prolonged drug release.

Reference

1. El-Ghannam et. al., J Biomed Mater Res 94A: 308–316, 2010.
2. El-Ghannam et. al., J Biomed Mater Res Part B: AppBiomater 73B: 277–284, 2005.