Effect of Crystal Lattice Modification of α-Cristobalite on Drug Adsorption and Release Kinetics

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Statement of Purpose: The purpose of this study is to understand how functional groups of silica based biomaterials affect drug binding and release kinetics essential for therapy. Data in the literature focused on the porosity characteristics of the material or drug loading techniques in order to control binding and release kinetics [1-4]. In the present study, the surface chemistry of α-cristobalite (Cris) was modified via doping with phosphorous. The drug adsorption and release kinetics are correlated to the microstructure of the material.

Methods: Highly stable porous Cris particles (90-150μm) were doped with different mole percentages of phosphorous (0, 0.0625, 0.125, 0.25 or 0.5) using direct impregnation with orthophosphoric acid and heat treatment at 1000ºC/3hr to promote silica-phosphate ionic substitution. X-ray Diffraction (XRD) with Reitveld Refinement was used to analyze the crystalline structure of Cris before and after modification. Fourier Transform Infrared spectrometry (FTIR) was used to study surface chemistry. Cris samples were immersed separately in DI water and the concentrations of Si and P ions in the immersing solution were measured using inductively coupled plasma optical emission spectroscopy (ICP-OES). The Cris granules were immersed in 8mg/ml Vancomycin in PBS for 24 hr. The drug concentration was measured by HPLC before and after immersion and the amount of drug adsorbed on the material surface was calculated. All samples had 5 replicates, and statistical analysis was completed using the student's t-test, and all p values below 0.05 were considered statistically significant.

Results: XRD results show that the there is an increase in the size of unit cell of Cris after P doping. After doping with P, FTIR shows a P-O band at 1136.8 cm^{-1} and a shift in the Si-O band at 1094.4 cm^{-1} indicating Si-P ionic substitution. Fig.1, shows the effects of P doping on Si and P dissolution from Cris. As expected, a significant increase in the release of P ions is observed as the % of P dopant increases (p value < 0.5). However, a comparable release of Si ions among the samples was noticed regardless of the concentration of doped P. FTIR results of modified and non-modified Cris after loading with Vancomycin show peaks belonging to an aromatic ring (1423 cm^{-1}) and CO_2- (1398 cm^{-1}) [5]. This indicates that Vancomycin functional group CO_2- and aromatic ring is the binding site to the Cris functional group Si-O. The effect of releasing the P ions on Vancomycin adsorption can be seen in samples that were immersed in DI water for 2 days have adsorbed more drug than the samples without immersion (p value<0.05) (Fig. 2.).

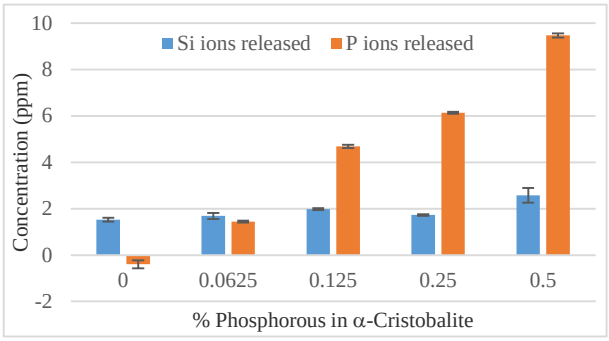

Figure 1. Effect of Phosphorous Doping on Silica and Phosphorous Ion Dissolution from α-Cristobalite

For the no immersion samples an increase in drug binding is observed after doping with 0.0625 % P, afterwards drug adsorption decreased with any further increase in P doping. The decreases in drug adsorption of both immersed and non-immersed samples maybe due to the availability of Si functional groups on the surface of Cris. If the samples were immersed for a longer period of time more Si functional groups would be exposed thus increasing the drug adsorption of the samples which still may have too much P on the surface.

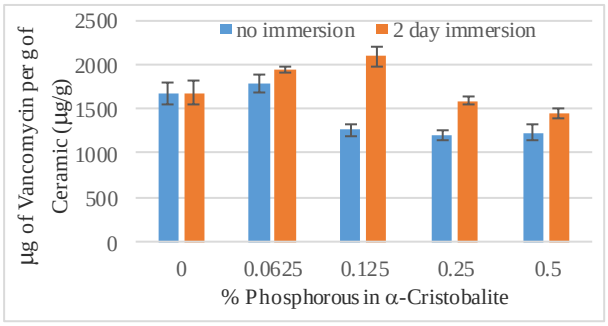

Figure 2. Effect of Releasing Phosphate Ions from α-Cristobalite on Drug Adsorption

Conclusions: Doping α-Cristobalite by P decreased Vancomycin adsorption. The release of phosphorus in DI water was associated by significant increase in Vancomycin adsorption due to the exposure of the silanol group on the material surface. These results suggests that Van has higher affinity to the silanol groups compared to the phosphate groups.

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