# Bioceramic drug delivery systems: what carrier for what drug?

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**Overview:** Calcium phosphate and silica-based bioceramics are very attractive for DDS applications. Silica-calcium-phosphate (SCPC) nanocomposite is a drug delivery platform that successfully demonstrated the ability to bind and release several therapeutics including antibiotics, peptides, anticancer drugs, and growth factors [1, 2]. The aim of the present work is to analyze on the molecular level the role of SCPC microstructure on binding and release kinetics of Cisplatin (Cis) and Vancomycin (Vanc). The main crystalline phases of SCPC are α-cristobalite ($SiO_2$, Cris) and β-rhenanite ($NaCaPO_4$, Rhe) were prepared and characterized separately. The ability of each phase to bind and release Vanc and Cis was investigated. The ceramics surface chemistry and their interaction with the different drugs were correlated with the loading capacity and linked to the release kinetics and ceramic dissolution. Moreover, the kind of drug tested (Vanc or Cis) demonstrated a significant influence on the loading capacity and release kinetics from the same carrier.

**Methods:** SCPC50 (containing a molar composition 36.8% CaO, 18.4% $P_2O_5$, 22.3% $Na_2O$ and 22.4% $SiO_2$), Cris and Rhe particles in the size range (250-425 μm) were synthesized. Ceramics composition, porosity and surface chemistry were analyzed by XRD, SEM, BET, mercury intrusion and FTIR, respectively. Loading of various ceramics were performed by immersion. Briefly: ceramic particles in a weight/volume 0.333 g/ml were immersed in 10mg/ml Cis/DMSO solution for 42 h or in 8 mg/ml Vanc/water solution at 37°C/100rpm/24h. Cis loaded on the ceramics was determined by washing the loaded particles with 70% $HNO_3$ and the [Pt] concentration in the solution was measured using ICP-OES. Vanc loading capacity was determined by HPLC and TG-DCS in an oxidative atmosphere. Release kinetics experiments were carried out by immersing 0.2 g of ceramic-drug hybrid and controls ceramic without drug in 10mL of PBS at 37°C/100rpm. An aliquot 1 mL from the immersing solution was withdrawn and replaced with fresh PBS after several time points. The concentrations of released drug were measured by: ICP-OES (Cis) and HPLC (Vanc). The therapeutic effect of the released drugs was analyzed in vitro. The data were expressed as the mean ± SD ($P<0.05$).

**Results:** Structural and compositional features of Cris, Rhe and SCPC50 ceramics demonstrated a significant influence on the loading capacity and release kinetics profile of Vanc and Cis. FTIR and DSC analyses demonstrated that the P-O functional groups in Rhe and SCPC have high affinity with the (C=O and N-H) of Vanc and (N-H and O-H) of Cis. Moreover, a weak chemical interaction between the two drugs and the Si-O functional group in Cris and SCPC was observed. Vanc loading per surface area increased in the order 8.00 μg Vanc/$m^2$ for Rhe > 4.49 μg Vanc /$m^2$ for SCPC>3.01 μg Vanc /$m^2$ for Cris ($p<0.05$). Cis loading capacity increased in the order 8.59 μg Vanc /$m^2$ for Cris, 17.8 μg Vanc/$m^2$ for Rhe and 6.03 μg Vanc /$m^2$ for SCPC ($p<0.05$). Drug release kinetics was both carrier and drug dependent. The percent drug release in the burst stage (during the first 2h) was: 50%, 50%, and 46% of Vanc; and 53.4%, 36.6%, and 30.6 % of Cis, for Cris, Rhe and SCPC50 respectively (Figure 1). Burst release was found to be correlated to the pore size distribution and surface area. Furthermore, the average rate of sustained release rates was: 9.8, 7.2 and 3.5 μg/h of Vanc and 4.5, 5.3 and 3.5 μg/h of Cis for Cris, Rhe and SCPC50, respectively, in the period between 8-216h.

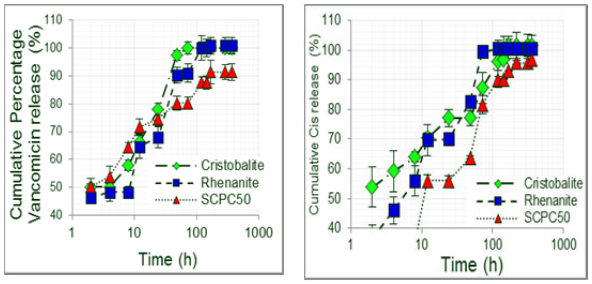


Figure 1. Release kinetic profiles of Cis and Vanc from Cris, Rhe and SCPC50

**Conclusion:** Inert Cris ceramic showed release kinetics controlled by its hierarchical porous structure and high surface area. On the other hand, the surface chemistry of bioactive Rhe overruled the effect of surface area. Therefore, it is possible to tailor drug release kinetics from SCPC platform by controlling the ratio of Cris and Rhe in the composite without affecting bioactivity of the drug.

**References:**

1. El-Ghannam et. al., J Biomed Mater Res 94A: 308–316, 2010.
2. Vedantham K, et al. J Biom Mat Res Part A 2012:100A:432-440. 2012.