**A New Bone Tissue Engineering Scaffold for the Release of Biological Molecules**

Kiarash J., El-Ghannam A.
Center for Biomedical Engineering, University of Kentucky, Lexington, KY-40506

**Introduction:** One approach to increase the efficiency of bone disease treatment is the use of sustained release systems that include drug supports in synthetic bioceramics. The advantage of a sustained release system of drug in the treatment of bone disease is the maintenance of a localized increase of the drug and thus a targeted control/treatment of microorganisms or malignant cells. Recently we reported on a novel porous, bioresorbable silica-calcium phosphate nano composite (SCPC) that has superior bioactivity and resorbability properties compared to traditional bioactive glass and calcium phosphate ceramics [1, 2]. In the present study, we examined the ability of SCPC to treat bone diseases by providing a controlled release of a therapeutic dose of drug molecules. The release kinetics of anti-cancer drug (5-Fluorouracil, 5-FU) and an antibiotic (vancomycin) from SCPC were analyzed and correlated to the physicochemical characteristics of the material.

**Materials and Methods:** SCPC particles in the size range of 90-425µm were prepared as previously described [1]. The surface area, porosity and pore size distribution were analyzed using mercury porosimetry. SCPC particles were immersed in simulated body fluid for 4 days. Surface modifications after immersion were analyzed by FTIR. For 5-FU loading on the ceramic, 0.2g SCPC particles were immersed in PBS solution containing 5.71mg/ml 5-FU for 24h. The amount of the drug adsorbed onto the surface of SCPC was calculated by measuring the concentrations of the drug solution before and after immersion. The SCPC-5-FU hybrid was immersed in 25ml of PBS and incubated at 37° C on an orbital shaker. At 24, 48, 96, 144 and 192h, 2ml were removed and replaced with 2ml of fresh PBS. The concentration of the drug in the immersed solution was determined using HPLC. For loading vancomycin on the ceramic, 0.2g SCPC particles were immersed in a vancomycin solution containing 8mg/ml for 1h. The particles were removed, dried and then immersed in 12ml of PBS. At 1, 3, 6, 24, 48, 96h and every 48h thereafter to 532h, 2ml were removed and replaced with 2ml of fresh PBS. The concentration of the released drug was measured by using a UV spectrophotometer at 280nm. Parallel experiments including SCPC samples without drugs were performed for comparison.

**Results:** SCPC particles were characterized by 54.9 % porosity, pore size range 3nm-352µm and specific surface area of 0.046 m²/g. Immersion of SCPC in SBF and drug solution did not change the porosity characteristics of the material. FTIR analysis showed the development of a hydroxyapatite (HA) surface layer after immersion in SBF or in drug solutions (Fig. 1). Data from the HPLC measurements indicated an adsorption of 2.78g 5-FU /m² of SCPC surface. An initial burst release of 1.2mg 5FU which constitutes 4.6% of the adsorbed drug was observed after 24h of immersion. After 24h, a sustained release of 5-FU from the SCPC-5FU hybrid into the PBS was observed and continued up to 192h. The average 5-FU concentration released in the solution was 50µg/ml. UV spectroscopy showed that SCPC adsorbed 0.56g/m². After 24h immersion in PBS 152.1µg constituting 3.16% of the originally loaded 4.8mg vancomycin was released. A sustained release of vancomycin was observed up to 532h. The average concentration of vancomycin released in the solution was 5.056µg/ml.

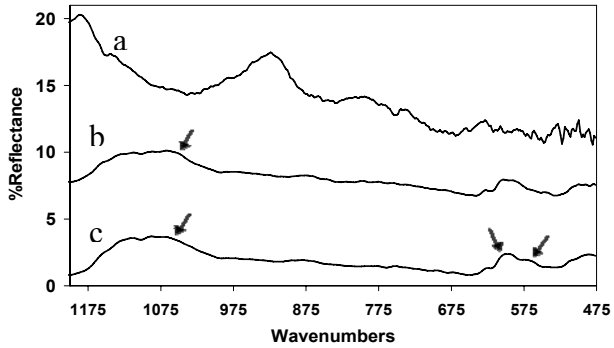


**Fig 1**. FTIR spectra for (a) SCPC unimmersed in SBF, (b) SCPC immersed in SBF for 4 days, (c) SCPC immersed in SBF for 4 day and loaded with 5-FU. Arrows show the characteristic peaks for HA.

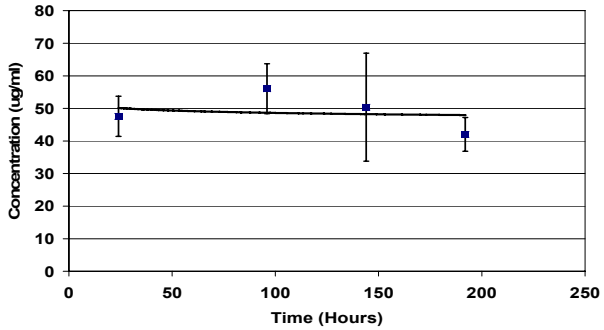


**Fig 2.** Release profile of 5-FU form SCPC-5FU hybrid.

**Conclusion:** SCPC has a great potential as a drug delivery system. When loaded with anticancer drug or antibiotic, SCPC provided a sustained release of a therapeutic dose of the drug. Drug loading onto the SCPC surface did not interfere with the precipitation of a hydroxyapatite layer on the material surface. The formation of the HA layer is critical for enhancement of bone cell function and tissue formation. Thus, SCPC can provide a targeted treatment for the disease and at the same time enhance tissue regeneration.

**Reference**: **1.** El-Ghannam, A; *J. Biomed Mater Res.* 2004, 69A: 490-501. **2.** El-Ghannam, et al; *J Biomed Mater Res A*. 2004 (3): 377-90.

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