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Author: T.S. Sampath Kumar K. Madhumathi B. Rajkamal S. Zaheatha A. Rajathi Malar S. Alamelu Bai

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## ACCEPTED MANUSCRIPT

### Enhanced protein delivery by multi-ion containing eggshell derived apatiticalginate composite nanocarriers

# T.S.Sampath Kumar $^{1,*}$ , Madhumathi $K^1$ , Rajkamal $B^1$ , Zaheatha $S^2$ , Rajathi Malar $A^2$ and Alamelu Bai $S^2$

- 1. Medical Materials Laboratory, Department of Metallurgical and Materials Engineering, Indian Institute of Technology, Madras, Chennai 600 036, India.
- 2. Department of Biochemistry, Asan College of Arts and Science, Chennai 600100, India.

#### **Abstract**

Eggshell is an attractive natural source of calcium for the synthesis of hydroxyapatite (HA) as it contains minor amounts of biologically relevant elements such as Mg, Sr, and Si. The mineral phase of the human bone is essentially a calcium deficient hydroxyapatite (CDHA) which shows more bioactivities and absorbance than stoichiometric HA does. Hence, we have attempted to develop a protein delivery system based on eggshell derived CDHA (ECDHA) nanoparticles for bone tissue engineering. Nanoparticles with Ca/P molar ratio of 1.67, 1.61 and 1.51 to form CDHAs with compositions covering the properties of stable HA phase (Ca/P=1.67) to degradable tricalcium phosphate (TCP) phase (Ca/P=1.5) were synthesized by microwaveaccelerated wet chemical synthesis using eggshell as well as synthetic calcium hydroxide as calcium precursors. The delivery profiles of bovine serum albumin (BSA), a model protein by the nanocarriers, were studied. Both eggshells derived and synthetic CDHA samples showed maximum amount of loading of 57% and 37% respectively at a Ca/P ratio of 1.51, comparing to stoichiometric HA. ECDHA also showed a much more BSA release (25%) than synthetically derived CDHA (6.5%) did. To further improve the release profile, alginate coating was carried out on CDHA nanoparticles and the BSA release profiles were evaluated. A maximum release of 65% was observed for alginate coated ECDHA at a Ca/P ratio of 1.51 for a period of 2 days. The ECDHA nanoparticle with a Ca/P ratio similar to degradable TCP and with alginate coating seems to be an ideal protein delivery agent.

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<sup>\*</sup>Corresponding author: "tssk@iitm.ac.in; Tel.:+91 4422574772; Fax: +91 4422570545.

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