Conversion of Coral Sand to Calcium Phosphate as a Drug Delivery System for Bone Regeneration

by

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Declaration

Candidate's Certificate

This is to certify that the work presented in this thesis was carried out by the candidate in the Faculty of Science at the University of Technology Sydney and has not been submitted to any other university or institution for a higher degree. This work contains no material written or published by any other person except where due reference has been made.

Joshua Chou

Sydney, April 2011

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Abstract

In this research, we have for the first time harnessed the architectural design of biospheres from coral beach sand, to capture and deliver the drug bisphosphonate alone, or in combination with antibiotics. Partnered with this we used lipid coatings to control drug elution by design. This is a study to utilise biomimetics for drug delivery using these marine structures. Importantly, release of the drug was sustained at physiologically relevant quantities for longer periods than those originating from other clinically practiced schemes such as, doping bone cements and oral administration. The simple concept of using natural structures directly for human therapeutics can yield enormous benefits to an increasingly ageing population. Currently researchers are striving to perfect the design and formulation of delivery vehicles that can be directed to an exact location and offload the pharmaceutical drugs at the site. There are many promising strategies including bio-inspired ones, but none using something as simple as coral beach sand with unique pore size, interconnectivity and architecture.

These calcium carbonate coral beach sand microspheres were converted to calcium phosphate and loaded with pharmaceutical drugs such as bisphosphonate. The drug bisphosphonate has an inherent affinity for calcium, and as the microspheres slowly degrade, the drug is released. Elution kinetics show sustained release of the adsorbed drug. This occurs for 21 days- long enough to influence early bone formation. Once the drug has been released, the spheres also safely dissipate. Drug functioning was positively determined by increased human osteoblast proliferation accompanied by osteoclast inhibition in direct association with bisphosphonate bio-spheres. The unique, complex topology and morphology enables the drug to be loaded and retained while the material is calcium phosphate and adsorbes the drug very efficiently.

In addition an antibiotic gentamicin was loaded at the same time to surmount the re-current problem of bacterial infections following bone and implant surgery. Biospheres therefore offer a more efficient and convenient alternative. Following complete drug release the vehicle degrades slowly in-situ. The elution kinetics can be further controlled by coating the spheres with lipid. In the future these can be incorporated with molecules that provide highly specific associations with a target tissue. Coral beach sand is plentiful and pre-designed to adsorb and release a variety of drugs, as indicated by this study. So far with this study we have shown this *in vitro,* but in principle this is applicable for any orthopaedic or maxillofacial drug of choice for bone repair and reconstruction. Biomimetics do not need to be complicated.

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Book Chapter

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