A NEW CALCIFICATION RESISTANT, BIOSTABLE, BIOCOMPATIBLE POSS-NANOCOMPOSITE POLYMER FOR DEVELOPING NEW GENERATION OF HEART VALVES

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INTRODUCTION: Recent advances in science and technology, especially in nanotechnology, offer novel materials with improved properties and potential application in medicine. Nanocomposites are among the widely studied novel materials for biomedical application. We have developed a new nanocomposite (NC) polymer based on polyhedral oligomeric silsesquioxane (POSS) nanoparticle and poly(carbonate urea)urethane polymer with potential application in biomedical devices. Our previous studies showed enhanced biocompatibility[1], improved degradative resistance[2], less thrombogenecity[3], and endothelialisation capability[4] which make it as a potential material of choice for blood containing devices such as artificial heart valve. Given these results, we studied calcification resistance properties of this new POSS-NC in an in vitro pulsatile flow circuit.

MATERIALS AND METHODS: Sheets (40 × 40 mm) of POSS-NC, 100 μm thickness, were manufactured and placed in an especial holder chamber. Patches of glutaraldehyde fixed bovine pericardium (BP) were used as control.
Accelerated physiological pulsatile flow system (APPFS): An especially designed APPFS was used to expose samples to the pulsatile mechanical stress in physiologic range. The rate and the pressure of the pulsatile pump were adjusted and monitored during the exposure to flow. A simulated physiologic solution (containing calcium and other electrolytes of human plasma) was used and the test was carried on into an incubator in 37˚C with adjusted physiological CO_2 and oxygen.
Calcification investigation: X-Ray study, quantitative chemical analysis (calcium assay), normal light microscopy, confocal microscopy, and scanning electron microscopy (SEM) were performed on the samples after 40×10^6 cycles in 31 days test period.

RESULTS: X-Ray studies showed massive calcium deposition on BP samples but no detectable calcification signs on POSS-NC sheets.
Chemical analysis: Quantitative analysis of calcium content of extracted solutions showed significant differences ($p<0.05$) between pericardium samples and NC samples. The average calcium detected in pericardium samples was 718.7±141.1 μg/cm^2, while in POSS-NC samples it was 120.1±33.0 μg/cm^2.
Microscopic examination: After staining with Von Kossa and Alizarin red, light and confocal microscopy showed areas of calcification within the tissue sections of BP samples, in comparison there were no sign of calcification in POSS-NC.
SEM: Surface studies using SEM were negative for both pericardium samples and BP suggesting no extrinsic calcification was found on samples.

CONCLUSION: The calcification properties of a novel POSS-NC polymer were assessed in an *in vitro* pulsatile flow circuit model specifically developed. The results showed that POSS-NC exhibits significant resistance to calcification in comparison with chemically fixed bovine pericardium, which is one of the main materials used clinically in current bioprosthetic valves. The calcium deposition on BP was intrinsic, not extrinsic. These findings suggest that this novel POSS-NC could be an attractive alternative to biological tissues for the manufacturing of artificial heart valves.

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