SCPP-EM-PVA composite as a promising scaffold for the prevention and treatment of aseptic loosening

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Statement of Purpose:

Our previous studies showed that erythromycin (EM) is effective in inhibiting periprosthetic tissue inflammation in patients with aseptic loosening (AL). Strontium (Sr)-doped calcium polyphosphate (SCPP) is an ideal bioceramics because of its biocompatibility, biochanical strength, and stimulation of bone growth. The aim of this study was to develop and characterize a SCPP-EM-Polyvinyl Alcohol (PVA) composite as a sustained EM release device for the prevention and treatment of AL.

Methods:

Preparation of SCPP-EM-PVA composite The frit of calcium phosphate monobasic monohydrate containing 1% Sr was calcined at 500ºC to polymerize into polyphosphate. After compressing to required formation, cylinder sample was sintered at 800ºC and cooled naturally. For EM incorporation, EM-ethanol solution was added into the SCPP matrix and the final EM concentration was adjusted to 1%, 5% and 10% (w/w). SCPP-EM composite was soaked in 7% PVA solution and then freeze at -80ºC, followed by being dried in a freeze dryer (-50ºC, 14Ap) for over 10h.

EM release assay SCPP-EM-PVA was put into simulated body fluids (SBF) and EM released into SBF was measured by an UV-spectrophotometer method.

Mechanical testing The maximum compress strength and Young's modulus were analyzed using a universal material tester.

Proliferation and differentiation of osteoblast ROS17/2.8 cells The cell proliferation was measured by MTT assay, and cell differentiation was measured by alkaline phophatase assay.

Results:

PVA coating significantly extends EM release time (Fig.1) PVA coating extends the EM release time from a few hours (no PVA coating) to more than one hundred hours, especially in the SCPP scaffolds containing 5% and 10% EM, respectively.

PVA coating improves compress strength (Fig. 2) As shown in Fig. 2 (a), the SCPP-PVA composite has the strongest compress strength, though the strength was compromised by the incorporation of EM. As shown in Fig. 2 (b), the composite fragility was reduced by PVA coating, as manifested by The Young's modulus of composite.

SCPP-EM-PVA composites enhance osteoblast differentiation. SCPP-EM-PVA composites are not cytotoxic when incubated with ROS17/2.8 cells for 6 days *in vitro*, as evaluated by MTT assay (Data not shown). As shown in Fig.3, The ALP activity was increased by EM-containing composites compared to SCPP-PVA composite only. However, no significant difference of ALP activity was found among composites with different EM addition.

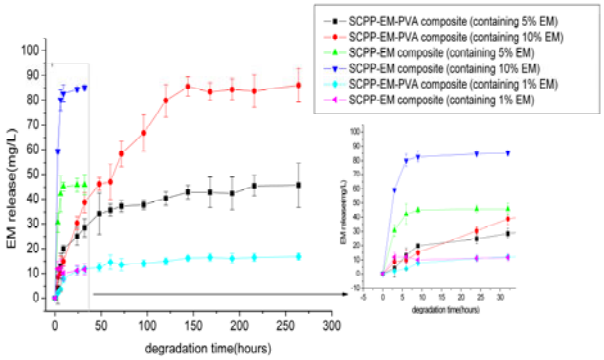

Fig.1 The cumulative release of EM into SBF for over 250 hours (n=8 for each SCPP composite, p<0.05).

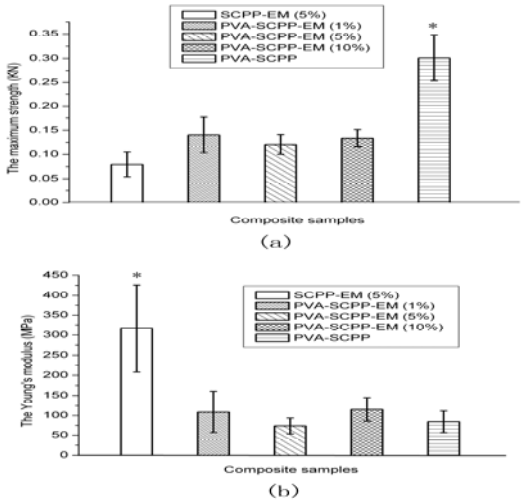

Fig.2 PVA coating improves (a) compress strength and (b) Young's modulus (n=5), p<0.05.

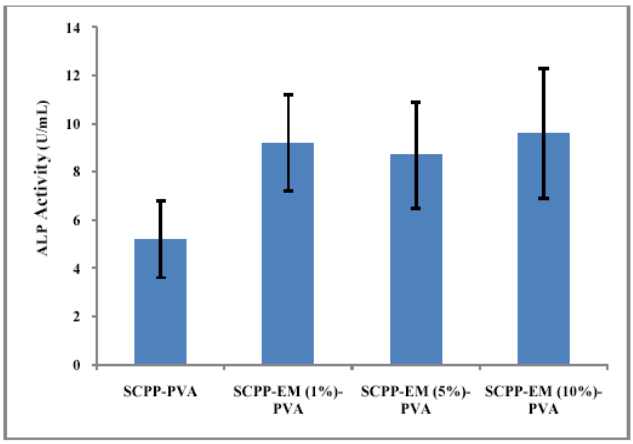

Fig.3 ALP activity of composites culturing with ROS 17/2.8 osteoblast for 2 days. n=5, p<0.05.

Conclusions:

EM represents one of the most promising drug candidates for AL. Delivering adequate levels of EM to the site of periprosthetic inflammation, without undesirable systemic side effects, presents a considerable challenge. PVA is a water-soluble polymer that can firstly swell and then partly dissolve in water solution. We found that SCPP-EM composite with PVA coating increases more than 10 folds of EM release time, as compared to composites without PVA coating. PVA coating also increases the mechanical strength and reduces the material fragility. The compress strength of cancellous bone ranges from 2 to 20MPa, and the SCPP-EM-PVA composites has the similar compress strength at the range of 4.2 to 15 MPa, indicating PVA-coated SCPP scaffolds can be used as a periprosthetic drug delivery device. Furthermore, our data showed that SCPP-EM-PVA composites are nontoxic to ROS17/2.8 osteoblast cells, and addition of EM in the composites enhances osteoblast differentiation, as evidenced by the increase of ALP activity. Taken together, we propose that the porous SCPP-EM-PVA composite can be used as a prosthesis coating matrix device that will allow us to deliver EM, or other anti-inflammatory drugs, to the periprosthetic tissue with sustained release for longer term inflammation inhibition.

Acknowledgments

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