

### 3D porous polycaprolactone-based magnesium scaffold for bone tissue engineering

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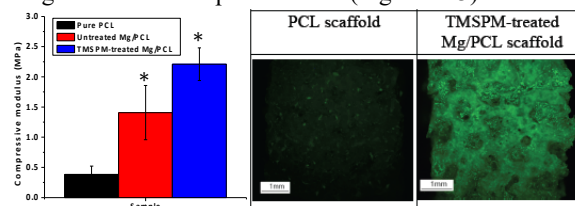
**INTRODUCTION:** Bone tissue engineering offers an alternative solution to the traditional bone substitutions e.g. autografts and allografts. This approach may help resolve the availability and donor site morbidity during autologous bone graft harvesting procedures and the risk of disease transmission with the use of allografts<sup>1</sup>. However, due to the poor mechanical and non-osteoinductive properties of the currently available synthetic grafting materials such as ceramic and polymeric materials, the scaffolds with superior bone regeneration ability are required. Magnesium (Mg), as a potential additive, plays an essential role in skeletal development<sup>2</sup>. Our previous study also showed that a specific amount of Mg ions is able to promote new bone formation<sup>3</sup>. Hence, our group has fabricated a hybrid porous scaffold made of polycaprolactone (PCL) and Mg micro-particles. This study aims to investigate the mechanical, *in vitro* and *in vivo* properties of the newly developed scaffold.

**EXPERIMENTAL METHODS:** The Mg/PCL scaffolds were prepared by incorporating 4.8% 150µm Mg granules into PCL using salt leaching technique. Silane coupling agent (TMSPM) was coated on the Mg granules in order to enhance the bonding between PCL and Mg. Compression test was conducted to study the mechanical property of the scaffolds. A 7-day stimulated body fluid (SBF) immersion test was conducted to test their bioactivity. After that, the surface composition was checked by energy dispersive x-ray spectroscopy (EDS). The cytocompatibility of the scaffolds was studied by direct culture of green fluorescent protein mouse osteoblasts (GFPOB). Finally, the *in vivo* response of the scaffolds was evaluated by rat model for 3 months. Giemsa staining was used to visualize the new bone formation.

**RESULTS AND DISCUSSION:** The compressive modulus of the Mg/PCL scaffold was doubled as compared to pure PCL scaffold, whereas increased 80% further after the TMSPM treatment (Figure 1). The result suggested the mechanical property of pure PCL scaffold could be significantly enhanced by incorporating Mg granules. The silane coupling treatment could further enhance its mechanical property. Calcium and phosphate deposition was detected on the hybrid scaffold but not on pure PCL scaffold after 7-day SBF immersion (data not shown). The apatite layer formation illustrated the enhancement of osteoconductivity of the PCL scaffold. Moreover, the hybrid scaffold was fully engulfed by living osteoblasts as compared to the pure PCL scaffold which indicated that the hybrid scaffold was able to enhance cell attachment and growth (Figure 2). This was possibly due to the effect of Mg ions release. In previous study, low level of Mg ions (i.e. 50ppm) was able to stimulate

growth and differentiation of osteoblasts<sup>3</sup>. Hence, this explained why more new bone formation was able to

grow inside the hybrid scaffold than pure PCL scaffold during animal implantation (Figure 3). The



interconnected porous scaffolds would allow fluid flow, thereby enhancing bony tissue in-growth. All these favourable observations may attribute to the bioactivity enhancement due to the consistent release of Mg ions. However, the release of Mg ions should be controlled carefully since bone loss will be resulted if too much ions are released<sup>4</sup>.

Figure 1 (Left) Compressive moduli of pure PCL and Mg/PCL hybrid scaffolds with and without TMSPM treatment. Significantly higher compressive moduli were found on the hybrid scaffolds than pure PCL scaffold. Figure 2 (Right) Microscopic view of the scaffolds after 3 days GFP mouse osteoblasts culture. More living cells were found on the TMSPM-treated Mg/PCL scaffold as compared to the pure PCL scaffold.

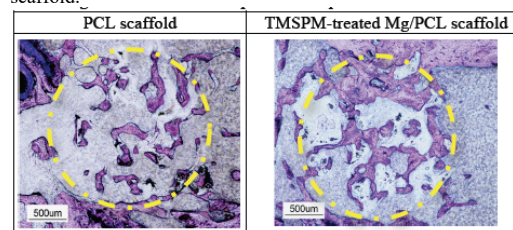


Figure 3. Giemsa stained histological photographs after 3 months of implantation. More newly formed bone was found within the hybrid scaffold as compared to the pure PCL scaffold.

**CONCLUSION:** This study demonstrates that the newly developed Mg/PCL scaffolds are able to enhance the mechanical property and inferior bioactivity of pure PCL scaffold so as to encourage bone formation and in-growth. TMSPM silane-coupling treatment can further enhance the mechanical property of the scaffolds. Hence, all these promising results have shown that the modified Mg/PCL hybrid porous scaffolds can be potentially applied in large bone defect fixation.

#### REFERENCES

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