A novel magnesium-based bone substitutes: An alternative to autologous bone grafting to treat large bone defects

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Statement of Purpose: Synthetic grafting materials offer an alternative solution to the traditional methods of bone replacement including autografts and allografts¹. However, due to the poor mechanical and non-osteoinductive properties of the currently available synthetic grafting materials such as ceramic and polymeric materials, other materials are needed to develop especially for treating large bone defects. Magnesium, as the biodegradable metallic material, plays an essential role in skeletal development². However, its fast degradation rate limited its use. Therefore, our approach is to develop a hybrid material made of Mg and a biodegradable polymer, polycaprolactone (PCL) to solve the problems³. TMSPM silane treatment was conducted on Mg prior hybrid fabrication so as to reduce the rapid corrosion rate of Mg. Additionally, PCL is used to form the hybrids with Mg since it has a slow degradation rate as compared to other polymers⁴. Therefore, by forming the hybrid material with PCL, it is then able to control the release of Mg during degradation. This study aims to investigate the mechanical, in vitro and in vivo properties of the newly developed bone substitute.

Methods:
(a) The Mg-PCL hybrids were prepared by incorporating 9% TMSPM-treated Mg granules with 2 different particle sizes (i.e. 45µm & 150µm), respectively.
(b) Compression test was conducted to study the mechanical properties of the hybrids. A 7-day stimulated body fluid (SBF) immersion test was conducted to test the bioactivity of the hybrids. After that, the surface composition was checked by energy dispersive x-ray spectroscopy (EDS).
(c) The cytocompatibility and osteogenic differentiation properties of the hybrids were studied by MTT and ALP assays using MC3T3-E1 pre-osteoblasts.
(d) The in vivo response of the hybrids was evaluated by rat model for 2 months. Micro-CT was used to monitor the volume change of new bone formation.

Results and Discussion: 36% higher compressive modulus was found on the hybrids as compared to pure PCL (Figure 1). The result suggested that the mechanical properties of pure PCL can be enhanced by incorporating Mg granules and the values fall within the range of cancellous bone (50-800 MPa)⁵. Calcium and phosphate deposition was detected on the hybrids but not on pure PCL after 7-day SBF immersion. The formation of the apatite layer illustrated that the hybrids may possess osteoinductivity. Moreover, significantly higher cell viabilities and specific ALP activities were found on the hybrids as compared to pure PCL, which suggested that the hybrids were cytocompatible and favored osteogenic differentiation (Figures 2 & 3). This was possibly due to the effect of Mg ions release. Our previous study showed that a low level of Mg ions (i.e. 50ppm) is able to stimulate the growth and differentiation of osteoblasts, whereas toxic effect was found when the Mg ions level was high. Hence, this showed the importance of controlling the released of Mg ions. This also explained why more new bone formation was found on the hybrids than pure PCL during animal implantation (Figure 4). More than 15% of new bone formation was found on the hybrids after 1 week of post-operation and 40% higher after 3 weeks. Hence, all the data presented here suggested our new bone substitutes maybe a potential candidate to treat large bone defects.

Conclusions: From the results of the compression test, in vitro and in vivo studies, the newly developed Mg-PCL hybrids are able to enhance the mechanical properties, osteoconductivity and also possess osteoinductivity so as to encourage bone formation. However, further studies including the in vivo osteoinductivity study is still needed.


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