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Biodegradable poly(L-lactide) composites by oligolactide-grafted magnesium hydroxide for mechanical reinforcement and reduced inflammation

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Biodegradable polymers, such as poly(L-lactide) (PLLA), are very useful in many biomedical applications. However, their degradation by-products have been much of a concern as they are the sources of inflammatory reactions in the body. In this work, we suggest a novel composite system composed of PLLA and oligolactide-grafted magnesium hydroxide (Mg-OLA) that can overcome drawbacks caused by poor mechanical properties and inflammatory response of PLLA for biomedical applications. Mg-OLAs were synthesized by ring opening polymerization and the structure, morphology, pH change, thermal, and mechanical properties were analyzed using FTIR, SEM, pH meter, TGA, and UTM. In particular, the tensile strength and modulus of PLLA/Mg80-OLA20 (0–20 wt%) were higher than those of PLLA/magnesium hydroxide. The PLLA/Mg80-OLA20 composite was also very effective in neutralizing the acidic environment caused by the degradable by-product of the PLLA matrix. *In vitro* cell viability and the expression levels of COX-2 and IL-6 proteins in the PLLA composites were also evaluated. Cell viability increased to around 100% with increasing the amount of Mg80-OLA20 from 0 to 20 wt%. The expression levels of IL-6 and COX-2 were reduced dramatically when increasing the proportion of Mg80-OLA20 from 0 to 50 wt%. As a result, the incorporation of Mg-OLAs into the PLLA matrix could reinforce the mechanical properties as well as reduce the inflammatory response of the hybrid PLLA. Therefore, this hybrid composite system blending oligomer-grafted magnesium hydroxide in biodegradable polymers would be a promising strategy for avoiding current fatal problems in biomedical applications.

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Introduction

Synthetic biodegradable and biocompatible polyesters, such as poly(L-lactide) (PLLA), polyglycolide (PGA), and poly(ε-caprolactone) (PCL), are useful materials for medical applications such as surgical implants, drug delivery, and tissue engineering.[1–4] Although these polymers are suitable for a number of the above-mentioned applications because they are well-processable, biocompatible, and biodegradable polymers, they have two critical shortcomings that restrict their applications including severe inflammatory response and relatively poor mechanical properties.[5,6]

In particular, PLLA-based materials have frequently shown sustained inflammatory responses upon implantation in the body. PLLA undergoes hydrolytic degradation *via* the bulk erosion mechanism by the random scission of the ester backbone. It degrades into lactic acid (LAc), a normal human metabolic by-product, which is broken down into water and carbon dioxide *via* the citric acid cycle.[7,8] Inflammatory response and cytotoxicity may be severe under conditions in which the acidic product accumulates and is concentrated. It becomes the cause of inflammation and cytotoxicity.[9–11] Anderson *et al.* demonstrated that the inflammatory responses occur on biodegradable PLLA microsphere.[12] Kontio *et al.* also reported the occurrence of a chronic inflammatory response from biodegradable PLLA.[13] Although there have been several efforts to address this problem using anti-inflammatory drugs and copolymers,[14–17] it still remains an unsolved issue till now.

Meanwhile, PLLA that is polymerized through ring opening polymerization (ROP) has a limitation in increasing the molecular weight due to trans-esterification and backbiting of the catalyst.[18] It is also known that condensation polymerization forms low molecular weight PLLA due to reversible reaction.[19] In addition to the inflammation problem, there were

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