Interfacial compatibilization of PLA and Mg in composites for bioresorbable bone implants

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Abstract. In this study, polylactide (PLA)/magnesium (Mg) composites were produced through extrusion and compression-molding. In order to enhance the interfacial adhesion between the hydrophobic matrix and the hydrophilic filler, an amphiphilic PEO-\textit{b}-PLLA block copolymer was used. The morphological study shows an effective improvement of the PLA/Mg interactions following the copolymer addition. Moreover, the surface contact angle test proves the decrease of the PLA hydrophobicity. Thus, a significant influence on the cell adhesion is expected. Furthermore, hydroxyapatite formation in bulk after eight weeks of the immersion in a simulated body fluid (SBF) is also shown, suggesting that the bioactivity will be noticeably improved. However, a decrease in mechanical properties and cell adhesion is observed.

1. Introduction
Stainless steel, cobalt-based alloys and especially titanium-based alloys have been the key materials for bone implants since the 1980s. However, these permanent implants present some disadvantages, such as side effect from long-term use: implant erosion and partial resorption, cortical bone erosion and fragmentation due to the high Young’s modulus of the implant requiring second/multiple surgical interventions [1]. Thus, alternatives to permanent metal implants already available on the market, such as bioresorbable implants, have been developed and continue to gain popularity. Together with the requirements for any implant (biocompatibility and suitable mechanical properties), the bioresorbable implants include biodegradability and bioactivity so as to achieve adequate strength and stiffness maintained during a required time interval, allow cell adhesion and proliferation, degrade and resorb for bone healing until its complete regeneration. For these reasons, the polylactide (PLA) is among the biodegradable and biocompatible polymers of choice [2]. However, PLA possesses low mechanical properties (Young’s modulus (GPa) = 3-4) compared to bone performance Young’s modulus (GPa) = 7-30), uncontrollable and relatively slow degradation time (> 6 months) and acidic degradation products (causing local inflammation issues) [3]. To successfully remediate this issues, (nano)fillers have often been incorporated to polymers. Among all, Mg present good osteoconductivity, high mechanical properties (compared to monolithic polymers) and lower degradation times (< 1 month) [4, 5]. Bearing in mind the published results, we propose here a combination of PLA and Mg. However, the poor interfacial adhesion between the hydrophobic PLA and the hydrophilic Mg is expected to negatively affect the matrix/filler (composite) properties. One of the possibilities to enhance the compatibility between a polymer and a filler involves modification of the filler surface using compatibilizing agents [6, 7]. We report on the testing of an amphiphilic copolymer to form a new interface between the matrix and the filler, thus improving the interfacial adhesion of PLA/Mg biocomposites and the composite’s biological activity.
2. Preparation of composites
The amphiphilic diblock copolymer poly(ethylene oxide-\textit{block}-polylactide), (PEO-b-PLLA) was synthesized via bulk ring opening polymerization (ROP) of L-lactide initiated by a PEO with a fixed chain length of 5000 g/mol. [8] The amount of copolymer was fixed to 10 wt.% in PLA. The filler amount was 5 wt.%, 10 wt.% and 15 wt.% of Mg and composites were prepared via extrusion and shaped into cylinders (12-mm length and 4-mm diameter) and rectangular specimens of 60×12×3 mm\(^3\) (length×width×thickness) via compression-molding.

3. Results and discussions

3.1 Morphology, surface hydrophilicity and dynamic mechanical analysis

3.1.1 Morphology
The morphology of all the composites was visualized using scanning electron microscopy (SEM) to evaluate the influence of PEO-\textit{b}-PLLA on the PLA/Mg interfacial adhesion. The samples were cryofractured and covered with gold prior to observation. As seen in Figure 1 (A), the poor interactions between the hydrophobic PLA matrix and hydrophilic Mg filler resulted in cavities left by the Mg particles after cryofracture. This behavior is considered as typical for incompatible composites with low interfacial adhesion between the matrix and the filler [5]. In contrast, the presence of the amphiphilic copolymer allowed an interestingly good compatibility between PLA and Mg as evidenced by the absence of cavities and the smooth and homogenous surface after criofracture (Figure 1 (B)).

![Figure 1. SEM images in bulk of (A) PLA/xMg and (B) PLA/10Copo/xMg composites (x = 0, 5, 10 and 15 wt. %).](image)

3.1.2 Surface hydrophilicity
Together with the surface-morphology, surface hydrophilicity is known to tailor the bioactivity of implants. [8] Therefore, the influence of the copolymer on the PLA/Mg surface hydrophilicity was evaluated using water contact angle (WCA) analysis. Interestingly, the addition of PEO-\textit{b}-PLLA showed a positive effect on the composite wettability. Indeed, the amphiphilic copolymer is able to enhance the hydrophilicity of the PLA/Mg composites by selective surface localization of the hydrophilic PEO blocks. [9] Thus, a decrease in the WCA from the first set (without copolymer) to the second one (with copolymer) was observed (table 1).
3.1.3 Dynamic mechanical analysis

Dynamic mechanical analyses (DMA) are often used to assess the mechanical properties of samples as a function of the temperature. The results obtained for all composites and the neat PLA are presented in table 2.

As seen, an improvement in the storage moduli (E’) was reached at 10 wt.% of Mg and 37 °C for the first set (PLA/xMg). Concerning the PLA/10Copo/xMg set, the E’ reproduces the same behavior of the first one with a decrease in the E’ values. In reality, the E’ decrease indicated the plasticizing effect of the PEO present in the P EO-b-PLLA copolymer [10]. After the copolymer addition, a significant drop in the loss factor tanδ was detected when the Mg amount increased. According to the literature, the decrease of tanδ is related to the highest intensity of interface adhesion [11]. Consequently, the composites reinforced with an amount of 10 wt.% of Mg filler will be more closely investigated in the following section.

Table 2. DMA results (storage modulus E’ and loss factor tanδ) of PLA/xMg and PLA/10Copo/xMg composites (x = 0, 5, 10 and 15 wt. %) at 37 °C.

| Mg amount (wt.%) | Water Contact Angle |
|------------------|---------------------|
|                  | PLA/xMg  | PLA/10Copo/xMg |
| 0                |  93      |  81             |
| 5                |  84      |  78             |
| 10               |  81      |  76             |
| 15               |  79      |  72             |

3.2 In vitro degradation study

In order to evaluate the bioactivity of the composites, an in vitro degradation test was performed by soaking the cylinders in the SBF at 37 °C and at pH 7.4. Prior to this test, the samples were taken out of the SBF and rinsed several times with distilled water, wiped off and dried in nitrogen. The visual aspect of the PLA/10Mg and PLA/10Copo/10Mg composites revealed the formation of a white friable layer on the composites surface. Its thickness for the PLA/10Copo/10Mg was found to also increase over time. This might be explained by the formation of hydroxyapatite ‘HAp’ (the major natural bone component) based on Mg degradation. [12] According to the literature [13], Mg degrades in SBF mainly through reactions with water by producing Mg cations (Mg^{2+}) and hydroxide anions (OH^-) and releasing hydrogen gas. The Mg^{2+} and OH^- form the magnesium oxide layer. Then, Ca^{2+} and Mg^{2+} react with phosphate to form small quantities of calcium phosphate (Ca_{3}(PO_{4})_{2} and magnesium phosphate (Mg_{3}(PO_{4})_{2})
Indeed, some cracks and pitting corrosion were observed in the composites (figure 2). This behavior is more pronounced in PLA/10Copo/10Mg compared to PLA/10Mg composite because of the hydrophilicity of PEO. In order to confirm the chemistry of the white layer, EDX analysis was performed on the composites surface and in bulk (cross-section). The data obtained revealed that after a period of eight weeks HAp was only formed at the surface of PLA/10Mg (Ca/P=1.6), while the mineral was present in the entire bulk of the PLA/10Copo/10Mg. Interestingly, the content of Ca and P was more prominent in the presence of copolymer in bulk. Indeed, the Ca/P ratio was 1.64 reached after eight weeks of degradation versus 1 for the PLA/10Mg composite. Thus, the copolymer-containing samples seem more beneficial for new bone tissue formation during the bone-healing process [14].

Figure 2. Degradation mechanism of the PLA/10Mg and PLA/10Copo/10Mg in the SBF.

4. Conclusion
As was shown above, the presence of an amphiphilic copolymer enhances the PLA/Mg interfacial adhesion and decreases the PLA hydrophobicity via creating a completely new interface between PLA and Mg. In fact, it is assumed that the more the surface is hydrophilic, the more the hydrophilic bone-like layer adheres. Moreover, HAp – the major component of natural bone – was formed in bulk only after eight weeks of immersion in the SBF for the PLA/10Copo/10Mg. However, the copolymer presence decreased the mechanical properties of the composite-based materials. In this regard, research is in progress to develop composites that meet the mechanical properties of natural bone by using novel co (polymers) to improve the PLA/Mg adhesion.

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