

Surface modification of poly(D,L-lactic acid) scaffolds for orthopedic applications: a non-destructive route via diazonium chemistry.

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Statement of Purpose: Scaffolds made with synthetic polymers such as polyesters are commonly used in bone tissue engineering due to their biocompatibility, biodegradability, and adequate mechanical¹. However, polyesters are hydrophobic, which implies that their surface is not ideal for cell adhesion and growth. Surface modification of these materials is thus crucial for enhancing the scaffold integration in the body. Different surface modification techniques have been developed to improve scaffold biocompatibility, such as physical adsorption, plasma treatment and wet chemistry techniques. Still, each of them presents some drawbacks: natural adhesive proteins can be physically adsorbed on the scaffold but the bond formed is weak; three-dimensional (3D) scaffolds cannot be homogeneously modified by plasma, because the plasma tends to modify the scaffold outer surfaces faster than the inner ones; wet chemistry techniques such as hydrolysis can be used to bind several functional groups to scaffold surfaces, but they often change the scaffold properties because they degrade the polymer. Here we show that diazonium chemistry² can be used to modify the outer and the inner surfaces of 3D Poly(D,L-lactic acid) (PDLLA) scaffolds with phosphonate groups, using a simple 2-step procedure. By changing reaction time and impregnation procedure we were able to tune the concentration of phosphonate groups present on the outer and inner surfaces of the scaffolds. Phosphonate groups should be able to enhance nucleation and growth of hydroxiapatite (HA) by attracting calcium cations³. To test this, we immersed the scaffolds in simulated body fluid (SBF), and characterized the scaffolds with various methods.

Methods: PDLLA scaffolds were fabricated by the casting and particulate leaching method, and their surface was modified by diazonium chemistry⁴. After generating an amino-rich layer, phosphonate groups were introduced by adding 2-aminoethylphosphonic acid (AEPa). To achieve a homogenous modification on the outer and inner scaffold surfaces, some samples were treated under vacuum conditions. Surface composition of the scaffolds was characterized by X-ray photoelectron spectroscopy (XPS) to confirm successful grafting of phosphonate groups. To see the effect of surface modifications, treated scaffolds were immersed in simulated body fluid solution (SBF) and characterized with XPS, Raman and FT-IR spectroscopy. Gel permeation chromatography (GPC) were also performed to check if diazonium treatment had an effect on degradation of PDLLA scaffolds.

Results: XPS showed that scaffolds treated with our method contained both N and P on their surface, and that the amount grafted was controllable by simply changing the functionalization time (compare “2 h treated” and “1 h treated” samples in Table 1). Using a vacuum

impregnation technique, we achieved homogeneous modification both on the inner and outer surfaces of the scaffolds (Table 1). The GPC results shows that the acidic conditions of the reaction solution did not cause degradation and changes in the polymer structure.

Table 1. XPS survey data measured on scaffolds functionalized with different methods. Standard deviations are calculated based on 10 points.

Modification	Surfaces	Element (%)	
		N	P
1h treated	Outer	1.6±0.28	0.65±0.18
	Inner	-	-
2h treated	Outer	3.4±0.22	1.3±0.14
	Inner	1.4±0.21	0.3±0.16
2h vacuum treated	Outer	4.1±0.23	1.1±0.21
	Inner	2.5±0.22	1±0.10

After immersion in SBF, larger and more abundant agglomerates were observed on the treated scaffolds (Figure 1). XPS analysis showed that these aggregates were composed of Ca and P, and more Ca and P were present on the surface of the treated scaffolds compared to non treated scaffolds. Raman and FT-IR spectroscopy revealed that the Ca/P precipitates were HA.

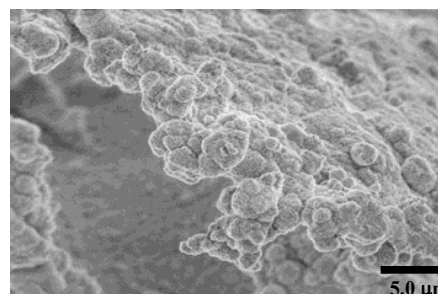


Figure 1. SEM images of and 2 h vacuum treated scaffolds immersed in SBF for two 4 weeks.

Conclusions: we have shown that PDLLA scaffolds can be easily and effectively modified with diazonium chemistry without degrading their polymeric structure. We successfully bound phosphonate groups, and showed that these enhanced nucleation and growth of HA particles on the surfaces of PDLLA scaffolds after immersion in SBF. The simplicity of diazonium chemistry, capability of bind various functional groups and the fact that PDLLA is not degraded during the treatment makes this method an ideal candidate to modify scaffolds for a variety of biomedical applications.

References:

- (1) Liu, X. H. *Ann. Biomed. Eng.*; **2004**, 32, 477.
- (2) Combellas, C. *Chem. Mater.*; **2005**, 17, 3968.
- (3) Zhang, R. Y. *Macromo. Biosci.*; **2004**, 4, 100.
- (4) Mahjoubi, H. *Chem. Mater.*; Submitted.