FROM MICRO TO NANO BIPHASIC CALCIUMPHOSPHATE/POLY-DL-LACTIDE-CO-GLYCOLIDE COMPOSITE BIOMATERIALS FOR HARD TISSUE RECONSTRUCTION

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PITTCON CONFERENCE & EXPO 2007

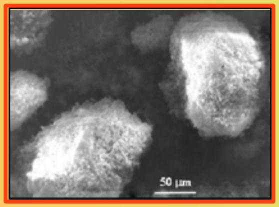
INTRODUCTION

Composite biomaterials have enormous potential for natural bone tissue reparation, filling and augmentation [1]. Ceramics/polymer composites play a significant role in these reparations, as their properties are very close to the natural bone tissue [2-4]. Calcium phosphate/poly-DL-lactide-co-glycolide (CP/DLPLG) composite biomaterials belong to this group of composites and due to their osteoconductive and biocompatible properties they can be successfully implemented in bone tissue reparation [5-7].

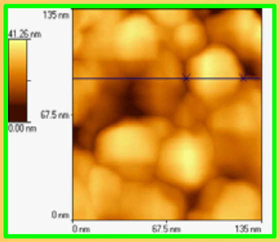
This paper shows possibilities of synthesizing CP/ DLPLG composite biomaterials formed as powders. CP/DLPLG composite biomaterial was produced in the form of spherical micro and nano granules. Each CP micro granule or nanoparticle was coated with amorphous DLPLG polymer.

MATERIALS AND METHODS

The influence of the processing technique on the structure and characteristics of the composite biomaterial was studied by X-ray diffraction analysis (XRD), differential scanning calorimetry (DSC), scanning electronic microscopy (SEM), atomic force microscopy (AFM). *In vitro* and *in vivo* research was used as the bases for the clinical application of the composite. Preliminary clinical research was done on women and man aged from 28 to 57 years.



b) 2D AFM image of nano CP/DLPLG



a) SEM image of micro CP/DLPLG

Figure 1. Microstructure of CP/DLPLG composite biomaterials

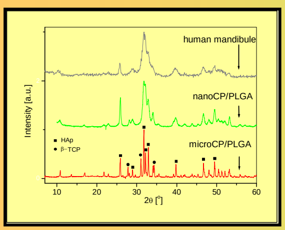
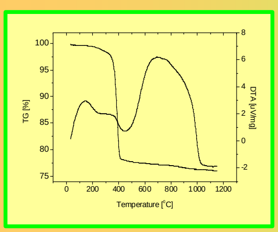
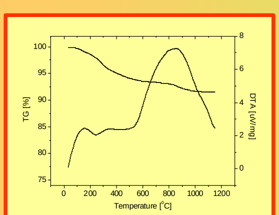


Figure 2. XRD analysis of CP/DLPLG and human bone

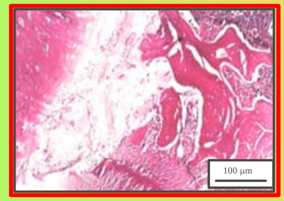


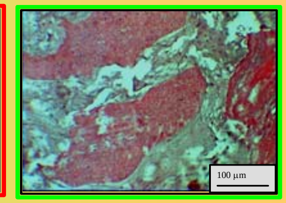
b) TGA/DTA curve of nanoCP/DLPLG



a) TGA/DTA curve of micro CP/DLPLG

Figure 3. Thermal analysis of composite biomaterials





a) micro CP/DLPLG b) nano CP/DLPLG

Figure 5. Histological preparation after 6 weeks of implantation

Table 1. Values of relative optical densities and alveolar ridge heights in the region of premolars

Variable	Control side of jaw (B)	Experimental side of jaw (A)	
		6 weeks after implanting	24 weeks after implanting
Number of patients	30	30	30
Relative optic density (g/cm^2) *	1.078 ± 0.144	0.865 ± 0.011	1.263 ± 0.150
Height of alveolar bone (cm)*	2.60 ± 0.16	2.52 ± 0.14	2.91 ± 0.19

RESULTS AND DISCUSSION

Figure 1a shows the morphology of CP/DLPLG composite biomaterial. Each CP particle was coated with DLPLG and the average particle diameter was between 150 and 200 µm. This composite was labeled micro CP/DLPLG because of the size range in which the particles fell. Using CP gel, spherical granules of CP/DLPLG composite biomaterial, 40 - 50 nm in diameter, were also obtained (Fig 1b). Based on average diameter of particles (1-100 nm), this composite was labeled nano CP/DLPLG. Figure 2 shows the XRD patterns of CP/DLPLG (micro and nano) composite biomaterials and human bone. TGA/DTA and DSC curves of micro and nano CP/DLPLG samples are given in Fig. 3. Figure 4 shows photos obtained during in vitro and in vivo research. Histological preparation after 6 weeks of implantation of micro and nano CP/DLPLG is snown in Fig 5. Rehabilitation of defects in the alveolar bone of maxilla are given in Tab. 1 and Fig. 6.

CONCLUSION

A calcium phosphate/poly-DL-lactide-co-glycolide (CP/DLPLG) composite biomaterial was synthesized by emulsion procedure using solvent non-solvent system. Average diameter of micro composite granules is from 150 to 200 µm, while the spheres of nano composite material are 40 ± 5 nm in diameter.

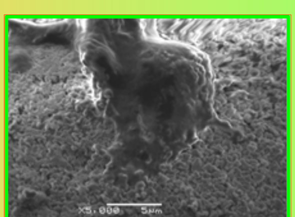
Thermal and XRD analyses confirmed that micro composite consists of well-crystallized biphasic calcium phosphate and nano composite of non-calcined, poorly crystalline calcium phosphate.

In vitro research on cellular cultures showed good adherence of fibroblast cells to the composite biomaterial surface. Nano CP/DLPLG composite showed the higher intensity of osteogenesis followed by regular bone structure formation compared to the micro CP/DLPLG composite.

A significant increase in optical density of alveolar bones in the region of premolars on the experimental side compared with the control one is noticed. These results indicate a high level of osteoregeneration and osteoblast activity.

a) consolidation of the supporting prosthetic tissue b) inserted fixed upper denture

Figure 6. Rehabilitation of defects in the alveolar bone of maxilla (with mikro CP/DLPLG)



a) body of fibroblast (MRC-5) on the surface of micro CP/DLPLG b) on mice

Figure 4. In vitro and in vivo tests

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