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# Bioactive glass-biopolymers-gold nanoparticle based composites for tissue engineering applications

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ABSTRACT

Biomaterials based on bioactive glass with gold nanoparticle composites have many applications in tissue engineering due to their tissue regeneration and angiogenesis capacities. The objectives of the study were to develop new composites using bioactive glass with gold nanospheres (BGAuSP) and gold nanocages (BGAuIND), individually introduced in alginate-pullulan (Alg-Pll) polymer, to evaluate their biocompatibility potential, and to compare the obtained results with those achieved when β-tricalcium phosphate-hydroxyapatite (βTCP/HA) replaced the BG. The novel composites underwent structural and morphological characterization followed by *in vitro* viability testing on fibroblast and osteoblast cell lines. Additionally, the biomaterials were subcutaneously implanted in Sprague Dawley rats, for *in vivo* biocompatibility assessment during 3 separate time frames (14, 30 and 60 days). The biological effects were evaluated by histopathology and immunohistochemistry. The physical characterization revealed the cross-linking between polymers and glasses/ceramics and demonstrated a suitable thermal stability for sterilization processes. The *in vitro* assays demonstrated adequate form, pore size of composites ranging from few micrometers up to 100 μm, while the self-assembled apatite layer formed after simulated body fluid immersion confirmed the composites' bioactivity. Viability assays have highlighted optimal cellular proliferation and *in vitro* biocompatibility for all tested composites. Furthermore, based on the *in vivo* subcutaneous analyses the polymer composites with BGAuNP have shown excellent biocompatibility at 14, 30 and 60 days, exhibiting marked angiogenesis while, tissue proliferation was confirmed by high number of Vimentin positive cells, in comparison with the polymer composite that contains βTCP/HA, which induced an inflammatory response represented by a foreign body reaction. The obtained results suggest promising, innovative, and biocompatible composites with bioactive properties for future soft tissue and bone engineering endeavours.

## 1. Introduction

Novel biomaterials based on bioactive glasses (BG) with metal nanoparticle composites have received much attention in the last few years [1–4]. The focus has been directed to biomedical applications in tissue engineering [5–7]. Gold nanoparticles (AuNPs) are attracting considerable interest due to their supportive effects in growth and proliferation of the living cells, thus solidifying a major role in the regeneration of damaged and diseased tissues [8,9]. As well, significant efforts are made to ensure the biocompatibility and bioactivity of mixed

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