Composites based on Biopolymers-Bioactive Glasses/Glass-ceramics containing Cu and Au for Tissue Engineering Applications

Klára MAGYARI[1,2] and Lucian BAIA*[1,2,3]
[1] *Interdisciplinary Research Institute on Bio-Nano-Sciences, Babeş-Bolyai University, Cluj-Napoca, Romania*
[2] *Institute for Research-Development-Innovation in Applied Natural Sciences, Babeş-Bolyai University, Cluj-Napoca, Romania*
[3] *Faculty of Physics, Babeş-Bolyai University, Cluj-Napoca, Romania*
lucian.baia@ubbcluj.ro

An excellent scaffold should be designed to simulate the natural mechanism of regeneration from the human body, and therefore, to obtain such a scaffold, the following requirements should be fulfilled: excellent bioactivity, good biocompatibility, osteoconductivity, osteoinductivity, simulate angiogenesis, relevant structural-mechanical properties, and biodegradable properties [1]. A promising approach for solving several mentioned issues is the use of composites with polymer, ceramics, metals, cells, and growth factors [2]. Particularly, alginate (Alg) and pullulan (Pll) were widely used as biomaterials for bone tissue engineering [3], while bioactive glasses and glass-ceramics (GC) with gold nanoparticles (AuNPs) were found to stimulate keratinocyte cell proliferation [4]. On the other hand, the use of CuO is justified by the improvement of the cell viability and angiogenesis properties as well as a good antibacterial effect [5].
Taking into consideration above mentioned aspects, our research group developed and investigated a series of novel composites based on a bioactive matrix (i.e., silicate glasses or GC), and biopolymers like Alg, Pll) containing CuO or differently shaped AuNPs by assessing their bioactive, biocompatible, and antibacterial properties. Our first interest was to combine Cu containing bioactive GC-based composites with Alg and Pll natural polymers for the synthesis of new biocompatible hydrogels and their use as support for *in vivo* tissue regeneration with antibacterial properties. In the beginning, it was shown that bioactive GC with relatively small amounts of CuO (*i.e.*, 0.5 and 1.5 mol%) have excellent cell viability and good antibacterial effect against Staphylococcus aureus. Further, evaluating the bone regeneration response of these Alg-Pll-GC composite scaffolds in an experimental long bone defect orthotopically implant it proved a very good in vivo quality, in terms of bone regeneration and osteogenic properties. Other studies demonstrated that Alg-Pll-bioactive glasses with gold nanoparticles (Alg-Pll-BGAuSP) are promising materials for soft and bone engineering endeavors [6]. The composites, including the control sample containing β-tricalcium phosphate-hydroxyapatite (β-TCP/HA), were implanted in bone defect in Wistar rats for 8 weeks, after that the remained materials were recovered. 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 a 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 indicated that the presented composites can be real promising candidates for use in future tissue engineering applications.

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References
1. S. Wu, X. Liu, K.W.K. Yeung, et al., *Mater. Sci. Eng. R Rep*. **2014**, *80*, 1–36.
2. J. Venkatesan, I. Bhatnagar, P. Manivasagan, et al., *Int. J. Biol. Macromol*. **2015**, *72*, 269–281.
3. R.P. Babu, K. O'Connor, R. Seeram, *Prog. Biomater*. **2013**, *2*, 1–16.
4. K. Magyari, T. Nagy-Simon, A. Vulpoi, et al., *Mater. Sci. Eng. C* **2017**, *76*, 752–759.
5. R.A. Popescu, K. Magyari, A. Vulpoi, et al., *Biomater. Sci*. **2016**, *4*, 1252–1265.
6. A. Dreanca, M. Moresan-Pop, M. Taulescu, et al., *Mater. Sci. Eng. C* **2021**, *123*, 112006.