Dextrin-based hydrogel for the development of injectable bone substitute

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The development of injectable bone substitutes (IBS) have garnered great importance in the bone regeneration field, as a strategy to reach areas of the body using minimally invasive procedures, and showing the ability of perfect fitting according to irregularities of bone tissue defects. In this context, the combination of injectable hydrogels and ceramic granules is emerging as a well-established trend. Particularly, *in situ* gelation hydrogels have arisen as a new IBS generation.

An injectable and *in situ* gelation hydrogel (HG) based on dextrin was developed aiming act as a carrier for bone graft granules and biomolecules [1] [2]. Dextrin is a low weight carbohydrate obtained by partial hydrolysis of starch that is already widely used in the cosmetic, textile and food industries. Furthermore, it is biocompatible, non-immunogenic and biodegradable, which renders dextrin a promising polymer for biomedical applications such as scaffolds and/or drug delivery systems.

To prepare the HG, dextrin was firstly oxidized with sodium periodate ($NaIO_4$) and then cross-linked with adipic acid dihydrazide, a non-toxic cross-linking molecule. Since HG will be a vehicle for medical application, a sterilization protocol for oxidized dextrin (ODEX) by gamma radiation was investigated, as well as, the effect of partial periodate oxidation effect on dextrin structure (oxidized derivatives), using mass spectrometry-based techniques. The results showed that gamma irradiation did not promote changes on the chemical structure of ODEX, and, so that, can be used as suitable terminal sterilization method for ODEX. *In vitro* cito- and genotoxicity assays performed in human lymphoblastoid TK6 cells revealed that HG displayed cytotoxicity depending on concentration, due to ODEX, but did not promote DNA damage. *In vivo* skin sentitization test showed that HG is not allergic.

The HG combined with commercial ceramic granules (macroporous Bonelike®, 250-500 μm) was tested in pre-clinical trials using a goat model, in two different bone defects: critical-sized calvarial defect (14 mm) and segmental tibial fracture (4 mm). The HG allowed the proper cohesion between the granules on the formulation and, also guaranteed mixture injectability. One the other hand, HG was able to stabilize *in situ* granules into the bone defects during tested periods (3-12 weeks) without affecting Bonelike® granules' osteoconductive properties neither impairing the bone repair/regeneration process.

References

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