ABSTRACT

THE EFFECT of GLUTARALDEHYDE as A CROSS-LINKING AGENT OF GENTAMICIN with GELATIN to THE EFFECTIVE IMPROVEMENT of BOVINE HYDROXYAPATITE - GELATIN for DRUG DELIVERY SYSTEMS and BONE FILLERS

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Background: *Bovine hydroxyapatite* and gelatin (BHA-GEL) composite were used as bone filler and a biodegradable drug delivery system (DDS) for the administration of gentamicin sulfate (GEN) in prevention and treatment infection of bone defects, were synthesized. The materials, which ovoid bone infection, are exclusively composed of gentamicin sulfate; bioactive *bovine hydroxyapatite* and gelatin were manufacture as pellet of the mixed components.

Methods: The pellets were characterized in vitro and in vivo. *Cross-linking* reaction was required to control the water penetration, swelling and release of gentamicin from the pellet. In vitro characterization with porosity, water absorption, swelling, SEM, MTT assay and gentamicin release from the pellet at conditions of pH and temperature body were studied for 4 weeks. In vivo characterization with implantation the pellet in rabbit femur for 2, 7, 14, 21, 28 days and GEN penetration to bone was evaluated.

Results: The charactererized in vitro that the BHA-GEL-GEN *cross-linking* with glutaraldehyde (GA) were porosity, water absorbtion and swelling smaller than *non cross-link* implan and nontoxic to human osteoblasts and promote their proliferation > 60%, and it was able to control release GEN above MIC which inhibit *Staphylococcus aureus* (ATCC 5923) growth for 28 days. After implanting the pellet into rabbit femur, we studied GEN penetration to bone, determining the concentration in proximal Css = 23.15 ±5.69 µg/ml at second day and distal bone 24.03 ±0.87 µg/ml at 28th day as function of time and bone growth as a consequence of the pellet reactivity in biological environment.

Conclusions: That BHA-GEL-GEN with GA non-toxic and cell-friendly are promising biomaterial of significantly prolonged antibacterial activity where they showed good carriers for local gentamicin release into the local osseous tissue; excellent biocompatibility and bone integration and promote bone growth during the resorption process.

Keywords: *bovine hydroxyapatite*; gelatin; gentamicin; *cross-link agent* glutaraldehyde; drug delivery system for bone defect; bone filler, biodegradable.