Ain Shams University
Women's College for Arts,
Science and Education
Zoology Department

Safety Evaluation of Some Polymers, Reinforced by Bioglass to Enhance Bone Regeneration in Albino Rats.

PhD Thesis

Doctor of Philosophy in Science

(Zoology)

By

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Karam Eldesoqi

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Dedication

I dedicate this work to GOD, my dear mother, father and wife who encouraged me during this work; I will not forget their continuous support.

Abstract

Bone grafts are performed to enhance healing of spine fusions and fractures and to regenerate bone in osseous defects and malformations. Bone tissue engineering provides a promising therapeutic option to improve the local bone healing response.

In the present study the possibility of using composite materials consisting of polymer [poly (L-lactide) (PLLA)] and bioglass (particles sizes 125 – 106 µm) as scaffold was investigated, Also loaded scaffolds with undifferentiated or differentiated Mesenchymal stem cells (MSCs) and Endothelial progenitor cells (EPCs) in bone tissue engineering.

Bioglass and PLLA were mixed for the prepration of bioglass scaffolds: PLA, BG 20% and BG 40%; (0, 20 and 40 %wt bioglass respectively). The scaffolds were in the form of disc shape 5 mm diameter and 1 mm thickness.

80 Adult male albino (Sprague Dawely Strain) rats weighing approximately 350-450g, were used and distributed in 11 groups; Control group; Negative control (defect) group; 3 groups were implanted only with PLA , BG 20 and BG 40 scaffolds; another three groups were implanted with PLA , BG 20 and BG 40 Scaffolds loaded with mesenchymal stem cells (MSCs) and endothelial progenitor cells (EPCs); The last 3 groups were implanted with PLA , BG 20 and BG 40 scaffolds were loaded with differentiated mesenchymal stem cells (MSCs) and endothelial progenitor cells (EPCs).

Osteoconductive properties of implanted specimens were evaluated by using the Skull Critical Size defect (CSD) model, 6 mm diameter, for 14 weeks. After sacrification cranium were removed for Micro CT analysis, histological (H&E) and histomorphometrical evaluation.

The area of new bone formation increased by increasing the percent of bioglass in the scaffold. This might be due to the release of calcium and silica ions which played an important role in the bone healing process.

EPCs and MSCs showed synergetic effect using bioglass scaffold by two mechanisms: EPCs increased micro vessel infiltration

which lead to increase of blood supply and oxygen to forming new bone tissue, also MSCs were differentiated and proliferated to osteocytes, which accelerate new bone tissue formation, especially when MSCs were predifferentiated to differentiated MSCs before loading the scaffold.

No behavioral changes or visible signs of physical impairment or neurological toxicity were observed during the 14 weeks observation period. The macroscopic analysis of the implant sites demonstrated a comparable scar formation and subsequent healing process in all groups. Serum NO_2, Leukocyte count, body temperature were determined with no systemic inflammation.

Liver (ALT, AST& ALP) and kidney (Urea & Creatinine) functions analysis showed no toxic effect. Occurrence of tumors was assessed macroscopically and histologically in slides of liver, kidney and spleen. Furthermore, the concentrations of malondialdehyde (MDA), sodium oxide dismutase (SOD) and total glutathione (GSH) concentration in the serum were used as indicators of free radicals activity. Previous analysis showed no organ damage, no systemic inflammatory reactions were assessed and no free radicals liberation.

In conclusion, Bioglass (particles sizes 125–106 µm), as scaffold, supports the bone formation and further enhanced in presence of EPC and MSC and more with d.MSCs. Bioglass scaffolds showed a good biocompatibility in *vitro* and in *vivo*, also didn't liberate free radicals. Furthermore additional EPC and MSC seeded onto the scaffold did not show side effects in vivo.

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