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In Vitro and in Vivo Evaluation of Vascular Endothelial Growth Factor Loaded Poly (Lactic-co-Glycolic Acid) Microspheres

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Objective: The aim of this study was to control the release of vascular endothelial growth factor (VEGF) from VEGF loaded Poly (lactic-co-glycolic acid) (PLGA) microspheres and produce nerve graft prefabrication.

Methods: VEGF was encapsulated into PLGA microspheres using a water-in-oil-in-water emulsification method. The size and the surface morphology studies were done and also in vitro release properties were assessed with the enzyme linked immunosorbent assay (ELISA). For the evaluation of the cytotoxicity of the formulations and proliferation effect of VEGF, the tetrazolium dye assay was performed.

In in vivo studies, epineural window was opened at the distal side of the siatical nerve trification and three separate groups were created. The amount of VEGF in blood was determined by ELISA and walking track for rats were done. The number and the average diameter of myelinated fibers were determined. The structure of axon and myelin sheath were examined by TEM analysis.

Results: The microspheres were found to be spherical with particle size ranges of 8 - 159 µm and controlled release of VEGF was achieved during a 30 days period. The formulations were non-cytotoxic making cell proliferation.

There were many myelinated fibers with large diameters in the partial incision and controlled release groups. Thereby, prefabrication was carried out for these groups. It was demonstrated that nerve graft can be prefabricated by the controlled delivery of VEGF.

Conclusion: VEGF loaded PLGA microspheres were successfully prepared and nerve graft can be prefabricated by the controlled delivery of VEGF without donor site morbidity for repairing segmental nerve defects.

Key words: Controlled release, microsphere, nerve graft prefabrication, PLGA, VEGF