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## **ENCAPSULATION OF LOCAL ANESTHETIC BUPIVACAINE IN BIODEGRADABLE PLGA NANOSPHERES: FACTORIAL DESIGN, CHARACTERIZATION AND CYTOTOXICITY STUDIES**

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Local anesthetics (LA) are able to induce pain relief by binding to the sodium channel of excitable membranes, blocking the influx of sodium ions and the propagation of the nervous impulse. Bupivacaine is an amide type local anesthetic widely used in surgery and obstetrics for sustained peripheral and central nerve blockade. The present work focuses on the preparation and characterization of nanospheres formulations containing BVC. To achieve these goals, BVC loaded poly(D,L-lactide-co-glycolide) nanospheres (PLGA-NS) were prepared by nanoprecipitation method and characterized. The full factorial experimental design was used to study the influence of four different independent variables on response of nanoparticle drug loading. BVC was assayed by HPLC, the particle size and zeta potential were determined using a Zetasizer. Free BVC was determined using a combined ultrafiltration-centrifugation technique. The results of optimized formulations showed a narrow size distribution with a polydispersity index of 0.05%, an average diameters of  $236.7 \pm 2.6$  nm and the zeta potential of  $-12,93 \pm 1,10$  mV. Toxicity studies with fibroblast 3T3 cells, BVC loaded-PLGA-NS increased cell viability, in comparison to the effect produced by free BVC. In this way, BVC-loaded PLGA-NS decreased BVC toxicity. This study is fundamental to characterize a potentially novel pharmaceutical form for the treatment of pain. (Supported by Fapesp Brazilian funding agency, Proc. 06/00121-9, 07/0127-9).