ISSN 0102-6593

caderno de farmácia

Órgão Oficial da Faculdade de Farmácia da Universidade Federal do Rio Grande do Sul
volume 26, Suplemento, 2010

DEVELOPMENT OF NANOSTRUCTURED SYSTEMS CONTAINING TACROLIMUS AS POTENTIAL FORMULATION FOR ORAL AND TOPICAL ADMINISTRATION

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Introduction: Tacrolimus (TAC) is an immunosuppressive agent that has been isolated from the fermentation broth of *Streptomyces tsukubaensis*. It is used as a potent immunosuppressant in transplantation medicine to prevent or reverse organ rejection such as heart, pancreas, bone marrow, small bowel and lung. It is also used in topical preparation for the treatment of atopic dermatitis, vitiligo and psoriasis.[1] After oral administration, absorption and bioavailability of TAC is highly variable, furthermore this drug causes side effects such as nephrotoxicity, neurotoxicity, hypertension, and diabetogenic effects, being the major causes of treatment interruption.[2] Over the last years many efforts have been made not only to improve the efficacy and bioavailability of drugs but also to reduce their adverse effects by means of the development of novel drug carrier systems polymeric nanocapsules.[3]

Objectives: The aim of this work is to develop lipid-core nanocapsules containing TAC, considering its immunosuppressive activity and the potential of nanostructures to increase the bioavailability after oral administration, to improve the cutaneous distribution of the drug and to reduce toxic effects.

Materials and Methods: Nanocapsule suspensions were prepared by the interfacial deposition of preformed polymer method using polycaprolactone as the biodegradable polymer and caprylic/capric triglyceride mixture and sorbitan monoestearat as the oil core. The formulations were characterized by means of drug content by high performance liquid chromatography (HPLC), mean size, pH and polydispersity.

Results: The formulations were obtained at TAC concentration of 1.00 $mg.ml^{-1}$, showing mean size of 376 ± 0.025 nm, pH of 5.9 ± 0.11 and SPAN values lower than 2. Validation of the HPLC assay demonstrated that this method was linear (r = 0.9993) in the range of 15 to 120 $\mu g.ml^{-1}$, precise (RSD: 0.48 % for repeatability and < 2.5 % for intermediate precision), and accurate. The specificity was tested in the presence of the adjuvant raw materials. The method is specific for TAC assay.

Conclusions: The results showed the technological feasibility to obtain tacrolimus-loaded lipid-core nanocapsules at a concentration of 1.0 $mg.ml^{-1}$ with narrow size distribution and average diameters in the nanometric range. Studies are in progress aiming a broader physical-chemical characterization of the formulations and their subsequent biological evaluation.

References:

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Acknowldgements: R.B.F thanks CAPES/Brazil for her fellowship. The authors thank CNPq/MCT, PRONEX-CNPq/FAPERGS and Universal CNPq.