TITLE: INTRANASAL THERAPEUTIC VACCINE FOR P10 PEPTIDE COMPLEXED WITHIN POLYMERIC NANOPARTICLES FOR THE TREATMENT OF PARACOCCIDIOIDOMYCOSIS IN MURINE MODEL.

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ABSTRACT:

Paracoccidioidomycosis (PCM) is a fungal infection caused by the dimorphic fungus *Paracoccidioides spp*. affecting mainly the lungs and also found in a systemic form. The main drugs for the treatment of PCM are polyenes, sulfanilamide and azole antifungal drugs. Another alternative to treat or prevent PCM is the use of vaccines for the elicitation of a Th1 type immune response, by producing IFN-gamma, important cytokine for the control of the disease. One of the most studied vaccine candidates is a P10 peptide-based vaccine, consisting of 15-mer amino acids, derived from the 43-kDa glycoprotein of *P. brasiliensis*. Although P10-based strategies for vaccination have been promising; however, short lifetime impairs its effectiveness due to premature degradation once inside the body by peptidases. An interesting alternative to overcome this problem is by its complexation within nanoparticles, because of their protective and stability characteristics. In addition, some nanoparticles have the capability of positively modulate the immune system. The main goal of this work was the production of a vaccine based on nanostructured particle complexed with P10 peptide. The technique used to prepare the nanoparticles containing P10 was the technique of ionic gelation. The physic-chemical characteristics of the complexes were evaluated by the measure of hydrodynamic size, polydispersity index, Zeta potential and peptide release from nanoparticles liberation assay. Hemolysis and MTT assays was also performed to evaluate cytotoxicity. The nanoparticles showed a hydrodynamic size of 220 nm, Zeta potential of + 20 mV, entrapment efficiency higher than 90% and the liberation rate was around 2%, suggesting a good stability for the formulation. Hemolysis and MTT assays indicated no cytotoxicity under a time of 24 hours. The complexation of P10 within nanoparticles showed a great capacity for *in vivo* application, characterized by no cytotoxicity, great size and zeta potential, high efficiency of entrapment and slow release of P10 peptide. With this work, we expect to achieve a high lifetime for P10 by reducing its quickly *in vivo* degradation and reducing its concentration to improve a Th1 response. It is also expect by using the nasal route to deliver the vaccine, a better immune response because of the site of PCM. Moreover, using a mucoadhesive polymer it is expected a delayed contact between the nanoparticles and the respiratory mucosa improving even more the immune response.

Keywords: Paracoccidioidomycosis, nanoparticles, P10, intranasal vaccine.

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