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# DEVELOPMENT OF A SYSTEM OF NANOPARTICLES CONTAINING CHITOSAN AND CHONDROITIN FOR IMPROVING THE TREATMENT OF LEISHMANIASIS

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**Resumo:**
Parenteral administration of pentavalent antimonials remains the first-choice treatment for leishmaniasis, however, the occurrence of side effects such as anorexia, myalgias, arthralgia, chemical pancreatitis, leucopenia, and cardiotoxicity, is an important problem in patients with leishmaniasis. . Amphotericin B (AmpB) has an effective leishmanicidal activity, but its clinical use is limited because of the high toxicity. To improve the therapeutic index of AmpB and reduce its cytotoxicity, lipid-based formulations such as AmpBisome®, AmphocilH® Abelcet® have been developed but, however, their use remains limited because of their high costs. Due to this, the present study aimed to develop, characterize and evaluate the in vitro pharmacokinetic and toxicological profile of a polymeric nanoparticle delivery system containing chitosan (Cs) and chondroitin sulfate (ChS) molecules loaded with AmpB for the improvement of Treatment of leishmaniasis, which presented promising results as efficacy and low toxicity.

**Palavras-chave:**
Nanoparticles, treatment, leishmaniasis.

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**Introdução:**
The parenteral administration of pentavalent antimonials continues to be the first choice to treat leishmaniasis, however, the occurrence of side effects, such as anorexy, myalgias, arthralgias, chemical pancreatitis, leucopenia, and cardiotoxicity, is an important problem registered in the patients. Amphotericin B (AmpB) presents an effective antileishmanial activity, but its clinical use is limited by high toxicity. To improve the therapeutic index of AmpB and to reduce its cytotoxicity, lipid-based formulations have been developed, such as AmpBisome®, AmphocilH® and Abelcet®, however, their use still remain limited due to their high costs. The present study aims to develop an optimized nanoparticle delivery system for AmpB using a polyelectrolyte complexation technique. For this, two opposite charged polymers presenting antileishmanial activity – chitosan (Cs) and chondroitin (ChS) – were used.

**Metodologia:**
Cs was used as a positively charged polymer, and ChS as a negatively charged polymer. The Cs (NQ), Cs-ChS (NQC), and Cs-ChS-AmpB (NQC-AmpB) nanoparticles presented a mean particle size of 79, 104, and 136 nm, respectively; and a polydispersity index (PI) of 0.2. The measured zeta potential of nanoparticles indicated a positive charge in their surface, while the scanning and transmission electron microscopes revealed spherical nanoparticles with a smooth surface. The attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR) analysis showed an electrostatic interaction between the polymers, whereas the release profile of AmpB from NQC-AmpB nanoparticles showed a controlled release.

## Resultados e Discussão:

The composed Cs, ChS, NQ, NQC, and NQC-AmpB nanoparticles proved to be effective against promastigotes of *Leishmania amazonensis* and *L. infantum*, with a synergistic effect observed between Cs and ChS. Moreover, the applied NQ, NQC, and NQC-AmpB compounds presented a low toxicity in murine macrophages, as well as null hemolytic activity in type $O^+$ human red blood cells. Pure AmpB presented a high toxicity in the macrophages. The results showed that cells infected with *L. amazonensis* and later treated with Cs, ChS, NQ, NQC, NQC-AmpB or pure AmpB presented significant reduction in the parasite number in the order of 24%, 31%, 55%, 66%, 90% and89%,respectively.

## Conclusões:

The data presented indicate that the engineered NQC-AmpB nanoparticles could potentially be used as an alternative therapeutic to treat leishmaniasis, mainly due to the low toxicity found in mammals' cells.

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