Synthesis and characterization of a copaiba oil-based nanoformulation for potential therapy against cutaneous leishmaniasis

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Área temática: F. Nanotecnología y salud

Cutaneous leishmaniasis is an endemic vector-borne parasitic disease transmitted by phlebotomine sandflies. It is a neglected tropical disease affecting low-income populations, with up to one million new cases annually. In Latin America, it is prevalent in Brazil, Colombia, Peru, and northern Argentina. It causes ulcerative lesions that may progress to severe forms if untreated. Current treatments are limited by toxicity, poor adherence, and rising parasitic resistance.

In recent years, there has been growing interest in safer natural products whose antileishmanial activity has been reported. Copaiba oil (CO) is an oleoresin extracted from trees of the *Copaifera* genus with demonstrated microbicidal and anti-inflammatory properties. Traditionally used in Amazonian folk medicine, the oleoresin evaluated in the present study was obtained from *Copaifera reticulata* in the Brazilian Amazon region.

In this work, Nanostructured Lipid Carriers (NLCs) were synthesized and characterized. These systems are composed of a combination of solid and liquid lipids, enabling the protection and controlled release of the active compound upon topical application for its skin delivery. The NLCs were prepared by forming an emulsion using Precirol as the solid lipid, copaiba oil as both the liquid lipid and active compound, and Poloxamer 188 as the surfactant. The emulsification process was carried out using an Ultra-Turrax® T18 at 25,000 rpm.

The stability of the formulation was evaluated over time by measuring particle size and zeta potential using Dynamic Light Scattering (DLS) and Electrophoretic Light Scattering (ELS), respectively, yielding an average hydrodynamic diameter of 150 nm and a zeta potential of −30 mV over 30 days. Colloidal stability was further assessed using Turbiscan analysis, showing a Turbiscan Stability Index (TSI) below 1.4 over the same period. Skin penetration capacity was studied using the Saarbrücken Penetration Method followed by both tape stripping analysis and Z-stacking of confocal laser scanning microscopy images, revealing penetration of the formulation into the shallow and medium *stratum corneum*. Morphology was analyzed by electron microscopy. Thermal properties, including melting behavior and crystallinity index, were also analyzed using Differential Scanning Calorimetry (DSC). Finally, a cellular uptake assay was performed. Also, the cytotoxic concentration range was determined, with cytotoxicity observed from 75 µg/mL of the formulation.