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Preparation and characterization of artemether-loaded niosomes in *Leishmania major*-induced cutaneous leishmaniasis

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Cutaneous leishmaniasis is the most prevalent form of leishmaniasis worldwide. Although various anti-leishmanial regimens have been considered, due to the lack of efficacy or occurrence of adverse reactions, design and development of novel topical delivery systems would be essential. This study aimed to prepare artemether (ART)-loaded niosomes and evaluate their anti-leishmanial effects against *Leishmania major*. ART-loaded niosomes were prepared through the thin-film hydration technique and characterized in terms of particle size, zeta potential, morphology, differential scanning calorimetry, drug loading, and drug release. Furthermore, anti-leishmanial effect of the preparation was assessed in vitro and in vivo. The prepared ART-loaded niosomes were spherical with an average diameter of about 100 and 300 nm with high encapsulation efficiencies of > 99%. The results of in vitro cytotoxicity revealed that ART-loaded niosomes had significantly higher anti-leishmanial activity, lower general toxicity, and higher selectivity index (SI). Half-maximal inhibitory concentration (IC50) values of ART, ART-loaded niosomes, and liposomal amphotericin B were 39.09, 15.12, and 20 µg/mL, respectively. Also, according to the in vivo study results, ART-loaded niosomes with an average size of 300 nm showed the highest anti-leishmanial effects in animal studies. ART-loaded niosomes would be promising topical drug delivery system for the management of cutaneous leishmaniasis.

Keywords Artemether, Niosomes, Topical drug delivery, Cutaneous leishmaniasis, *Leishmania major*, Promastigote

Leishmaniasis is an infectious disease caused by protozoan parasites from different species of Leishmania. Leishmaniasis has three main clinical forms including cutaneous leishmaniasis (CL), visceral leishmaniasis (VL), and mucocutaneous leishmaniasis, among which the CL is the most common form[1]. Cutaneous leishmaniasis is mainly caused by *Leishmania tropica*, *Leishmania major*, and *Leishmania aethiopica*[2]. *Leishmania major* (*L. major*) is considered as the most common cause of cutaneous leishmaniasis in the Middle East area[3]. Disease severity can be varied from a self-limited skin lesion (cutaneous leishmaniasis; CL) to lesions spread from the initial skin lesion to the mucosa (mucosal leishmaniasis; ML), or lesions spread through the body uncontrollably (disseminated or diffuse cutaneous leishmaniasis; DCL). DCL causes a potentially fatal systemic disease with multi-organ failure including the spleen, liver, and bone marrow (kala-azar or visceral leishmaniasis; VL)[4,5]. According to the World Health Organization (WHO) reports, 700,000 to 1 million cases of leishmaniasis are diagnosed annually. Moreover, about 200,000 new cases of CL are annually reported to WHO, while since a large number of infected patients usually do not refer to the physician, the real incidence rate is more than 600,000 to 1 million cases annually[6].

The main therapeutic agents in the management of all clinical forms of leishmaniasis are pentavalent antimonial drugs including meglumine antimoniate (Glucantime®) and sodium stibogluconate (Pentostam®)[7], which

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Competing interests

The authors declare no competing interests.

Additional information

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