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Mannosylated Oral Amphotericin B Nanocrystals for Macrophage Targeting: In vitro and Cell Uptake Studies

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Abstract : The aim of the present research was to develop oral Amphotericin B (AmB) nanocrystals (Nc) grafted with suitable ligand in order to enhance drug transport across the intestinal epithelial barrier and subsequently, active uptake by macrophages. AmB Nc were prepared by liquid anti-solvent precipitation technique (LAS). Poloxamer 188 was used to stabilize the prepared AmB Nc and grafted with mannose for actively targeting M cells in Peyer's patches. To prevent shedding of the stabilizer and ligand, N,N'-Dicyclohexylcarbodiimide (DCC) was used as a cross-linker. The prepared AmB Nc were characterized for particle size, PDI, zeta potential, X-ray diffraction (XRD) and surface morphology using scanning electron microscope (SEM) and evaluated for drug content, in vitro drug release and cell uptake studies using caco-2 cells. The particle size of stabilized AmB Nc grafted with WGA was in the range of 287-417 nm with negative zeta potential between -18 to -25 mV. XRD studies revealed crystalline nature of AmB Nc. SEM studies revealed that ungrafted AmB Nc were irregular in shape with rough surface whereas, grafted AmB Nc were found to be rod-shaped with smooth surface. In vitro drug release of AmB Nc was found to be 86% at the end of one hour. Cellular studies revealed higher invasion and uptake of AmB Nc towards caco-2 cell membrane when compared to ungrafted AmB Nc. Our findings emphasize scope on developing oral delivery system for passively targeting M cells in Peyer's patches.

Keywords : leishmaniasis, amphotericin b nanocrystals, macrophage targeting, LAS technique
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