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Tuftsin coated Ampho-NanoLip constructs for improved targeting and enhanced efficacy of leishmaniasis

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Leishmaniasis parasites are one of the intracellular protozoan parasites which reside primarily in host mononuclear phagocytes and usually lethal if untreated. Amphotericin B is a broad antimycotic agent and a highly antiparasitic one having severe nephrotoxicity and hematologic toxicity as the major limiting factors. These side effects led to extensive research in formulations in the form of liposomes, emulsions, lipid and polymeric nanoparticles which reduce the amount of free AmB in blood stream, thereby reducing its toxicity but their non-targetability and higher cost restricts their use to poorest to poor. Among all these colloidal carriers lipid nanoparticles have been extensively explored due to their ideal characteristics of better storage stability and higher drug loading which make it a promising candidate for novel drug delivery owing to its versatile nanotherapeutic applications. The nanoparticles surface was modified with a peptide sequence containing tuftsin. Tuftsin is known to stimulate the immune function of various cells, including macrophages (primarily), neutrophils, and monocytes. Surface modification with tuftsin was investigated on the basis of the fact that this tetrapeptide has been used for macrophage specific targeted delivery. The tuftsin modified nanoparticles could be used for effective delivery of biopharmaceuticals into the macrophages because of better accumulation in macrophage rich organs when compared with other colloidal systems due to their preferential phagocytosis. Therefore, we have developed tuftsin modified novel AmB lipid nanoconstructs. The main objective of this study was to develop and evaluate a new novel formulation of AmB as a cost effective and target oriented alternative. Various formulations were developed with the use of microfluidizer (optimized by varying pressure and number of cycles) and characterized for various parameters (particle size, zeta potential, % entrapment efficiency, morphology, stability, *in vitro* release and toxicity). The entrapment efficiency of AmB was achieved up to 88.4% for AmB-NLC and 83.5.3% for Tft-AmB-NLC with particle size 142±6.2nm and 162.6±4.4nm, and zeta potential of -28±1.6 mv and +32+1.3 mv, respectively. The optimized formulations were found stable for more than 3 months in terms of particle size and size distribution. The morphological characterization of the formulations was done using Transmission Electron Microscopy. The *in vitro* release profile of the AmB-NLC and Tft-AmB-NLC showed 62.6% and 60.2% drug release within 24 hours, respectively. The toxicity profile showed the permissible range of haemolysis and cytotoxicity.

The findings suggested that it would be preferable to deliver AmB through tuftsin anchored nanostructured lipid carriers.

Biography:

I, Priyanka Tripathi, am a full time Ph.D. student in Division of Pharmaceutics, CSIR-Central Drug Research Institute, Lucknow, India. I have passed B. Pharm. in 2006 and M. Pharm. (Pharmaceutics) in 2008 with honours (hold rank in university). I am also a post graduate diploma holder in drug regulatory affairs. I have published total 18 international research papers including 5 papers in first authorship. I have presented 9 oral, 8 poster and attended 5 national/international events. I am active member of AAPS, CRS and secretary of BRG's steering committee. I am CSIR-Senior Research Fellow in Division of Pharmaceutics, CSIR-CDRI, Lucknow, India from 02/04/2012 to till date and worked as Project Assistant Level-II in the same division from 11/06/2010 to 01/04/2012. I have also worked as Assistant Professor at SRNS College of Pharmacy, Gormi, India from 10th June 2006 to 22nd Oct. 2006 and from 30th Sept. 2008 to 24th May 2010.