

Development of Methotrexate Nanostructured Lipid Carriers for Topical Treatment of Psoriasis: Optimization, Evaluation, and in vitro Studies

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Abstract : Methotrexate is effective in controlling recalcitrant psoriasis when administered by the oral or parenteral route long-term. However, the systematic use of this drug may provoke any of a number of side effects, notably hepatotoxic effects. To reduce these effects, clinical studies have been done with topical MTx. It is useful in treating a number of cutaneous conditions, including psoriasis. A major problem in topical administration of MTx currently available in market is that the drug is hydrosoluble and is mostly in the dissociated form at physiological pH. Its capacity for passive diffusion is thus limited. Localization of MTx in effected layers of skin is likely to improve the role of topical dosage form of the drug as a supplementary to oral therapy for treatment of psoriasis. One of the possibilities for increasing the penetration of drugs through the skin is the use of Nanostructured lipid Carriers. The objective of the present study was to formulate and characterize Methotrexate loaded Nanostructured Lipid Carriers (MtxNLCs), to understand in vitro drug release and evaluate the role of the developed gel in the topical treatment of psoriasis. MtxNLCs were prepared by solvent diffusion technique using 3(2) full factorial design. The mean diameter and surface morphology of MtxNLC was evaluated. MtxNLCs were lyophilized and crystallinity of NLC was characterized by Differential Scanning Calorimetry (DSC) and powder X-Ray Diffraction (XRD). The NLCs were incorporated in 1% w/w Carbopol 934 P gel base and in vitro skin deposition studies in Human Cadaver Skin were conducted. The optimized MtxNLCs were spherical in shape, with average particle size of $253(\pm 9.92)\text{nm}$, zeta potential of $-30.4(\pm 0.86)\text{mV}$ and EE of $53.12(\pm 1.54)\%$. DSC and XRD data confirmed the formation of NLCs. Significantly higher deposition of Methotrexate was found in human cadaver skin from MtxNLC gel ($71.52 \pm 1.23\%$) as compared to Mtx plain gel ($54.28 \pm 1.02\%$). Findings of the studies suggest that there is significant improvement in therapeutic index in treatment of psoriasis by MTx-NLCs incorporated gel base developed in this investigation over plain drug gel currently available in the market.

Keywords : methotrexate, psoriasis, NLCs, hepatotoxic effects

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