Abstract

Title: "Formulation and Evaluation of Certain Skeletal Muscle Relaxants in New Dosage Forms"

The purpose of the current study was to develop nanotransfersomes-loaded thermosensitive *in situ* gel for rectal administration of tizanidine HCl, aiming to bypass the hepatic first pass effect with improved bioavailability and sustained release of the drug. Tizanidine HCl-loaded transfersomes were prepared by thin-film hydration method followed by characterization of the prepared vesicles for various parameters such as entrapment efficiency, particle size, *in vitro* release study and *ex vivo* permeation study. Tizanidine HCl-loaded transfersomal formula composed of phosphatidylcholine and tween 80 at a weight ratio of (85:15) gave satisfactory results. It exhibited encapsulation efficiency of 52.39 %, particle size of 150.33 nm, controlled tizanidine release over 8 h and good permeation characteristics. It was then incorporated into pluronic based thermo-reversible *in situ* gel using HPMC as a mucoadhesive polymer. *In situ* gel was further characterized in term of physical parameters, *in vitro* drug release, *ex vivo* permeation study, *in vivo* localization and histopathological evaluation. Finally, pharmacokinetic study of transfersomes-loaded *in situ* gel was performed after its rectal administration to rabbits and compared with rectal tizanidine HCl *in situ* gel

and oral drug solution. The study revealed that the formulation successively enhanced the bioavailability of TIZ by about 2.2 fold and increased the half-life of the drug to about 10 h. It can be concluded that the incorporation of nanotransfersomes into gel vehicle can achieve a dual purpose of prolonged tizanidine HCl release and enhanced bioavailability. Thus, tizanidine HCl transfersomes-loaded *in situ* gel was found to be a promising drug delivery system for the treatment of spasticity.

Keywords: Tizanidine HCl; transfersomes; rectal; *in situ* gelling systems; pharmacokinetics.