Development and Characterization of Tizanidine Hydrochloride Loaded Polymeric Nasal Insert

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Abstract

Muscle spasm is defined as a sudden involuntary contraction of one or more muscle groups and is usually an acute condition associated with muscle strain (partial tear of a muscle) or sprain (partial or complete rupture of a ligament). Tizanidine hydrochloride is centrally acting muscle relaxant believed to act by increasing presynaptic inhibition of spinal motor neurons use in muscle pain. Tizanidine hydrochloride has very low oral bioavailability of 34-40% due to high first pass hepatic metabolism suggests an ideal drug candidate for nasal drug delivery system. The aim of present investigation was to develop and characterize tizanidine hydrochloride loaded polymeric nasal insert. Drug excipients compatibility was determined using Fourier Transform Infra Red Spectroscopic (FTIR). Nasal insert was prepared by lyophilization technique using xanthan gum–guar gum and chitosan-pectin combination. Various ratios of xanthan gum–guar gum and chitosan-pectin were optimized for better characteristics. Nasal insert was characterized for water uptake, bioadhesion potential and drug content. *In vitro* drug release study was performed using cellulose acetate membrane for all batches and goat nasal mucosa for optimized batch. Scanning electron microscopy was performed for nasal insert to evaluate surface porosity. Nasal toxicity study was also performed using goat nasal mucosa to observe cell necrosis and removal of epithelium from the mucosa. Stability was performed at room temperature and accelerated condition. Absence of incompatibility between drug and excipients was observed that confirmed by FTIR. Optimized batch M_9 containing xanthan gum to guar gum weight ratio 9:1 showed good water uptake (1091.5±19.09 %), bioadhesive potential (0mm) and drug content (95.675±6.61). *In vitro* drug release was found to be 98.85±0.73 and 96.58±0.31 up to

six hour using cellulose acetate membrane and goat nasal mucosa respectively. Stability study results indicated that nasal insert stored at room temperature remains stable with almost no change in nasal insert characteristic. Nasal toxicity study indicates no pathological changes in nasal mucosa of goat. The present investigation provides a practical approach used to prevent rapid clearance of tizanidine hydrochloride from the nasal mucosa. Mucoadhesive polymer may improve residence time of drug on mucosa. So more drug can absorb through nasal mucosa leads to higher bioavailability of drug via nasal route. Developed nasal insert of tizanidine hydrochloride may be useful for unconscious patient for relief in post-operative pain because these patients are unable to take medicine via oral route

***Keywords*:** Tizanidine Hydrochloride; Muscle pain; water uptake; chitosan; pectin; xanthan gum; guar gum