Lamotrigine loaded solid lipid microparticles: preparation, formulation and in vitro characterization

S. Mohammad Samani*, F. Ahmadi, F. Jalali

Department of pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Background and Aims: Lamotrigine (LTG) is an antiepileptic drug which shows regeneration effect on nerve injuries. This research aims at designing an optimized formulation of solid lipid microparticles (SLMs) containing LTG to achieve an injectable controlled release system.

Methods: The method of preparation was melt dispersion. 50 mg LTG was dispersed in 500 mg melted lipid mixture (stearic acid and cholesterol) which followed by adding hot (80-90°C) aqueous solution of Tween 80 under drive mixer. Finally, all formulations were rapidly cooled under stirring. By experimental design, the effect of different cholesterol percentages (0, 20 and 40 % w/w of lipid mixture), surfactant percentages (0.5%, 1% and 1.5% w/v) and duration of mixing (2, 5 and 10 min) were studied. To study the effect of cholesterol on entrapment efficiency and release behavior, three levels of cholesterol (0%, 20% and 40% w/w of lipid mixture) were selected. The release medium consisted of 10% V/V ethanol in PBS. To evaluate the effect of freeze drying on size distribution, three cryoprotectants (mannitol, lactose and trehalose) in three levels (25%, 50% and 100% w/w) were used. Morphology, stability and DSC analysis of SLMs were performed.

Results: Higher levels of Tween 80 provided smaller SLMs. Formulation containing 40%w/w cholesterol released the drug faster than two others while SLMs containing no cholesterol released drug in a slower manner than others. Increasing amount of cholesterol resulted in decreasing size distribution. The formulation containing 20% w/w cholesterol showed the highest entrapment efficiency. SLMs containing mannitol as cryoprotectant (100% w/w of SLMs) presented higher stability in freeze drying and showed lower change in size distribution.

Conclusions: Cholesterol fastened the release of LTG and provided smaller SLMs and surfactant percentage was the most important factor on size distribution. Using cryoprotectant for lyophilization of SLMs made them stable in drying process especially in higher amounts.

Keywords: Lamotrigine; Solid lipid microparticles; Lyophilization