In vitro and in vivo evaluation of self-nanoemulsifying drug delivery systems of cilostazol for oral and parenteral administration

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Abstract

The current investigation was aimed to improve the solubility of poorly soluble drug, cilostazol (CLZ). Self-nanoemulsifying drug delivery system (SNEDDS) composed of oil, surfactant and co-surfactant for both oral and parenteral administration of CLZ was formulated. The components for SNEDDS were identified by solubility studies, and pseudo-ternary phase diagrams were plotted to identify the efficient self-emulsification regions. The optimum formula, composed of Capryol 90 as an oil phase, Cremophor EL as a surfactant, and Transcutol HP as a co-surfactant in a ratio of 19.8:30.5:49.7 by weight, was able to solubilize CLZ 2000 times higher than its solubility in water. This formula was able to form grade "A" nanoemulsion when diluted with water, resulted in emulsification time of 50 ± 1.1 s, particle size of 14.3 nm, PDI of 0.5 and % transmittance was 97.40% ± 0.65. It showed excellent in vitro dissolution of 93.1% and 81.5% after 5 min in 0.3% sodium lauryl sulphate solution and phosphate buffer pH 6.4, respectively when compared with the marketed tablet formulation and drug suspension as the tablets showed only 44.3% and 9.9% while CLZ suspension showed 33.9% and 8.8% in 0.3% sodium lauryl sulphate solution and phosphate buffer pH 6.4, respectively. It was found to be robust to dilution, thermodynamically stable with low viscosity values of 14.20 ± 0.35 cP. Invivo study revealed significant increase in bioavailability of CLZ in rabbits to 3.94 fold compared with the marketed tablet formulation after oral administration. This formula could be sterilized by autoclaving and did not cause significant hemolysis to human blood which indicates its safety for intravenous administration with a 1.12 fold increase in bioavailability compared with its oral administration. Our study illustrated the potential use of SNEDDS of poorly soluble CLZ orally, and its successful administration of parenterally when required in acute cases of myocardial and cerebral infarction.

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