Olmesartan Medoxomil-Loaded Self-Nanoemulsifying Drug Delivery Systems: Design, In-Vitro Characterization, and Pharmacokinetic Assessments in Rabbits Via LC-MS/MS

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Abstract

Olmesartan medoxomil (OLM) is a lipophilic (log P = 4.31) antihypertensive drug suffering from limited oral bioavailability in humans (26%) due to its low aqueous solubility, uncontrolled enzymatic conversion to the active metabolite (olmesartan; OL) and efflux by drug resistance pumps. Surmounting such limitations via incorporation of OLM into self-nanoemulsifying drug delivery systems (SNEDDS). Based on OLM-equilibrium solubility studies in various oils, surfactants and co-surfactants, Capmul® MCM, Tween® 20, Cremophor® EL and polyethylene glycol-400 (PEG) were combined in different ratios to plot ternary phase diagrams. OLM-loaded SENDDS were developed and evaluated for particle size, polydispersity index (PDI), zeta potential, self-emulsification time, morphology, drug released percentages after 5-min (Q5min%), 1-hour (Q1h%) and dissolution efficiency percentages (DE1h%). The OL pharmacokinetics from SNEDDS (F6) and Benicar® tablets were evaluated (LC-MS/MS) in rabbits. Spherical OLM-loaded SNEDDS were developed. The best-achieved SNEDDS (F6) showed short emulsification time (13 s), fine droplet size (60.00 nm), low PDI (0.25), negative zeta potential (-14.4 mV), promising dissolution parameters; Q5min% (29.78%), Q1h% (66.69%) and DE1h% (47.96%) and enhanced in vivo absorption characteristics; shorter Tmax, higher Cmax and larger AUC(0−48h; suggesting its potential for the enhancement of the oral absorption of practically insoluble drugs; like OLM.

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