Development, characterization and comparative *in vitro* evaluation of Iloperidone solid self microemulsifying delivery system and liquisolid compacts for improved oral delivery.

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Abstract:

Iloperidone (ILO), an atypical anti-psychotic drug used to treat schizophrenia. It is a BCS class II drug with low oral bioavailability (36%) due to poor aqueous solubility. The purpose of this study is to develop and compare the relative performance of solid self microemulsifying drug delivery system (SMEDDS) and liquisolid compacts (LSC) of ILO for improved oral delivery. Solubility studies were performed to select Oil, Surfactant and Cosurfactant which showed more solubility of ILO. Capmul MCM, Labrafac WL 1349 were selected as oils, Lauroglycol 90 and PEG 600 were selected as surfactant and cosurfactant respectively. Pseudoternary phase diagrams were plotted. Here, both oils containing Smix (1:1 ratio) of surfactant and cosurfactant showed more emulsion zone when compared to that of Smix (2:1 ratio). Liquid SMEDDS (A1) containing Capmul MCM (15%) with Smix ratio 1:1 resulted in globules having the average size of 133.2 ± 4.34 nm, PDI of 0.183 ± 0.09 and ZP of -20.4 ± 1.17 mV respectively. LSC of ILO were prepared using PEG 600 as non volatile solvent to solubilize the drug. The optimized formulations were adsorbed on to different carriers like Syloid 244 FP, Syloid XDP and Mannitol. Syloid XDP carrier was optimized for smedds (A1X1), and Syloid XDP carrier and coating material (Aerosil 200) in 15:1 ratio was optimized for liquisolid compacts (S3). The optimized solid smedds (A1X1) resulted in globules having size, PDI, and ZP of 145.3± 1.30 nm, 0.225 ± 0.01, -19.6 ± 0.96 mV respectively. Drug content of the optimized solid smedds and liquisolid compacts (S3) were 97.76% ± 0.58 and 97.30% ± 0.90 respectively. Dissolution studies for solid smedds (A1X1), liquisolid compacts (S3), and pure drug were performed using USP type II dissolution apparatus using size 00 capsules. The pure drug release was 45.49% ± 0.26 at 120 min, where as the solid smedds and liquisolid compacts showed 95.70% ± 0.29 and 93.78% ± 0.65 release respectively at 30 min. Differential Scanning Calorimetry (DSC) of pure ILO drug was performed and a sharp endothermic peak was found at 126.88 ºC. Scanning Electron Microscopy (SEM) and Powder X-ray Diffractometry (PXRD) studies were conducted for pure drug, optimized solid SMEDDS, LSC, Syloid XDP and Aerosil 200 and the results showed the drug has lost its crystallinity in both solid SMEDDS and liquisolid formulations. This resulted in the rapid drug release from both solid SMEDDS and liquisolid compacts. Powder flow characteristics were done for solid SMEDDS and liquisolid compacts and resulted in an average angle of repose value of 28.6 ± 0.72 and 24.3 ±0.10 respectively. Taken together, no significant difference was observed in the drug release profiles and flow characteristics of the two developed systems.

Keywords: Iloperidone, Bioavailability, SMEDDS, Liquisolid compacts, Crystallinity.