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Dermal Flurbiprofen Nanosuspensions: Optimization with Design of Experiment approach and *in vitro* evaluation

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Abstract

Flurbiprofen (FB) is the one of the non-steroidal anti-inflammatory drugs (NSAIDs) which has low water solubility and dissolution. Nanosuspensions are promising drug delivery systems consisting pure drug particles to overcome poor water solubility issues. Recently, Design of Experiment (DoE) approaches have often been used to develop new formulations include nanosuspensions. The main objective of this study was to prepare FB nanosuspensions in existence of Plantacare 2000 (PL) as stabilizer using DoE approach to evaluate the critical formulation attributes (CFAs) and critical process parameters (CPPs). Particle size, particle size distribution and zeta potential values were selected as dependent variables and FB%, FB: PL and homogenization cycles were independent variables. Both 2^3 and 3^3 factorial designs were used to achieve optimum nanosuspension formulation. The final nanosuspension was freeze-dried and then crystalline state, morphological and thermal properties were investigated using X-ray diffraction, scanning electron microscopy and differential scanning calorimetry, respectively. The saturation solubility studies of nanosuspensions were conducted in comparison with the coarse powder and the physical mixture. The *in vitro* permeation of nanosuspension and FB solution were determined through dialysis membran and rat skin. The particle size, polydispersity index and zeta potential values were found to range 665 nm- 700 nm, 0.200- 0.300 and approximately -30 mV, respectively. Nanosuspensions were obtained with spherical shape and no polymorphic or crystalline state change were observed. The saturation solubility of FB was 5.3 fold increased in nanosuspension formulation. Permeability of FB nanosuspension was higher than FB solution in rat skin. It was concluded that the DoE approach is a useful tool to prepare FB