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EFAVIRENZ DISSOLUTION ENHANCEMENT III: COLLOID MILLING, PHARMACOKINETICS AND ELECTRONIC TONGUE EVALUATION

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Abstract

Efavirenz (EFV), a non-nucleoside reverse transcriptase inhibitor (NNRTI), is part of first-line therapy for the treatment of human immunodeficiency virus type 1 infection (HIV-1/AIDS). This drug shows relatively low oral absorption and bioavailability, as well as high intra- and inter-subject variability. Several studies have shown that treatment failure and adverse effects are associated with low and high EFV plasma concentrations, respectively. Some studies suggest different EFV formulations to minimize inter-patient variability and improve its solubility and dissolution; however, all of these formulations are complex, using for instance, cyclodextrins, dendrimers and polymeric nanoparticles, rendering them inviable industrially. The aim of this work was to prepare simple and low-cost suspensions of EFV for improvement of solubility and dissolution rate by using colloid mill, spray or freeze-drying, and characterization of the powders obtained. The results demonstrated an increase in the dissolution rate of EFV, using 0.2% of sodium lauryl sulfate (SLS) and 0.2% of hydroxypropylcellulose (HPC) or hydroxypropylmetilcellulose (HPMC) in both freeze and spray dried powders. The pharmacokinetic studies demonstrated improved pharmacokinetic parameters for the formulation containing SLS and HPC. The powders obtained, which present enhanced dissolution properties, can be incorporated in a solid dosage form for treatment of AIDS in paediatric patients with promising results.

Keywords: Efavirenz, dissolution, bioavailability, colloid milling, drying, electronic tongue.

Abbreviations: EFV, efavirenz; NNRTI, non-nucleoside reverse transcriptase inhibitor; HIV-1/AIDS, human immunodeficiency virus type 1 infection; SLS, sodium lauryl sulfate; HPC, hydroxypropylcellulose; HPMC, hydroxypropylmetilcellulose; NRTIs, nucleoside reverse transcriptase inhibitors; API, active pharmaceutical ingredient; CD. Cyclodextrin; FDA, Food and Drug Administration; AUC, area under the curve