Dissolution Behavior of the Poorly Soluble Weak Acid Drug Valsartan upon Entry in the Small Intestine

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Abstract

The objective of this study was to investigate the transfer behavior of the weakly acidic BCS class II model drug valsartan from the stomach to the small intestine during fasted and fed states. An in vitro transfer model previously introduced by Kostewicz and coworkers based on a syringe pump and a USP paddle apparatus was used to obtain the concentration profiles of the weak acid valsartan in the small intestine. Donor phases of simulated gastric fluid during fasted and fed states (FaSSGF pH 1.6 and FeSSGF pH 5.0, respectively) were used to predisperse Diovan® immediate release tablet (160 mg valsartan). The initial concentrations of valsartan in the donor phases FaSSGF and FeSSGF were 6.2 % and 91.8%, respectively. The predispersed dispersions of valsartan were then transferred to acceptor phases that simulate intestinal fluid and cover the physiological properties (pH, buffer capacity and ionic strength) during fasted and fed states at a flow rate of 2 mL/min. The pH measurements were reported at time intervals corresponded to those of the transfer experiments to investigate the effect of % dissolved of valsartan in the donor phase on lowering the pH of the acceptor media. The similarity *f*2 test was used to compare the

concentration profiles in the acceptor media. The concentration profiles of valsartan predispersed in FaSSGF ranged between 33.1 -89.4% after 240 min. Whereas valsartan predispersed in FeSSGF was fully dissolved in all acceptor media within a range of 94.5-104.9% after 240 min. Therefore, the transfer model provides a useful screen for the concentrations of valsartan in the small intestine after oral administration during fasted and fed states.