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Development of controlled release bi-layered tablets containing oxycodone hydrochloride

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Oxycodone hydrochloride is a semi-synthetic opioid agonist that provides very effective relief for moderate to severe pain in cancer and post-operative patients. Controlled release oxycodone formulations have been studied to enhance the therapeutic effect by providing constant release over the whole dosing interval and improve patient's convenience by reducing the frequency of administration as well. The aim of this study was to develop once-a-day controlled release formulations containing oxycodone hydrochloride by modulating the release barrier in bi-layered tablet and investigating the IVIVC.

Controlled release formulations containing 20 mg of oxycodone were prepared by bi-layered tablet technology consisting of drug contained layer and barrier layer. In vitro drug dissolution test was conducted according to USP Apparatus 2 at 150 rpm in pH 6.8 media and analyzed the released drug using reversed phase HPLC at a wavelength of 230 nm. Three CR formulations having different drug releasing profiles were orally administrated to six subjects of Beagle dog. The plasma

samples were analyzed by LC-MS/MS and calculated pharmacokinetic parameters. IVIVC was investigated using fraction dissolved and fraction absorbed data from three different formulations. The bi-layered tablets were successfully manufactured by simple direct compression and showed more continuous drug release kinetics than the monolayer tablets. In vitro dissolution profiles were controlled by the viscosity of hypromellose in the barrier layer. In the pharmacokinetic study of three different CR tablets, modulating the release rate by different barrier layers affected the absorption of oxycodone. Fraction dissolved and fraction absorbed were well correlated with superior correlation coefficients (0.9930, 0.9949, and 0.9688). Bi-layered controlled release formulations consisting of drug contained layer and barrier layer including hypromellose were established with respect to well controlled dissolution profiles and IVIVC in Beagle dog model. The findings of the present study provide the potential of once-a-day controlled released oxycodone hydrochloride.

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