Pharmacokinetics of Etodolac in Rabbits: Effect of Food and Antibiotics

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Etodolac, 1,8-diethyl-1,3,4,9 tetrahydropyrano [3,4-b]-indole-1-acetic acid, is a NSAID drug which have analgesic and anti-inflammatory effect on human body by inhibiting COX-2 enzyme [1]. The main aim of this study was to develop a new reverse phase high performance liquid chromatography method with fluorescence detection (HPLC-FLD) in rabbit plasma. In addition, the pharmacokinetics of etodolac in rabbits were evaluated after single oral dosing with and without food; and together with administration of oral and intravenous of two different antibiotics. In this study, liquid-liquid extraction method was performed for extraction of etodolac from rabbit plasma. Valsartan was used as internal standard (IS). The chromatographic separation was carried out using C18 column. The mobile phase consisted of 0.5% TFA and methanol (26/74, v/v) was delivered at a rate of 1 mL/min and also excitation and emission wavelengths were 215 nm and 348 nm, respectively. Six rabbits were used in order to carry out this study and then the pharmacokinetic parameters (t1/2, Cmax and AUC) were calculated.

Calibration curve of etodolac was linear in the range of 1-50 µg/mL. Intra- and inter-day accuracy and precision were lower than 3.7% and 7.6%, respectively. Percent recovery and limits of detection (LOD) and quantification (LOQ) were found to be 98%, 0.25 µg/mL and 0.80 µg/mL, respectively. The developed method was successfully applied to the determination of etodolac in rabbit plasma samples. The single oral dose of Etol Fort (400 mg) was administrated to following groups: 1- with food; 2- without food; 3- together with oral administration of antibiotics (Atorvastatin 10 mg); 4- together with administration of intravenous of antibiotics (Moxiflactatin 400 mg). After oral dosing without food, etodolac was rapidly absorbed and reached maximum concentrations by 4.0 h; absorption was delayed 6.8 h when administrated with food. The absolute bioavailability of etodolac was lower when it was given together with antibiotics. The proposed method can be successfully used in pharmacokinetic studies and routine clinical experiments in order to determine the plasma concentration of etodolac with good linearity, precision and accuracy data.

KEYWORDS: etodolac, pharmacokinetic, rabbit

REFERENCES: