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Pharmacokinetic Evaluation of Modified Release Formulations of Diclofenac Potassium Tablets Prepared for IVIVC Studies

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***SUMMARY*. This pharmacokinetic study was performed in cross over manner on 12 male healthy volunteers. Study was ethically approved and prior informed consents of all subjects were obtained. Optimized formulations of diclofenac potassium tablets *i.e.* intermediate release (IntR, F12) and slow release (SR, F25) were given in this investigation to each volunteer in a randomized way with two weeks washout period. Cannula was inserted to draw the blood samples. A validated liquid chromatographic method was used to determine the concentration of diclofenac potassium in plasma. Time vs. plasma profile of these formulations was elucidated by using PK/PD software (Kinetica® 4.4.1). The C_{max} and T_{max} of F12 and F25 were in order of 0.778 ± 0.004 μg/mL, 1.844 ± 0.010 h and 0.330 ± 0.007 μg/mL and 5.581 ± 0.045 h. While area under the curve (AUC) values for IntR and SR were found to be 4.734 ± 0.058 mg/L×h and 4.778 ± 0.057 mg/L×h. No significant differences were determined between compartmental and non compartmental parameters. Furthermore it was also observed from these finding that HPMC K15M at variable concentrations has efficiently controlled the *in vivo* and *in vitro* release of drug from trial SR and IntR formulations. These pharmacokinetics parameters were determined in Pakistani populations in order to develop an *in vitro*/*in vivo* correlation (IVIVC).**

RESUMEN. Se realizó un estudio farmacocinético cruzado en 12 voluntarios sanos de sexo masculino. El estudio fue éticamente aprobado y se obtuvieron los consentimientos previos de los participantes. Dos formulaciones optimizadas, de liberación intermedia (IntR, F12) y de liberación lenta (SR, F25) se les dio en esta investigación a cada voluntario de una manera al azar con dos semanas de periodo de descanso. Las muestras de sangre se extrajeron con cánulas. Se utilizó un método validado de cromatografía líquida para determinar la concentración de diclofenaco de potasio en plasma. El tiempo vs. perfil plasmático de las formulaciones fue establecida mediante el uso de software de PK/PD (Kinetica® 4.4.1). La $C_{máx}$ y $T_{máx}$ de F12 y F25 estaban en el orden de 0,778 ± 0,004 mg/mL y 1.844 ± 0.010 h y 0.330 ± 0.007 mg/mL y 5,581 ± 0,045 h, mientras que los valores del área bajo la curva (AUC) para IntR y SR resultaron ser 4,734 ± 0,058 y 4,778 ± 0,057 mg/L×h, respectivamente. No hubo diferencias significativas entre los parámetros compartimentales y no compartimentales determinados. Además, también se observó que HPMC K15M a concentraciones variables ha controlado de manera eficiente la liberación *in vivo* e *in vitro* del fármaco tanto en la formulación SR como Intr. Estos parámetros farmacocinéticos se determinaron en poblaciones de Pakistán con el fin de desarrollar una correlación *in vivo* e *in vitro* (IVIVC).

KEY WORDS: compartmental and non-compartmental, diclofenac potassium, IVIVC, optimized formulations, pharmacokinetics.

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