



Pharmacokinetics and Evaluation of the Safety of Cefepime Administered to Rabbits

Roberto RULE ^{1,2}, Sergio VILLAGRA ², Adriana PETINELLI ²,
Carlos CORDIVIOLA ³, Guillermo PROZZI ² & Osvaldo H. FARINA ²

¹ Commission of Scientific Research of the Province of Buenos Aires, Argentina.

² Applied Pharmacology. Faculty of Medical Sciences, University of La Plata, La Plata, Argentina.

³ Department of Animal Production. Faculty of Agricultural and Forestry Sciences.
University of La Plata, Argentina.

SUMMARY. The aim of this study was to determine the kinetic behaviour and the safety of cefepime administered to rabbits. For this, rabbits ($n = 29$) were used and distributed in Groups 1 (G1), 2 (G2) and Control (CG). Animals from G1 ($n = 21$) received a monodose of cefepime intravenously, (20 mg/kg weight) and, after this, blood samples were collected, controlling the time. Rabbits from Group G2 ($n = 4$) received multidoses of cefepime (20 mg/kg weight, intravenously), and blood and urine samples were taken in order to analyse them. Animals from Groups G2 and CG were controlled electrocardiographically (ECG) throughout the treatment. Rabbits from Group CG ($n = 4$) were evaluated and samples were obtained in the same way and within the same time periods as G2. The concentration-time curves of cefepime were determined using a biological method, and it was analysed through a non-compartmental model. The pharmacokinetic results (Mean \pm S.D.) were: $t_{1/2} = 1.6 \pm 0.4$ h; $AUC = 212.1 \pm 82.1$ $\mu\text{g}/\text{mL}\cdot\text{h}$; $AUMC = 387.4 \pm 132.2$ $\mu\text{g}/\text{mL}\cdot\text{h}$; $V_{ss} = 216.7 \pm 63.4$ mL/kg; $CL = 99.7 \pm 19.4$ mL/kg y $TMR = 2.0 \pm 0.4$ h. The cefepime administered to rabbits in therapeutic doses did not produce any biochemical, electrocardiographic or renal modification.

KEY WORDS: Cefepime, Pharmacokinetics, Rabbits, Safety.

*Author to whom correspondence should be addressed. *E-mail:* robertorule@yahoo.com.ar