STUDY OF THE INTESTINAL ABSORPTION OF CIPROFLOXACIN IN RATS.

M. Rodríguez, A. Ruiz-García, G. Sánchez, M. Bermejo, V. Merino, J.M. Plá-Delfina
Department of Pharmacy and Pharmaceutics, Valencia University, SPAIN.

Introduction

Numerous compounds including fluoroquinolones have been reported to be actively secreted by intestinal efflux systems as P-glycoprotein (P-gp)[1,2,3]. The clinical relevance of this secretion remains unclear since only a few reports have demonstrated an increase in oral bioavailability of some drugs after cotreatment with a P-gp reversal agent[4]. The existence of a intestinal secretion process for some fluorquinolones seem to be demonstrated in biological systems like Caco-2 cells[5,6].

The aim of this work is to establish the importance of the reported efflux process of ciprofloxacin (C) in our experimental conditions.

Materials and Methods

An intestinal in situ perfusion technique[7] was used to calculate first order absorption rate constants, k_a, of C at 0.5, 5 and 50 µg/mL. In order to study the influence of Verapamil HCl in the absorption process of C it was perfused at the concentration of 2 mM in the presence of 0.5 µg/mL of C.

The output of the efflux system was checked by iv infusion[8] of C (0.5 mg) and measure of the recovery at 30 min in the in situ preparation (Q_{30}), as well as the area under the cumulative concentration in the luminal fluid versus time curve (AUC) in the presence (2mM) and absence of V in the intestinal lumen.

Quantification of C was achieved by fluorimetry after HPLC.

Results and Discussion

Figure 1 shows k_a values. No influence of the concentration can be seen, probably due to the large variability of k_a (around 30 % CV). Nevertheless, at the lower concentration of C k_a significantly increases in the presence of V ($p=0.005$), pointing out the existence of an efflux process. The active carrier transport represents a high percentage of the apparent k_a (155.8 %) and could be responsible for the variability obtained in the results.

When considering the iv administration, Q_{30} represents about a 2% of the total dose infused in both cases; and there are no statistical differences of AUC values (Figure 2).

Figure 1

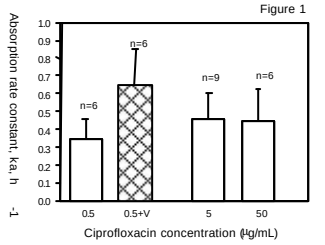
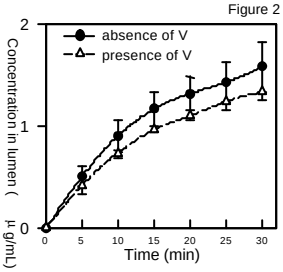


Figure 2



Conclusions

Even if there is a strong evidence of an efflux of C in situ, this process has little importance if iv administration is used at this dose.

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