

INFLUENCE OF P-GLYCOPROTEIN ON THE INTESTINAL ABSORPTION OF GREPAFLOXACIN.

Sánchez-Castaño G, Ruiz-García A, Merino V, Bermejo MV, Garrigues TM, Plá-Delfina JM.
Department of Pharmacy and Pharmaceutics, Valencia University, SPAI N.



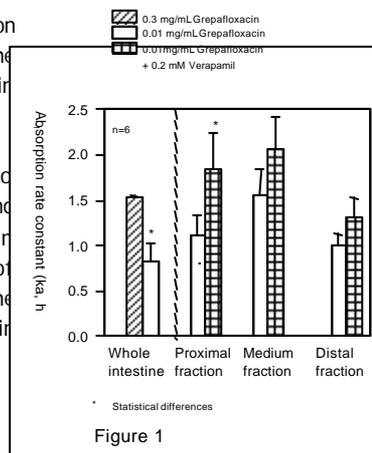
√ Purpose

Numerous compounds including fluoroquinolones have been reported to be actively secreted by intestinal efflux systems as P-glycoprotein but the clinical relevance of this secretion remains unclear^{1,2,3}.

The aim of the study was to determine the influence of intestinal P-glycoprotein (Pgp) on intestinal absorption of grepafloxacin (donated by GLAXO), and to investigate regional differences in proximal, medium and distal portions of small intestine of rat.

k_a was calculated in every condition by non linear regression of the remaining concentration of GRX in lumen versus time.

The lower concentration was also studied in proximal, medium and distal portions of the intestine in the absence and presence of verapamil HCl (V) 0.2 mM, and the apparent k_a value was calculated in each condition.



√ Results and Conclusions

Figure 1 shows k_a values. In the whole intestine, k_a increases as the concentration is raised ($p < 0.0001$), showing the possible activity of an intestinal efflux system. When the lower dose is assayed, no regional differences in k_a were found. The addition of a Pgp inhibitor (V) modifies the apparent k_a in the proximal fraction of the intestine ($p = 0.019$). In medium and distal portions no statistical differences were found. These results confirm that there are regional differences of Pgp functionality in

the rat.

√ Acknowledgements

This work is part of the SAF96-1710 Project of the MEC-Spain. A. RG and G. S. participated with grants from the MEC.

√ References

- Hunter J. and B. H. Hirst. 1997. Adv. Drug. Deliv. Rev. 25:129-157.
- Tsuji A. and I. Tamai. 1996. Pharm. Res. 13:963-977.
- Terao T., E. Hisanaga, Y. Sai, I. Tamai and A. Tsuji. 1996. J. Pharm. Pharmacol 48:1083-1089.
- Merino, V., J. Freixas, M. V. Bermejo, T. M. Garrigues, J. Moreno and J. M. Plá-Delfina. 1995. J. Pharm. Sci. 84:777-782.

√ Materials and Methods

The in situ intestinal absorption rate constant (k_a) of grepafloxacin was determined in the whole intestine of rats at two different concentrations (0.3 and 0.01 mg/mL). The grepafloxacin solutions were perfused in the whole intestine of the anesthetized rats and samples of the luminal content were taken every 5 minutes over a period of 30 minutes⁴.