ORAL BIOAVAILABILITY OF TRIAMTERENE IN THE RAT.

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√ Objetive

To determine the oral bioavailability of triamterene HCl in solution, in order to know the factors responsible for the low and erratic bioavailability[1] of the oral dosage forms available on the market.

√ Materials and Methods

Male Wistar rats, cannulated in the jugular vein[2] for sampling and drug administration, were randomly assigned to two groups. Group A (n=5) and Group B (n=6). Group A received a dose of 2 mg/Kg orally and Group B received the same dose intravenously. Triamterene solution was prepared in propileneglycol-saline solution (50% V/V). Blood samples were taken over a period of 240 minutes in both groups. Samples were centrifuged and after precipitation of proteins with methanol (1:3), were analyzed by HPLC (fluorimetry detection). AUC was calculated by the trapezoidal rule. Bioavailability was estimated as the AUC_{oral}/AUC_{iv} ratio.

√ Results and Conclusions

Mean plasma levels are shown in Figure 1. Pharmacokinetic parameters are listed in Table 1 along with AUC values. Oral bioavailablity is about 100%.

Figure 1

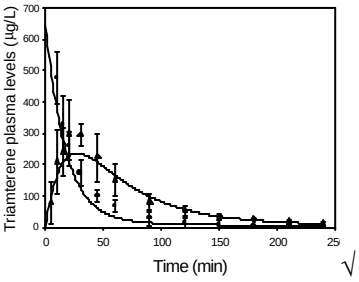

Table 1

	Value	Standard Error
Vd (L)	0.7758	0.3161
$k_{10}(min^{-1})$	0.0484	0.0142
$k_{12}(min^{-1})$	0.0086	0.0043
$k_{21}(min^{-1})$	0.0088	0.0051
$k_{01}(min^{-1})$	0.0236	0.0048
F	1.63	0.42

The results obtained suggest that triamterene, whose elimination depends primarily on metabolism and is very quick, is not subject to any intestinal or hepatic first pass effect.

On the other hand, the characteristics of the absorption process of triamterene (saturable, proton-dependent; data not shown) have no impact on bioavailability at the studied dose. It can be concluded that technological aspects, that condition the dissolution of the oral dosage forms are probably responsible for the reported low and erratic bioavailability of triamterene in human.

√ Acknoledgements

Ana Ruíz-García and Gloria Sánchez-Castaño are granted Ph.D. Students of MEC-Spain.

√ References

[1]Kapoor V.K. Analytical profiles of drug substances and excipients. Vol.23: 571-605

[2]Peris-Ribera J. E., F. Torres-Molina, M. C. García-Carbonell, J. C. Aristorena and J. M. Plá-Delfina. 1991. J. Pharmacokin. Biopharm. 19:647-665..