# STUDY OF THE INTESTINAL ABSORPTION OF TRIAMTERENE IN RAT: DOES IT USE THE SAME TRANSPORT SYSTEM THAN FOLIC ACID?.

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# Introduction

The aim of this study was to go insight the mechanism implied into the absorption of triamterene in rat and to evaluate the possibility that this diuretic uses the same transport system than folic acid, since both compounds have similar structures [1].

## **Experimental Methods**

The structure of Triamterene and Folic acid are shown in Figure 1.





The determination of the intestinal Permeability coefficient was made by a method of perfusion in situ without recirculation. The animals used were male Wistar rats weighting between 270-300 g. Five different solutions of triamterene, ranging from 0.008 to 8 µg/mL were perfused in the small intestine in the presence and in the absence of folic acid 3.15 mM. The analysis of the samples was made by liquid chromatography (HPLC) with fluorimetric detection. The absorption coefficients were obtained by nonlinear fitting of a monoexponential equation to the luminal concentrations versus time These data. apparent first order absorption rate coefficients were transformed into permeability values (Peff) with the following equation: Peff= effective (Ka\*2)/R where R is the intestinal radius calculated from the perfused volume and the intestinal segment length.

A model that considers both, passive and active transport through the membrane was fitted to data in order to determine the magnitude of both processes [2]. The remaining luminal concentrations in every conditions were fitted to a system of differential equations of a combined passive and Michaelis-Menten kinetics with the aid of Winnonlin v.01 software.

$$\frac{\partial C}{\partial t} = -k_d + \frac{V_m \cdot C}{K_m + C} \qquad \text{Eq (1)}$$

This allows to obtain the passive  $(k_d)$  and active  $(K_m \text{ and } V_m)$  parameters.

## **Results and Discussion**

The permeability values of Triamterene in presence and absence of folic acid are displayed in Figure 2. The parameters of eq (1) are displayed in Table 1. The concentration versus time values are plotted in Figure 3.

The one way analysis of variance (ANOVA) showed statistically significant differences between the Permeability values at the different concentrations of triamterene assayed in the absence of folic acid. The post-hoc Scheffé analysis revealed that permeability values were different except between the two higher concentrations. When the luminal concentration of triamterene was increased the permeabilitity coefficients decreased, according to an active transport from the luminal side of the membrane, being the magnitude of both processes (active and passive) very similar. No statistical differences were observed when the mixed solutions were perfused, and the permeability values obtained in these conditions were the same than the obtained at the highest concentrations of triamterene alone. Accordingly, the active component of transport is inhibited by folic acid.





### Conclusion

The results obtained point out the possible existence of а combined kinetic transport for triamterene from the intestine. Moreover, as expected, due to structure analogies between the two molecules assayed, the transport system used by triamterene seems to be the same than the used by the antidote folic acid.

#### References

1. Zimmerman J, Selhub J, Rosenberg IH. Competitive inhibition of folic acid absorption in rat jejunum by triamterene. J. Lab. Clin. Med. 1988, 108 (4): 272-276.

2. Makhey VD, Guo A, Norris DA, Hu P, Yan J, Sinko PJ. Characterization of the regional intestinal kinetics of drug efflux in rat and human intestine and in Caco-2 cells. Pharm Res. 1998, 15: 1160-1167.