STUDY OF THE INTESTINAL ABSORPTION OF TRIAMTERENE IN RATS.

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Objective
The aim of the work was to study the intestinal absorption process of triamterene (T) in rats. T is currently used as a diuretic in therapeutics and have a low bioavailability probably due to its low solubility. This study intends to go insight the absorption mechanism of T to find other possible causes to its bioavailability problems.

Materials and Methods
The concentration dependence was studied by perfusion of three different concentrations of T ranging from 0.08µg/mL to 8 µg/mL, using an intestinal in situ perfusion technique performed in rats. The proton dependence was checked by comparing the absorption rate constants, k, at pH=5.00 and pH=7.00. The solutions where perfused in the whole intestine of the anesthesized rats and samples of the luminal content were taken every 5 minutes over a period of 30 minutes. k was calculated in every condition by non linear regression of the remaining concentration of T in lumen versus time. Inhibition studies were performed using Verapamil HCl (4mM, V), a mixed inhibitor of P-glycoprotein (pgp) and Multidrug Resistance-Associated Protein (MRP).

Results and Conclusions
The absorption rate constant of triamterene in each condition are listed in Table 1 and graphically outlined in Figure 1 for better comparison.

<table>
<thead>
<tr>
<th>Triamterene concentration (µg/mL)</th>
<th>pH 5.00</th>
<th>pH 7.00</th>
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<tr>
<td>0.08</td>
<td>0.85(0.21)</td>
<td>0.94(0.22)</td>
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<tr>
<td>0.08 + 4mM V</td>
<td>1.37(0.32)</td>
<td>0.98(0.48)</td>
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When the physiological pH (7.00) is used there are no statistical differences between k. In these conditions, the presence of V produces an increase (not significant) in k that might suggest the influence of an efflux system for which V is not specific.

Further studies are therefore necessary in order to characterize the kinetics of the process.

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References