POSSIBLE RENAL EXCRETION MECHANISM OF XANTHINE DERIVATIVES, 3-METHYLXANTHINE AND ENPROFYLLINE (3-PROPYLXANTHINE) IN RATS

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Some xanthine derivatives, including theophylline, possess bronchodilatory effect mediated via cAMP phosphodiesterase inhibition and/or adenosine antagonism. It is reported that N³-substituted xanthine derivatives, 3-methylxanthine (3MX) and enprofylline (3-propylxanthine, ENP), are excreted into the urine by active tubular secretion in human and rats. However, the active transport system for xanthine derivatives from blood to urine through the tubular epithelial cells remains unclear, although the tubular secretion of ENP is reported to be inhibited by N-benzoyl-β-alanine, which may be an organic anion transport inhibitor. To determine the transport system involved in the tubular secretion of xanthine derivatives, we investigated the effects of organic anion and cation drugs on the renal clearance (CLR) of 3MX and ENP in rats. The clearance ratio (CLR/GFR) of 3MX and ENP was significantly decreased by coadministration of probenecid, but not p-aminohippurate. On the other hand, the cation drugs tetraethylammonium and cimetidine significantly reduced the values of CLR and CLR/GFR for 3MX and ENP. Probenecid is reported to be a substrate for organic cation transporters as well as organic anion transporters. These findings at least suggest that some organic cation transport systems are involved in the tubular secretion of 3MX and ENP in rats.