Uptake of Cefadroxil derivatives into rat intestinal brush-border membrance vesicles

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Abstract

Uptake of cefadroxil and its two acetyl-derivatives, N-acetyl- and O-acetyl-cefadroxil, into the brush-border membrane vesicles (BBMV) was measured at [pH]o = 5.5, 7.4 and [pH]i = 7.4. Both acetyl-derivatives showed a significantly slower uptake than cefadroxil at [pH]o = 5.5 and 7.4. Cefadroxil and the two derivatives showed a higher uptake rate in the presence of an inward H+ gradient ([pH]o = 5.5, [pH]i = 7.4). At [pH]o = 5.5, uptake of cefadroxil into BBMV was inhibited by N-acetyl-, O-acetyl-, N-BOC-, and N-BOC-O-acetyl-cefadroxil, but not by cephalothin and cefuroxime. At [pH]o = 7.4, no inhibition of cefadroxil uptake was evident for any inhibitors. There were two different transporters responsible for the uptake of cefadroxil at pH 5.5 and 7.4. One is the H(+)-coupled dipeptide transport system, and the other is the neutral pH-preferring system. The alpha-amino group may be essential for the transport of cefadroxil by both transport systems. Although the phenolic group in the side chain is not an essential functional group of beta-lactam antibiotics, an additional derivation on the phenolic group of cefadroxil also inhibited both the H(+)-coupled dipeptide transport system and the neutral pH-preferring transport system.