

Mechanisms of Carboxylic Acid Transport in Rat Jejunum

THE TRANSPORT OF BENZOIC ACID has been investigated with *in vitro* preparations of the rat small intestine. Preliminary studies were made with the everted sac preparation. It was found that sacs made from the jejunal region, incubated in Krebs bicarbonate saline containing 10 mM benzoic acid, transported benzoic acid from the mucosal to the serosal sides. A concentration gradient was established during the incubation, and the final serosal concentration was significantly greater than the final mucosal concentration. The capacity of the intestine for transport of benzoic acid was greatest in the mid- and distal-regions of the jejunum. No transport against a concentration gradient was observed in the ileum.

Jejunal transport of benzoic acid was stimulated by metabolizable sugars, such as glucose and fructose, and was inhibited by the actively transported sugar, galactose, which is not metabolized. The transport of benzoic acid was also inhibited by metabolic inhibitors and by sodium depletion. Furthermore, the rate of benzoic acid transfer was inhibited by high concentrations of benzoic acid, and it was not possible to demonstrate unequivocal saturation kinetics for the transport process. However, the structural analogues, benzoic acid and phenylacetic acid, did exhibit mutual inhibition in rate of transfer. No interaction was observed between benzoic acid and *p*-aminobenzoic acid.

Further studies with a flux chamber preparation showed that benzoic acid transfer was affected by the pH of the incubation medium, but the transfer could not be explained by the pH partition hypothesis. Studies using the voltage clamp technique showed that the intestine is relatively impermeable to benzoate anion and that the transport of benzoic acid is not electrogenic.

These characteristics can be explained by a model system consisting of three compartments in which the intermediate compartment has a pH value different from that of the bulk phases. Two alternative forms of this model can be described: one in which the pH of the intermediate compartment is greater than that of the bulk phases, and the other in which the pH of the intermediate compartment is less than that of the bulk phases. Consideration of these two alternatives showed that a distinction between them could be made from studies of the interactions between the fluxes of transported acids. The observed interactions between benzoic acid and phenylacetic acid and between benzoic acid and pentanoic acid are consistent with the predictions of the high pH version of the model, and are inconsistent with the low pH version or a carrier-mediated transport process.

It was concluded that carboxylic acid transport can be explained by a system having the characteristics of the high pH model, and this conclusion was found to be consistent with the unique pattern of acid-base transport in rat jejunum. The location of this high pH microclimate compartment has not been identified, but studies of the intracellular concentrations of the transported acids suggested that the intracellular space is unlikely to be the high pH intermediate compartment. It is suggested that the microclimate of high pH might be represented by the lateral channels of the intestinal epithelial cells.