Relationship between Structure and Permeability of Tryptophan Derivatives Across Human Intestinal Epithelial (Caco-2) Cells

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L-Trp and its derivatives were used as model compounds to clarify structural factors which influence the intestinal epithelial permeation and metabolism of amino-acid derivatives. Permeability of model compounds through Caco-2 cells was used as an *in vitro* absorption model for human intestinal epithelial cells. The influence of compound concentration, the effects of various transporter substrates on permeability coefficients, and pH dependency of permeability coefficients were investigated. The transcellular permeability of Trp and Trp-NH_2 in the direction from the apical side to the basolateral side, in which nutrients and drugs were ordinarily absorbed, declined with increasing concentration and saturated at more than 1 and 0.4 mM, respectively. The permeability coefficients for *N*-terminal protected Trp derivatives and Ac-Trp-NH_2 showed similar and constant values in both from the apical-to-basolateral and basolateral-to-apical directions. In addition, significant inhibition of the apical-to-basolateral permeation of Trp by Leu and Phe was observed. The permeability coefficient ratio at pH 6.3 to that at pH 7.3 was explained by the ratio of the ionic form to the neutral form of the compounds. Based upon these results and the partition coefficients in the 1-octanol/water system, possible absorption mechanism of Trp and its derivatives across Caco-2 cells was proposed.

Key words: Caco-2, Structure-Permeability Relationships, Tryptophan Derivatives