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消化管における難吸収性薬物の透過性及びに吸収性に及ぼす各種溶解補助剤の影響

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Recently, various solubilizing agents have been widely used to dissolve many poorly water-soluble compounds and evaluate their intestinal transport and absorption. However, these solubilizing agents might sometimes alter the intestinal barrier function and affect the function of intestinal transporters including P-glycoprotein (P-gp) and PEPT1. Therefore, we examined the effect of various solubilizing agents on the intestinal barrier and the function of P-gp and PEPT1 by an *in vitro* diffusion chamber and an *in situ* closed loop method. The model drugs used were 5(6)-carboxyfluorescein (CF), rhodamine123 (a p-glycoprotein substrate) and cephalexin (typical substrate for PEPT1). DMSO, ethanol, PEG400, propylene glycol, Cremophor EL, Tween 80, Labrasol, HCO-60, Transcutol P, Gelucire44/14, sodium taurocholate (NaTC) and 2 hydroxypropyl-β-cyclodextrin (2HP-β-CyD) were used as models of common solubilizing agents. Among these solubilizing agents, NaTC (20 mM and 50 mM) increased the transport of CF and cephalexin, suggesting that it might alter the intestinal barrier function. The results of CF seemed to correlate well with that of cephalexin, suggesting that passive diffusion might also contributed to the absorption of cephalexin. On the other hand, Labrasol also increased the transport of CF altogether with NaTC in the case of absorption study. Moreover, various solubilizing agents including Cremophor EL, Tween 80, PEG400, Labrasol, DMSO and ethanol increased the absorptive transport of rhodamine123 and decreased its secretory transport in the rat small intestine, suggesting that they might inhibit the function of P-gp in the intestine. However, other P-glycoprotein substrate drugs might be used in order to confirm this condition. Therefore, care should be taken when these solubilizing agents are used for evaluating the intestinal transport and absorption of poorly absorbable drugs.