QUANTITATIVE ASSESSMENT OF SMALL INTESTINAL METABOLISM: CURRENT STATE AND ISSUES
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Not only the liver but also the intestine, lungs and kidneys are well known as drug metabolizing organs. Quantitative assessment of organ metabolism (availability or extraction ratio) should be done from two viewpoints, presystemic metabolism and systemic metabolism. Both presystemic and systemic organ availability (or extraction ratio) are assessed by the equation based on the well-stirred model for organs except the intestine [1]. In contrast, the assessment method of presystemic intestinal availability is different from that of systemic intestinal metabolism. Pathways of orally administered drug molecules shown in Figure 1 clearly indicate that presystemic metabolism (Fpg) should not be assessed by the equation based on the well-stirred model although systemic intestinal metabolism (Fg) is assessed by the model equation.

Figure 1. Comparison of pathways of orally administered drug molecules.

This difference in the pathway of drug molecules also means that even if the intrinsic clearance of the intestine is comparable to that of the liver, presystemic intestinal availability is less than presystemic hepatic availability. Although intestinal metabolism has been recognized as a process impacting on oral bioavailability, the quantitative assessment method of presystemic intestinal metabolism has not been established so far. Several assessment methods have been reported in animal studies, though.

Current issues for the quantitative assessment of small intestinal metabolism are to differentiate presystemic intestinal availability (Fpg) from systemic intestinal availability (Fg) [2], and to establish a kinetic model equation to predict and evaluate intestinal pharmacokinetics.

References:

Biography
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