## The Relationship of Gastrointestinal Membrane Permeability and in vivo Bioavailability of Four Beta-blockers in Rats

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On the basis of recognizing that physicochemical properties, gastrointestinal permeability and pharmacokinetic characteristics of drug are the fundamental parameters controlling the rate and the extent of drug absorption, the biopharmaceutics drug classification system for correlation between drug solubility, gastrointestinal membrane permeability and *in vivo* bioavailability is proposed. The objective of this study was to assess whether the partition coefficient and *in vitro* gastrointestinal permeability of beta-blockers can be correlated with *in vivo* bioavailability. *In vitro* gastrointestinal membrane permeability was determined by using the diffusion chamber method. Bioavailability parameters were evaluated after intraveneous, intraportal and oral administrations of the beta-blockers such as atenolol, metoprolol, pindolol, propranolol. There were good correlations between log P (n-octanol/buffer), intestinal membrane permeability and gastrointestinal first-pass effect. The correlations obtained in this study indicated that *in vitro* diffusion chamber method could be used to predict *in vivo* bioavailability such as gastrointestinal first-pass effect of beta-blockers in rats.

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## Toxicokinetics of 4-tert-octylphenol

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4-tert-Octylphenol(OP) is a surfactant additive widely used in the manufacture of a variety of detergents and plastic products. Also, OP is known to have estrogenic activity by interacting with development and functions of endocrine system. This study was carried out to obtain toxicokinetic parameters of OP in male Sprague-Dawley(SD) rats. Male SD rats were administered OP, either single oral applications of 50, 100 or 200 mg/kg body weight, or a single intravenous injections of 1, 5 or 10 mg/kg body weight. Blood samples taken at several time intervals after administration were obtained from the femoral artery. Analysis of blood samples for OP was performed by gas chromatography with detection by mass spectrometry(GC/MS). The detection limit of OP was 1.9 ng/m² at SIM mode of GC/MS. Calibration curve for analysis of the concentrations of OP in plasma was (OP/BP peak area ratio) =  $0.0294 \times (\text{plasma conc.}) + 0.028 \text{ (r2} = 0.9991)$ . The OP plasma concentration was  $\sim 3921 \text{ ng/}$ ml immediately after single intravenous applications decreased rapidly within 45 min, and was detectable low concentration up to 6 hr after application. When administered orally in SD rats (50, 100 and 200 mg/kg), OP was detected in blood early after oral administration, indicating rapid initial uptake from gastrointestinal tract, with Tmax obtained from 0.67~0.83 hr. Using the AUC of blood concentration vs. time, low oral bioavailabilities of 1.2, 5.0 and 5.3% were calculated for the 50, 100 and 200 mg/kg groups, respectively.

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