Pharmacokinetic Study of Ursodeoxycholic Acid and Its Glycine Metabolite after Oral Administration of Ursodeoxycholic Acid in Healthy Chinese Subjects
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Purpose
Ursodeoxycholic acid (UDCA), a secondary bile acid naturally found in human plasma, is used in the treatment of chronic cholestatic liver diseases. In liver, UDCA is rapidly metabolized into its glycine conjugate, i.e. glycoursodeoxycholic acid (GUDCA). However, the pharmacokinetics of both UDCA and GUDCA are barely studied and not available in Chinese subjects. The present study aims to determine the pharmacokinetics of UDCA and GUDCA in Chinese subjects after a single oral dose of 500 mg UDCA.

Methods
Protocol was approved from the local ethics committee prior to the study. Healthy male subjects were administered with a single oral dose of 500 mg Ursofalk capsule after an overnight fast of 10 h. Venous blood samples were collected at pre-dose (0 h) and at 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 10, 12 and 24 h post-dose. Simultaneous quantification of UDCA and GUDCA in plasma was conducted using a validated LC/MS/MS method. Pharmacokinetic parameters of UDCA and GUDCA were calculated by non-compartmental model from the plasma concentration vs time profiles. The metabolic ratios of GUDCA to UDCA (i.e. AUC_{GUDCA}/AUC_{UDCA}) were evaluated and compared with the previous published data from Finnish healthy subjects.

Results
Totally 26 adults completed the study. The T_{max}, C_{max} and AUC_{0-24h} of UDCA was ~3 h, 10.4 ± 4.3 µmol/l and 61.9 ± 38.5 µmol•h/l, respectively. A slight rebound of UDCA was observed after 10-12 h post-dose, due to enterohepatic cycling. GUDCA plasma level increased rapidly after a warm meal, as is reported previously. The AUC_{0-24h} of GUDCA was 59.8 ± 28.6 µmol•h/l. Compared with Finnish subjects (at 150 mg dose), the mean AUC_{GUDCA}/AUC_{UDCA} ratio observed in Chinese subjects (~1.14) was lower than that in Finnish subjects (~2.37), indicating potential difference in metabolism of UDCA among ethnic groups.

Conclusion
Different metabolic ratio of GUDCA to UDCA was observed in Chinese subjects when compared to that of Finnish subjects. Further studies on phenotyping and geneotyping of UDCA may warrant its clinical usage. (Funded by Europharm Laboratories Co. Ltd., Hong Kong. 7050413)