Green tea elevated the blood level of indoxyl sulfate, a nephro - cardiovascular toxin, in renal failure rats through inhibition on OAT1 and OAT3

Yu-Hsuan Peng, Douglas H. Sweet, Shiuan-Pey Lin, Chi-Sheng Shia, Yu-Chi Hou,

Pei-Dawn Lee Chao

School of Pharmacy, China Medical University, Taichung, Taiwan, R.O.C.

Department of Pharmaceutics, Virginia Commonwealth University, Richmond, USA

Abstract

Green tea (GT) is one of the most popular beverages worldwide. GT contains plenty of catechins such as epicatechin, epigallocatechin and epigallocatechin-3-gallate etc. Indoxyl sulfate (IS) is a highly protein-bound toxin, which cannot be removed via hemodialysis. The serum IS concentration was a predictor for the progression of renal and cardiovascular diseases as well as all-cause mortality. The excretion of IS was associated with organic anion transporters (OATs) 1 and 3. Based on the metabolic fate of GT, the major molecules in bloodstream were the glucuronides/sulfates of catechins, which are putative substrates of OATs. We hypothesized that the metabolites of GT might inhibit the excretion of IS mediated by OATs. This study investigated the effect of GT on the elimination of intravenous IS in elderly normal rats. In addition, a chronic renal failure rat model was established to investigate the effect of GT on endogenous serum IS level. The serum concentration of IS was assayed by HPLC. The results showed that GT significantly decreased the elimination of IS in both elderly and CRF rats. Furthermore, cell line studies indicated that GT metabolites inhibited the uptake functions of OAT1 and OAT3. In conclusion, ingestion of GT elevated the serum levels of endogenous IS in renal failure rats through inhibition on OAT1 and OAT3.