Basic study for green tea-simvastatin interaction

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Food components and drugs may interact in several ways leading to consequences for health. Some well-known examples of clinically relevant food-drug interaction are those of green vegetables and oral anticoagulants, St. John's wort and antiretroviral drugs or grapefruit juice and statins. Food components may, indeed, augment or reduce the efficacy of drugs and/or reduce their tolerability through diverse mechanisms of interaction. Very recently, Werba et al. observed that consumption of green tea doubles the bioavailability of simvastatin (SIM), a compound widely used for reduction of abnormally high atherogenic lipoproteins in a hypercholesterolemic patient (Ann Intern Med, 149:286, 2008). Based on the available information about metabolic pathways of SIM and green tea, we speculate that the interaction observed may be related to competition for the mechanisms of transport and/or metabolism between green tea cathechins and SIM. The use of statins, which is diffuse in western countries, is increasing in the eastern hemisphere. This leads to foresee a growing number of people taking both green tea and statins.

The objective of our study is to elucidate scientifically pharmacokinetic and pharmacodynamic interaction between green tea and SIM from basic and clinical point of view. In basic experiments, female Sprague-Dawley rats received single or repeated oral administration of green tea extract (GTE, 400 mg/kg), then they were orally administered SIM (20 mg/kg). Plasma concentrations of SIM and its active metabolite simvastatin acid (SVA) in rats were periodically measured by LC/MS/MS and their pharmacokinetic parameters were estimated. It was found that single and repeated oral administration of GTE in rats increased significantly the AUC and C_{max} but not $t_{1/2}$ of SIM. Further, in these GTE-pretreated rats, the AUC, C_{max} and $t_{1/2}$ of SVA showed a tendency of increase as observed in the case of SIM. In conclusion, these data indicate that GTE may affect pharmacokinetics of SIM. The underlying mechanism and pharmacological significance for GTE-SIM interaction may be clarified by further detailed experiments such as in vitro experiments and pharmacodynamic study. We are now planning a clinical study in Italy and in Japan to assess the consistency of putative interaction in two ethnically different populations.