JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
CORRESPONDENCE/REBUTTAL

DOI:10.1021/jf1009846

Comment on Lymphatic Absorption of Quercetin and Rutin in Rat and Their Pharmacokinetics in Systemic Plasma

We have read the paper by Chen et al. (*1*) on lymphatic absorption of quercetin and rutin in rats with great interest. The authors were able to detect intact rutin in blood plasma and lymph of rats that had received this quercetin glycoside by duodenal administration. As mentioned in the manuscript, this finding is in contrast to the majority of published studies, which could not detect intact rutin in plasma. The authors of another study in which rats received rutin at a similar dosage (around 200 mg/kg) via gastric gavage could not detect the intact glycoside in plasma (*2*). We believe that the surprising observation by Chen et al. (*1*) could be likely due to the specific experimental conditions chosen. In their study, the administered rutin was dissolved in a PEG400/ethanol solution that might have facilitated permeation of the glycoside through the intestinal wall. However, we believe that this finding does not challenge the current consensus that under more physiological conditions hydrolysis of rutin by intestinal microflora is required for absorption of its aglycone quercetin (*3*).

Unfortunately, Chen et al. analyzed rutin and quercetin without considering their metabolites derived from intestinal and hepatic metabolism. It is widely known that the major part of quercetin circulates in the form of conjugated and methylated metabolites, whereby the latter ones are especially abundant in rats (*4*). In rat lymph, Murota and Terao (*5*) detected the metabolite 3′-*O*-methylquercetin in substantial amounts, whereas unmodified quercetin represented only a very minor fraction in this body fluid.

A major focus in the paper by Chen et al. is the statistical comparison between the pharmacokinetic parameters in lymph fluid with those in blood plasma. However, as the authors noted themselves with regard to fluid volume, the lymph is a different body compartment than the blood. Thus, time−concentration courses of compounds in lymph are different from those in blood just for this reason alone. Chen et al. quoted another study to support their methodological approach (*6*). However, the authors of the latter study used their pharmacokinetic profiles of lymph in a very different way. In the study part, in which those authors used a noncompartmental analysis, the ratios of lymph and plasma AUC values were compared between two different methods of drug administration (in that case intravenous and subcutaneous administration). Obviously, the cited study cannot be used to support the unusual pharmacokinetic analysis performed by Chen et al. (*1*).

Thus, unfortunately, the conclusions drawn by Chen et al. in their study are, in our opinion, of only very limited value with regard to lymphatic and plasma pharmacokinetics of quercetin and rutin.

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Received for review March 15, 2010.

Published on Web 07/07/2010