Impact of the changes in P-glycoprotein activity on domperidone pharmacokinetics in rat plasma

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Abstract:
The effect of quinidine (QD) and grapefruit juice (GFJ) extract, P-glycoprotein inhibitors, on the domperidone (DOM) concentration in rat plasma was investigated. DOM, a dopamine D2-receptor antagonist, is a substrate for P-glycoprotein. DOM (10 mg/kg) was administered orally 2 h after GFJ extract (0.2 ml/kg) or QD (2.5 mg/kg). DOM concentration in plasma samples was determined by HPLC with fluorescence detection. The GFJ extract and QD administration significantly increased $C_{\text{max}}$ of DOM by 19% and 36%, respectively, and the AUC_{0-25} (area under the concentration-time curve from time zero to 15 min) by 29% and 44%, respectively. In addition, QD significantly increased the DOM AUC_{0-25} (32%), whereas a 19% increase was observed after GFJ extract administration. In conclusion, GFJ and QD significantly influenced DOM at plasma concentration during the first two hours after DOM administration indicating that interaction takes place during absorption phase.

Key words:
domperidone, P-glycoprotein, quinidine, grapefruit juice