Introduction: Grapefruit juice (GFJ) is known to decrease the plasma concentrations of several drugs by inhibiting organic anion-transporting polypeptide (OATP) 2B1. We aimed to determine the duration of the inhibitory effect of GFJ on OATP by comparison with the duration of the GFJ-mediated effects on cytochrome P450 (CYP) 3A4 activity.

Patients (or Materials) and Methods: Seven Japanese healthy subjects were enrolled and administered celecoxib (Cel) and midazolam (Mdz), which are substrates of OATP2B1 and CYP3A4, respectively, on days 1, 3, and 7 (0, 48, and 144 hours after the ingestion of GFJ). On the control day, Cel (100 mg) and Mdz (15 µg/kg) were orally administered with water. Three days later, all subjects drank GFJ (200 mL 3 times a day) for 3 days. On day 1, the same doses of the drugs were administered with GFJ. On days 3 and 7, the subjects were administered the same doses of the drugs with water.

Pharmacokinetics and hemodynamic parameters of both drugs were evaluated on each day. The plasma concentrations of Cel and Mdz were determined by LC-MS/MS. The study protocol was approved by the ethics committee of Hamamatsu University School of Medicine and University of Shizuoka, and all participants provided written informed consent before the study was initiated.

Results: Plasma concentrations of Cel were lower on day 1 than on the control day. AUC0–8 and Cmax of Cel were significantly decreased on day 1, and the mean ratios of these values and the corresponding control-day values were 0.21 and 0.13, respectively. The Cmax and AUC0–8 returned to the corresponding control levels on days 3 and 7. In contrast, AUC0–8 of Mdz was higher on days 1 and 3 than on the control day, with the mean ratios of the corresponding values and control-day value being 2.60 and 1.42, respectively. The AUC0–8 returned to the control level on day 7. Systolic and diastolic blood pressure or heart rate at 1 and 3 hours after administration of drugs did not change by the intake of GFJ.

Conclusion: GFJ greatly reduced Cmax and AUC0–8 of Cel suggesting that it strongly inhibited OATP2B1. However, the OATP2B1 inhibition caused by GFJ dissipated faster than the GFJ-mediated alterations in CYP3A4 activity, which were sustained for at least 48 hours. Our results are clinically relevant because many patients take OATP substrates daily, and knowing the duration of inhibition would help patient interactions.

Disclosure of Interest: None declared.

PP178—ANTIPELLEPTIC DRUGS: PRESCRIBING PATTERNS AND INTERACTION RISK IN GENERAL PRACTICE

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Introduction: In the last years, a growing trend in antiepileptic drug (AED) use was observed, but few data concerning indication of use and drug interaction risk are available in general practice. The aims of this study were: to analyze the prevalence, incidence of use, and the prescribing pattern of newer and older AEDs; to assess the exposure to potential interactions between AEDs and other drugs in a general practice setting of Southern Italy.

Patients (or Materials) and Methods: We analyzed a population of almost 150,000 individuals living in Caserta and registered in 123 general practitioners’ lists. Patients who received at least 1 AED prescription during 2005–2011 were identified. The use of newer and older AEDs was calculated as 1-year prevalence and incidence; AEDs consumption was evaluated as defined daily dose (DDD)/10,000 inhabitants/d. Clinically relevant interacting drugs were identified and the risk of drug interactions was calculated as overlapping days between the exposition days of AEDs and interacting drugs.

Results: Prevalence of old AED use slightly increased from 10.7/1000 inhabitants in 2005 to 13.0/1000 in 2011, while a strong increase of newer AED use was observed from 14.7/1000 to 22.3 until 2006, followed by a deep fall to 16.2/1000 in 2011. Among older AEDs, phenobarbital and valproate were the most widely used in 2011,