

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Interaction of statins with grapefruit juice

Grapefruit juice has been extensively studied for its ability to interact with drugs. As a naturally occurring product, the interacting substance(s), not fully identified, appear in different quantities in different fruit. The commercial juicing process forces large quantities of potentially interacting substances normally present in the pith and rind into juice. This has led to the suggestion that the whole grapefruit is less likely to interact as the fruit juice.

Furanocoumarins have been identified as ingredients in grapefruit juice that inhibit intestinal cytochrome P450 isoenzyme CYP3A4, meaning that there may be increased plasma concentrations of the substrates of CYP3A4 during consumption of the juice. The interaction of grapefruit juice with statins is of interest, due to the common use of these drugs, sometimes as primary prevention in currently healthy people.

The expression of statin-grapefruit juice interactions may vary, depending on the specific statin drug involved, the quantity of juice consumed and the timing of this. Pravastatin seems not to interact with grapefruit juice. Fluvastatin and rosuvastatin are not significantly metabolised by CYP 3A4 therefore an interaction is not expected. The interaction occurs with simvastatin and to a lesser extent with atorvastatin. Consumer advice ranges from no recommendation, to restricting juice, to avoiding juice.

Quantity of grapefruit juice taken seems important. In one study 200 ml grapefruit juice three times a day followed by a single dose of Atorvastatin 40 mg in healthy subjects lead to an increase in the area under the plasma level–time curve (AUC), of 2.5 fold and an increase of total HMG-Co-A reductase inhibition by 50%. However a single 240 ml glass of juice caused an increase of only 37% in AUC of atorvastatin.

If the juice is given at the same time as the statin, greater increases in AUC and peak plasma levels occur. In healthy subjects given 200ml double strength juice three times a day for 2 days and on day 3 given 60mg simvastatin plus juice then more juice 30 and 90 minutes later, the mean peak serum simvastatin and simvastatin acid rises 9 fold and 7 fold respectively. When simvastatin was given 24 hours after grapefruit juice the effect was only 10% of that observed during concurrent use. Rhabdomyolysis has been reported four days after a patient started to eat 1 fresh grapefruit daily while taking simvastatin 80 mg daily for the previous six months

Grapefruit juice interactions are hard to manage because one specific dose adjustment is unlikely to be suitable for all preparations and quantities of juice taken. Adverse clinical effects can be minimised by avoidance of the combination with drugs of a narrow therapeutic range or potentially serious consequences.

This E-Bulletin is based on work by Nicky Gordon, Senior Pharmacist, RGH

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