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Grapefruit juice interactions

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Questions about the interaction of drugs with grapefruit juice have increased. I have therefore collated available data to produce a table which may help when assessing the significance and clinical relevance of an interaction. [The full table is available with this article](#) on the *Australian Prescriber* web site (www.australianprescriber.com).

The CYP3A4 enzyme system is found in the liver and in enterocytes. Some drugs are therefore metabolised as they are absorbed by the enterocytes. Drugs can also be pumped back into the intestinal lumen by a P-glycoprotein (Pgp) transporter. Pgp and CYP3A4 may therefore act in tandem as a barrier to drugs getting from the gut to the systemic circulation. Inhibition of either or both systems can increase the bioavailability of a drug.¹ Grapefruit juice appears to selectively inhibit CYP3A4 in the small intestine. However, the interactions are not simple competition for substrate metabolism, grapefruit juice acts by selective post-translational downregulation of enzyme expression in the intestinal wall.^{2,3} The inhibition can last up to 24 hours with a maximal effect when the juice is given with the drug or up to four hours before the drug.⁴

All interactions studied so far have used grapefruit juice.⁵ There are no useful studies with whole grapefruit.⁶ Sweet orange juice does not interact, however, Seville (or bitter) orange juice can inhibit CYP3A4 (although this does not affect cyclosporin⁷).

Of the many interactions studied only cyclosporin can be definitely said to have a clinically significant interaction. The clinical significance of increased concentrations of sirolimus and tacrolimus is less clear. Other interactions which may be clinically significant occur with amiodarone, atorvastatin, carbamazepine, felodipine and simvastatin.

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FURTHER READING

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