Summer ripe pomegranate

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PIC QUESTION OF THE WEEK: 7/13/09

Q: Does pomegranate juice result in drug interactions similar to those observed with grapefruit juice?

A: Grapefruit juice interacts with drugs by inhibiting the intestinal source of the CYP3A4 isoenzyme resulting in increased bioavailability and potential adverse effects of many medications. These include amiodarone, buspirone, itraconazole, sertraline, and several anticonvulsants, benzodiazepines, calcium channel blockers, and *statins*. Other citrus fruits such as Seville oranges, limes, pomelos (an Indian grapefruit), and tangelos (a combination of pomelos and tangerines) can potentially produce the same effect. In recent years, there has been increased consumption of pomegranate juice, a fruit native to India and the Mediterranean region. Pomegranates appear to possess several medicinal properties including antimicrobial activity, antidiarrheal effects, and ability to reduce blood pressure and serum lipids. The juice may contain up to three times the antioxidant activity of red wine and green tea. There is, however, some data to suggest that the fruit can interact with drugs by inhibiting CYP450 (cytochrome P450) isoenzymes. An *in vitro* study concluded that pomegranate could weakly inhibit CYP2D6, thus potentially increasing the levels of drugs metabolized by this isoenzyme. These include a number of antidepressants, antipsychotic agents, narcotic analgesics, propoxyphene, tramadol, etc. There is also some evidence that pomegranate inhibits the 3A4 isoenzyme in the gastrointestinal tract, but not the liver. Animal studies, primarily in rats, indicate that the juice may produce a $\geq$ effect on CYP3A4 activity as compared to grapefruit juice. In most of these studies, the effect was dose dependent and did not extend beyond 72 hours. Other studies do not support a similar conclusion. There is one reported case of rhabdomyolysis in a patient drinking pomegranate juice while treated with rosuvastatin and ezetimibe. A causal relationship in this report appears remote. This particular *statin* is metabolized by the 2C9 isoenzyme. Lastly, an 8 ounce glass of pomegranate juice did not alter the clearance of intravenous or oral midazolam while grapefruit juice did increase bioavailability of the drug. In summary, there is currently little evidence that drugs metabolized by CYP450 isoenzymes will interact with pomegranate juice to the same extent they do with grapefruit juice. A daily 8 ounce serving of either of these juices should not produce a significant effect on metabolism and clearance of most drugs.

References:

- Farkas D, Oleson LE, Zhao Y, et al. Pomegranate juice does not impair clearance of oral or intravenous midazolam, a probe for cytochrome P450-3A activity: Comparison with grapefruit juice. J Clin Pharmacol 2007;47:286-94.
- Pomegranate. In: Jellin M, Gregory PJ, et al. Natural Medicines Comprehensive Database. www.naturaldatabase.com (Accessed 7/06/09).
- Summers KM. Potential drug-food interactions with pomegranate juice. Ann Pharmacother 2006;40:1472-3.

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