

Potential Drug Interactions With Grapefruit

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Drug(s)	Findings	Implications
Amiodarone (<i>Cordarone</i>)	Increases blood levels of the drug.	Watch for irregular heart rhythm.
Alprazolam (<i>Xanax</i>) Diazepam (<i>Valium</i>) Midazolam (<i>Versed</i>) Triazolam (<i>Halcion</i>)	Increases blood concentrations by inhibiting the intestinal metabolism.	Watch for possible increased sedation. Clinical significance on cognitive function is not known. One reference indicates alprazolam may have a small or negligible effect.
Buspirone (<i>BuSpar</i>)	Increases absorption and blood concentrations.	Despite significant effects, the action of the drug does not appear to be affected significantly.
Caffeine	Decreases caffeine metabolism.	Watch for possible increase in side effects, such as nervousness or insomnia.
Amlodipine (<i>Norvasc</i>) Diltiazem (<i>Cardizem</i>) Felodipine (<i>Plendil</i>) Nicardipine (<i>Cardene</i>) Nifedipine (<i>Procardia, Adalat</i>) Nimodipine (<i>Nimotop</i>) Nisoldipine (<i>Sular</i>) Verapamil (<i>Calan, Verelan</i>)	Increases blood concentrations, most likely the result of grapefruit inhibiting the intestinal metabolism.	Look for signs of toxicity, such as flushing, headache, fast heart rate, and low blood pressure. Some references dispute the clinical relevance of the interactions with amlodipine, diltiazem, and verapamil. However, there is considerable interindividual variability in the effect of grapefruit on drug metabolism.
Carbamazepine (<i>Tegretol</i>)	Increases blood concentrations.	Look for signs of toxicity, such as dizziness, poor balance and coordination, drowsiness, nausea, vomiting, tremor, and agitation.
Carvedilol (<i>Coreg</i>)	Increases blood levels.	The clinical significance of this interaction is not known.
Cyclosporine (<i>Neoral, Sandimmune</i>)	Increases blood concentrations.	Look for signs of toxicity, such as kidney and liver damage, and immune suppression.
Estrogens	Increases absorption and blood concentrations.	Effects are unknown at this time.
Fexofenadine (<i>Allegra</i>)	Might decrease oral absorption and blood	The clinical significance of this interaction is unknown. Tell

	levels.	patients it's best to take fexofenadine with a plain glass of water.
Atorvastatin (<i>Lipitor</i>) Lovastatin (<i>Mevacor</i>) Simvastatin (<i>Zocor</i>)	Increases absorption and blood concentrations. Grapefruit interaction unlikely with pravastatin (<i>Pravachol</i>) or fluvastatin (<i>Lescol</i>).	Look for increased toxicity, such as headache, GI complaints, and muscle pain.
Itraconazole (<i>Sporanox</i>)	Impairs absorption.	The clinical significance of this interaction is not known. Theoretically it could decrease efficacy of itraconazole.
Losartan (<i>Cozaar</i>)	Might reduce the blood levels of the drug.	Might reduce the effectiveness of losartan, but further studies are needed to determine significance.
Methylprednisolone (cortisone)	Increases plasma concentration of methylprednisolone.	Consumption of large amounts of grapefruit might increase the risk of adverse effects.
Quinidine	Decreases drug elimination.	The clinical significance of this interaction is unknown.
Sertraline (<i>Zoloft</i>)	Increases serum concentrations.	The clinical significance of this interaction is unknown.

Background

Grapefruit juice has been shown to affect the metabolism of several drugs. Included in the list of potential target drugs are diazepam, cisapride, cyclosporine, felodipine and other dihydropyridine calcium channel blockers, midazolam, nisoldipine, triazolam, saquinavir, lovastatin, and atorvastatin. The mechanism of this interaction appears to primarily result from inhibition of enzymes in the intestinal wall.

Several constituents of grapefruit juice have been implicated including the flavonoids naringin and naringenin, along with the furanocoumarins, bergapten and 6,7-dihydroxybergamottin. Unfortunately, the content of these varies between different grapefruit juices and varieties of fruit, making it impossible to determine if one is safer than another.

How Long Does the Inhibition Last?

In studies of healthy volunteers, the effect of grapefruit juice appears to last for at least three days following ingestion, and could perhaps be longer in some patients. For drugs that are significantly impacted by this interaction, one glass (8 ounces) of grapefruit juice is enough to cause the interaction, and following regular ingestion, the effect can last for up to three days following the last glass. Since most patients

take medications on a somewhat regular basis, it appears that the safest approach is to avoid grapefruit juice altogether.

Since these studies were done in healthy volunteers, patients who are taking these drug for diseases may have much greater and risky effects. It would be very difficult to say that these changes would not be important for real patients waiting to take their medication later in the day after ingesting juice. The only way to avoid these interaction is to advise patients to not ingest grapefruit juice. Other alternatives, such as orange juice, may be more appropriate.

In addition to grapefruit juice, many researchers are warning that the fruit itself could also cause problems. Several studies now indicate that the fruit should also be avoided in patients taking interacting drugs. Health Canada is now advising consumers NOT to drink grapefruit juice or eat grapefruit in any form if they are taking medications that might interact, until they have talked to their doctor or pharmacist about the potential for side effects.

While sweet oranges and their juice do not appear to cause the same reaction, sour orange juice such as that from Seville oranges, may have an effect similar to grapefruit juice. Preliminary research suggests lime juice might also have this effect. Tangelos are a hybrid of grapefruit and may also interfere with drugs. Most other citrus fruits, such as lemons, citrons, naturally sweet oranges and tangerines are considered safe.