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The Gravity of Weight

A Bitter Pill to Swallow: Grapefruit Juice and Medication

Some fruit juices may not be for breakfast anymore.

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Giuseppe Arcimboldo's "*The Summer*" (from "*The Seasons*"), 1563, Kunsthistorisches Museum, Vienna. Grapefruit is most commonly associated with potential interactions with medications, but many other fruits may decrease or increase medication blood levels.
Source: Wikimedia Commons/Public Domain.

We have all heard of the benefits of fresh fruit as part of a healthy diet. Fruits are rich in antioxidants that help protect against cell damage caused by exposure to unstable compounds called free radicals, and they have fiber that is naturally filling and may aid in digestion. Sometimes, however, fruit and fruit juices may interfere with a drug's pharmacokinetics and create a food-drug interaction. In other words, sometimes they can affect the bioavailability of a medication and may adversely interfere with blood levels, causing either lower levels of medication that are ineffective or higher levels that may be toxic. The juice most commonly implicated is grapefruit juice, but pineapple, pomegranate, and even some kinds of orange juice have also been found to interact with medications.

Canadian researcher David G. Bailey and his colleagues had discovered the interaction of grapefruit juice and medication serendipitously in the early 1990s. They had been experimenting with the effects of alcohol on felodipine, one of the calcium channel blockers, medications used to treat hypertension. Wanting to mask the taste of the alcohol, Bailey said they tried "every juice in a home refrigerator one Saturday evening." White grapefruit juice from frozen concentrate proved the most effective to disguise the taste, but unexpectedly, they found that their patients developed an increase in their heart rate, lower standing blood pressure, and orthostatic hypotension, as well as medication blood levels that were fivefold higher with grapefruit juice than when the medication was given with water. It turns out that the primary pathway by which grapefruit juice interfers with medications is by way of CYP3A4, an isoenzyme of the cytochrome P450 enzyme family, that is found in the small intestine. This cytochrome P450 family, incidentally, is the same one involved in the metabolism of the selective serotonin reuptake inhibitors such as fluoxetine (Prozac), and is, in fact, responsible for the metabolism of the majority of medications currently in use. As a result, when less of the medication is metabolized, more remains in the blood. In grapefruit juice, furanocoumarins are the main chemicals that are responsible for the toxic interaction.

The actual effect of the medication-grapefruit juice interaction is, though, quite variable among people, suggesting a genetic component. Furthermore, some patients are more susceptible to the effects because of preexisting (and particularly chronic) medical conditions such as hepatic insufficiency that predispose them to drug sensitivities and abnormal drug effects. In those susceptible, one glass of juice can be enough to affect blood levels and these effects can last for 24 hours and even become cumulative over time. Researchers believe that juice that is more concentrated and of a greater quantity causes "more marked interactions," but factors like storage and preparation of the juice can factor in as well.

Since that initial chance association, researchers have found the grapefruit juice-medication interaction is far more common than originally thought and as noted, occurred not just with grapefruit juice but with other juices and foods as well. For example, in a more recent study by Methlie and colleagues reported in the *European Journal of Endocrinology* (2011), both grapefruit juice and licorice increased cortisol levels in patients given exogenous cortisol for treatment of Addison's Disease, a disease (from which President John F. Kennedy suffered) characterized by a deficiency of the body's own cortisol. Increased medication levels have been seen with many medications, including beta blockers, cardiovascular drugs, statins for lowering cholesterol, benzodiazepines, antihistamines, anti-epileptics, anti-depressants, and immunosuppressants. Most interactions result in increased blood levels. Commonly used medications, such as methadone (a synthetic opioid), cyclosporine (used for psoriasis and rheumatoid arthritis), midazolam (Versed, used as a mild anesthetic for relaxation and sedation prior to surgery), triazolam (Halcion, used for sedation), verapamil (a calcium channel blocker used to treat hypertension), and sertraline (Zoloft, an anti-depressant), have been shown to have their blood levels affected by grapefruit juice. For the statins, (e.g. lovastatin (Mevacor), atorvastatin (Lipitor), and simvastatin (Zocor), all used to lower cholesterol, grapefruit juice seems to be associated with adverse effects such as muscle pains (myalgias) and rhabdomyolosis (rapid destruction of skeletal muscle.) With the medication fexofenidine (Allergra, used to treat allergies), grapefruit juice, orange juice, and even apple juice have been reported to reduce blood levels and hence its effectiveness.

Bottom line: Consult your physician and pharmacist about any known interactions your medication may have with common foods, juices, or even other medications. Some will be completely contraindicated, whereas others may suggest cautious use, particularly because there can be such individual variation in response. Sometimes medications will come with warnings, including a warning to wait four hours between drinking juice and taking a drug. For those interested in a more complete (but far from exhaustive) list of potential interactions, please see the review article by Seden and colleagues in the journal *Drugs*, 2010, "Grapefruit-drug Interactions."

Jan Matejko, "*Alchemist Sendivogius*," 1867. Museum of Art in Lodz, Poland. The old alchemists or apothecaries would mix together compounds to make primitive medicines.
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