Drug interactions with grapefruit

I was glad to see James Maskalyk's review of grapefruit and drug interactions,[1] as I have been concerned for some time about the need to increase awareness of this issue.[2,3] However, I would like to comment on drugs that were listed as if the effects were equal. Some patients enjoy grapefruit, and it is unkind to impose an unnecessary prohibition.

The magnitude of the grapefruit effect is related to the bioavailability of the drug. Felodipine, with a bioavailability of only 15%, had on average a tripling of blood levels with grapefruit, whereas nifedipine, with a bioavailability of 60%, had only a 30% increase in area under the curve (AUC). Amlodipine, which is approximately 80% bioavailable, is hardly affected by grapefruit.[4] Similarly, whereas simvastatin and lovastatin, which are only 5% bioavailable, have a 15-fold increase in AUC with grapefruit,[5,6] levels of atorvastatin increase only by 2.5-fold.[7]

I therefore tend to tell patients on amlodipine and atorvastatin that grapefruit is likely to have only a minor effect.

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Folic acid fortification: time for a concentrated effort

Vidia Persad and colleagues[1] nicely show that folic acid fortification of cereal grains is rapidly followed by a remarkable reduction in the incidence of spina bifida and anencephaly. Their data indicate that countries that do not fortify grain are allowing thousands of babies to be born each year with these preventable defects.[2,3]

As wonderful as this prevention is, data suggest that increased concentration of folic acid in flour would further reduce these birth defects. Although the rate of spina bifida that is not preventable with folic acid is unknown, data from a community trial in China showed that taking 400 mg/d of folic acid reduced the prevalence to about 6 per 10 000 in high- and low-risk areas.[4] The Chinese data suggest that increasing the concentration of folic acid in grains in Canada would reduce the incidence of spina bifida and anencephaly in Canada by least an additional 50%.

Before fortification, it was estimated that fortification at 140 mg/100 g of flour (the concentration required in the US and Canada) would increase the average women's daily consumption of folic acid by 100 mg. Some subsequent estimates suggest that the average woman consumes 200 mg/d of folic acid. The US Public Health Service and Institute of Medicine recommend that all women of reproductive age consume 400 mg/d of synthetic folic acid.

The US Centers for Disease Control and Prevention and the March of Dimes suggest that fortification concentration should be at least 350 mg/100 g of grain. In 2000 the UK Committee on Medical Aspects of Food and Nutrition Policy (COMA) recommended a concentration of 240 mg/100 g of grain.[5] Chile has implemented a concentration of 220 mg/100 g; however, women in Chile consume about twice as much flour as women in Canada and the United States.

Canadian nutrition regulators discouraged the US Food and Drug Administration from requiring fortification, saying that Canadians did not need folic acid fortification. Persad and colleagues have shown this not to be the case. Fortunately for Canadian children and their families, commercial interests forced Canadian regulators to adopt the US standard. Perhaps Canadian regulators will now show leadership in North America by increasing folic acid fortification concentration to at least 240 mg/100 g, as recommended by COMA.

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[Two of the authors respond:]

We thank Godfrey Oakley for his comments on our article[1] and agree that current folic acid fortification levels may be inadequate. Unfortunately, it is difficult to determine the lowest level needed to minimize the occurrence of open neural tube defects; some suggest that there is no need for fortification, although others recommend as much as 350 mg/100 g of grain. A consensus will be difficult to achieve. Meanwhile, it is important that further population-based studies on the effects of fortification be undertaken not only to help determine such a level but also to rule out theoretical adverse effects. It is also impor-