

# DRUG & THERAPEUTICS LETTER



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### Meals and medicines

Understanding the possible clinical implications of taking medicines with or without a meal is important for achieving quality use of medicines. Although the effect of food is not clinically important for many drugs, there are food-drug interactions which may have adverse consequences. Often these interactions can be avoided by advising the patient to take their medicines at the same time with respect to meals.

#### The effect of food on drug absorption

The formulation of a drug influences its absorption. Food can affect both the rate and extent of absorption.

Meals slow down gastric emptying

and this can delay drug absorption.

The composition of the meal influences the rate of gastric emptying eg. high fat meals lead to delayed gastric emptying. A delay in the drug reaching the small intestine can delay its subsequent absorption into the systemic circulation. Based on these observations, oral administration of a medicine under fasting conditions is often recommended when rapid absorption (and hence rapid onset of therapeutic effect) is needed. For most medicines, especially those used for chronic conditions, a delay in the onset of absorption is of no clinical consequence as long as the amount of drug absorbed is unaffected.

Food has the potential to either increase or decrease the extent of drug absorption. Understanding food-drug interaction mechanisms enables the clinician to provide appropriate advice to patients about taking medicines with respect to the timing and composition of meals. The effect of food depends on the physicochemical and pharmaco-

kinetic characteristics of the drugs. For example, the poorly water soluble antiretroviral drug saquinavir should be taken with food to allow bile enhancement of its dissolution which then facilitates absorption.

Delayed gastric emptying after a meal and the associated gastric acid secretions can reduce the bioavailability of some medicines that are acid labile. The constituents of a meal may also specifically interact with drugs. Calcium and other cations in food can form insoluble chelates with some medicines preventing their optimal absorption. Bisphosphonates are therefore recommended to be taken with plain water to prevent the formation of chelates which significantly reduce bioavailability.

Prescribing a drug regimen that fits in with the patient's daily routine can enhance the patient's adherence to treatment. This leads to the general recommendation that patients should take their medicines at prescribed and consistent times relative to their meals. This is despite the fact that the absorption of some medicines may be significantly reduced when taken with food, for example atorvastatin and thyroxine. Patients should also be informed if particular foods can interfere with their treatment such as

calcium rich foods chelate and reduce the absorption of tetracyclines and quinolones.

Some medicines (eg. NSAIDs and metformin) are taken with food to minimise the risk of gastrointestinal adverse effects. Repaglinide and the sulfonylureas should be taken before a meal to avoid the risk of significant hypoglycaemia. Similarly, taking acarbose with meals is essential to ensure its maximum efficacy in delaying the intestinal absorption of carbohydrates.

### **Interaction with Grape juice**

Co-ingestion of grape juice and certain drugs (eg. nifedipine, diazepam, cyclosporine, simvastatin, atorvastatin, saquinavir etc.) significantly increases their bioavailability because the constituents of the juice inhibit pre-systemic drug metabolism or transport. This increase in bioavailability can lead to excessive beneficial or adverse effects. The effects of grape juice are complex and have been widely studied.

A single glass of grape juice is enough to increase the bioavailability of some drugs. If the juice is drunk over several days the effects are long-lasting, so simply separating the dose

of medicine and the ingestion of grape juice does not prevent the interaction. For this reason grape juice ingestion should be avoided completely with certain drugs.

**Conclusion :** Meals may have variable and often unpredictable effects on drugs via a range of mechanisms. By understanding and appreciating the clinical consequences of these effects, health professionals can provide advice about the appropriateness of ingesting medicines with respect to the times and the composition of meals. This has become an important issue with significant impact on the quality use of medicines.

**Reference :**

Andrew Mc Lachlan and Iqbal Ramzan. Meals and medicines. Australian Prescriber 2006;29(4):40-2

***Brief Information***

**Drug Interactions with Macrolides**

The macrolide antibiotics (erythromycin, roxithromycin, clarithromycin and azithromycin) are well-known to interact with other drugs. The most commonly reported interacting drugs have been warfarin, statins, cisapride, anticonvulsants

and ergot derivatives. The basis for these interactions is considered to be cytochrome P450 , particularly 3A4. It is also possible that the interactions with warfarin have a mechanism which does not involve CYP3A4.

Roxithromycin is often considered to have less potential for interactions than erythromycin due to its much lower affinity for CYP3A4, but reports to ADRAC suggest otherwise. The majority of these have described interactions with warfarin but there are also reports of interactions with anticonvulsants, statins, digoxin and cyclosporine.

Clarithromycin, a potent inhibitor of CYP3A4, has a similar level of reported interactions. Azithromycin is considered to have little potential for interactions but of the 111 reports received to ADRAC for this drug, 6 have described interactions with either warfarin or tacrolimus.

Prescribers should be aware of the potential for interactions with all of the macrolides, especially with those medicines known to be subject to interactions such as warfarin, digoxin, anticonvulsants, statins and immunosuppressants, many of which also have a low therapeutic index.

### Drug Monitoring and Toxicology Laboratory

This laboratory under the Department of Clinical Pharmacology is providing services since 1987. It provides qualitative estimation of some drugs and quantitative estimation of phenobarbitone, phenytoin, carbamazepine, paracetamol, salicylate, theophylline and cholinesterase enzyme.

The total number of patients who utilized the service from October 2005 to March 2006 was 549. The summary of samples received by the laboratory during last 6 months is as follows:

S. No.	Drug / Enzyme	Reference range (normal limit)	Total samples	Results within normal limits	Results beyond normal limits
1.	Carbamazepine	4 -12 µg/ml	219	158	61
2.	Phenytoin	10 -20 µg/ml	134	37	97
3.	Phenobarbitone	15 – 40 µg/ml	30	21	9
4.	Paracetamol	10 – 20 µg/ml	41	7	34
5.	Cholinesterase	3500 – 8500 U/l	125	27	98
6.	Total	–	549	250	299

"Drug and Therapeutics Letter" is also available in the following websites:  
<http://www.teachinghospital.org.np/diu.html>, <http://www.iom.edu.np/diu.html>

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