by Sarah E. Bland, RPh
Column Editor: Lee Vermeulen, MS, RPh,
Director, Center for Drug Policy, University of Wisconsin Hospital and Clinics

Drug-Food Interactions

The use of computerized drug interaction screens, built into community pharmacy computer systems and used by many on-line, point-of-sale prescription claim adjudication systems, have become an important tool for pharmacists in preventing negative outcomes associated with drug-drug interactions. Food-drug interactions are more challenging (since food consumption is not documented on patient profiles), but often pose equally substantial risk of negative outcome. Consider this brief case-in-point adapted from the records of the University of Wisconsin Hospital and Clinics (this describes an actual case, but many details have been modified).

Case: A forty-nine year old male patient with a history of severe depression is placed on a monoamine oxidase inhibitor (MAOI) after failing on treatment with tricyclic antidepressants and selective serotonin re-uptake inhibitors. The patient was warned of possibly severe hypertensive reactions associated with the consumption of foods high in tyramine (a pressor amine) while on the MAOI. The patient remained adherent to a tyramine-free diet for several months, and was showing dramatic response to the new therapy. As the patient's depression diminished, his appetite returned, and on one occasion he consumed a substantial quantity of chocolate (known to contain some tyramine, but generally considered safe for consumption in moderation in tyramine-free diets). Two hours later, the patient presented to the Emergency Department complaining of a severe headache. A diagnosis of hypertensive crisis was made and treatment with nitroprusside was begun. Unfortunately, the patient suffered a stroke and died within 20 minutes of treatment initiation.

Despite the appropriate education and warnings provided by the patient's physician and pharmacist, this food-drug interaction caused the death of a patient. In this issue, Sarah Bland provides a thorough reference tool that can be referred to as patients are counseled on diet considerations that affect their medication therapy. It is critical that pharmacists remain aware of potential food-drug interactions, recognize that they will not be warned of potential interactions by their standard drug-drug interaction software, and intervene with information and education when necessary. —Lee Vermeulen

Summary

Interactions between foods and drugs can have profound influence on the success of drug treatment and on the side effect profiles of many drugs. The interactions are not always detrimental to therapy, but can in some cases be used to improve drug absorption or to minimize adverse effects. These interactions have received more attention recently, especially drug interactions with grapefruit juice. As new drug approvals occur with ever-increasing speed, there is less information available about their adverse effects and interactions when the drugs reach the market.

A second area of concern is the use of herbal medicines and dietary supplements. These products are not rigorously monitored, and may contain little if any of the substance indicated on the label. Some of the herbs used can interact adversely with prescription drugs. Two notable examples are ma huang (ephedra) and feverfew. Ma huang is a stimulant that can cause hypertensive crises in patients taking monoamine oxidase inhibitors. Feverfew has anticoagulant properties that can augment the effects of warfarin.

Most food-drug interactions occur through three mechanisms: reduced rate or extent of absorption, increased rate or extent of absorption, or through chemical/pharmacologic effects.

With some drugs, the presence of increased amounts of stomach acid results in the destruction of acid-labile drugs, such as penicillin G, ampicillin and dicloxacillin. In other cases, the components of the food, such as calcium or iron, may form complexes with the drug that are less easily absorbed. Examples include tetracycline, sodium fluoride and ciprofloxacin. The absorption of alendronate is impaired by food, calcium and almost everything, including orange juice and coffee. It should be taken with plain water and nothing else should be consumed for at least 30 minutes. In many cases, the actual mechanism by which food interferes with absorption is not known. Delayed absorption does not necessarily reduce the total overall exposure to the drug; the area under the curve (AUC) may be equivalent regardless of how the drug is taken.

Sarah Bland is a Clinical Pharmacist in the Center for Drug Policy and Clinical Economics, Department of Pharmacy, University of Wisconsin Hospital and Clinics, and is a Certified Specialist in Poison Information in the UW Hospital Poison Control Center.

A reduced rate of absorption may sometimes be useful in reducing the side effects of a drug, as in the case of ibuprofen, without reducing bioavailability.

The bioavailability of some drugs may be enhanced by food. For example, an acid environment is necessary for the absorption of ketoconazole. The absorption of griseofulvin is increased by fat in a meal. Fenofibrate, mebendazole, isotretinoin, tamsulosin, carbamazepine and labetalol are examples of drugs that will be better absorbed when taken with food. Improved absorption of a drug may or may not have a significant effect on the drug's efficacy.

Chemical or pharmacologic interactions occur through a wide variety of mechanisms. A very common interaction is that between beverage alcohol and drugs that have sedative effects. The effects of sedative drugs will usually be potentiated by the consumption of alcohol. Opiates, benzodiazepines and antihistamines are well-known examples of this phenomenon. Another alcohol-related interaction is the competitive inhibition of the enzyme aldehyde dehydrogenase, often called the "Antabuse®" reaction. Nausea, vomiting, flushing, dizziness and tachycardia may occur with exposure to alcohol in patients taking some cephalosporins, ketoconazole, metronidazole and sulfonylureas. In addition, chronic alcohol overuse can increase the toxicity of some drugs, as with acetaminophen and methotrexate, or reduce the drug's efficacy, as with phenytoin.

Components of food may antagonize the desired effect of the drug, as in the case of warfarin. Foods which are high in vitamin K, or which enhance vitamin K production by intestinal microorganisms, can reduce the effectiveness of warfarin in diminishing the body's supply of vitamin K, which is needed to activate clotting factors. Changing to a diet with increased consumption of leafy and/or dark green vegetables, such as spinach and turnip greens, could lessen the degree of anticoagulation made possible by warfarin by supplying additional vitamin K.

Perhaps the most feared food-drug interaction is that between monoamine oxidase inhibitors (MAOIs) and the amino acid tyramine, which is found in a variety of aged, fermented, overripe or pickled foods and beverages and, to a lesser extent, chocolate and yeast-containing foods. Tyramine is indirectly sympathomimetic. When its metabolism is suppressed, as it is by MAOIs, it can cause a significant release of norepinephrine, resulting in markedly increased blood pressure, cardiac arrhythmias, hyperthermia and cerebral hemorrhage.

The interaction between grapefruit juice and a variety of drugs has been widely reported. It appears that one or more flavonoids found in grapefruit juice inhibit some of the enzymes in the cytochrome P450 system. This results in reduced metabolism of drugs that are cleared by the same system; bioavailability may increase by as much as 200%. Patients should avoid drinking grapefruit juice for two hours before and four hours after taking drugs in this category. If the drug is in an extended-release dosage form, patients should wait until six hours have passed before drinking grapefruit juice.

Additional information about drug-food interactions can be found in these references:

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12. Lippman SB, Nash K. Monoamine oxidase inhibitor update: potential adverse food and drug interactions. *Drug Safety* 1990;5:195-204.
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Note: The list of drugs on the following pages includes only drugs that have been or are currently on the UW Hospital & Clinics formulary. The absense of a drug on this list does not necessarily mean that it has no drug-food interactions.

DRUG-FOOD INTERACTIONS

DRUG	EFFECT	NOTE
Acetaminophen	reduced rate of absorption; chronic alcohol ingestion increases hepatotoxicity	N *
Acetaminophen/ butalbital +/- caffeine	increased sedation with alcohol	*
Acetaminophen/ codeine	reduced side effects with food; increased sedation with alcohol	F *
Acetaminophen/ Hydrocodone	reduced side effects with food; increased sedation with alcohol	F *
Acetaminophen/ oxycodone	reduced side effects with food; increased sedation with alcohol	F *
Acetohexamide	altered glycemic control with alcohol	*
Alendronate	reduced absorption	E
Alfentanil	chronic alcohol use reduces sensitivity to alfentanil	*
Allopurinol	reduced side effects; reduced clearance of active metabolite with protein-poor diet	F *
Alprazolam	increased sedation with alcohol; clearance may be inhibited by grapefruit juice	*
Aminophylline	see theophylline	*
Amitriptyline	increased sedation with alcohol	*
Amlodipine	grapefruit juice inhibits metabolism slightly	*
Amobarbital	increased sedation with alcohol	*
Amoxapine	increased sedation with alcohol	*
Amoxicillin/ clavulanic acid	reduced side effects	F
Ampicillin	reduced absorption	E
Antacids (aluminum)	reduced effectiveness with high-protein meals	N
Aspirin	reduced side effects with food; increased GI blood loss with alcohol	F *
Aspirin/caffeine/ butalbital	reduced side effects with food; increased sedation with alcohol	F *
Astemizole	reduced absorption; metabolism may be inhibited by grapefruit juice	E *
Atenolol	reduced absorption	N
Atovaquone	greatly increased absorption, especially with fatty food	F

DRUG	EFFECT	NOTE
Azathioprine	reduced side effects	F
Azithromycin	reduced absorption	E
Baclofen	reduced side effects	F
Bethanechol	increased side effects	E
Bisacodyl	dissolves enteric coating	E
Bromocriptine	reduced side effects with food; increased side effects with alcohol	F *
Bumetanide	delayed onset; reduced efficacy	C
Buspirone	delayed rate but increased total absorption	N
Butalbital	increased sedation with alcohol	*
Calcium carbonate	increased absorption except with phytates and oxalates	N
Captopril	reduced absorption	C
Carbamazepine	increased absorption	F
Carbidopa/levodopa	slows rate of absorption; reduced side effects; dietary fiber increases absorption	C
Carvedilol	slows rate of absorption	N
Cefaclor	slows rate of absorption; peak levels reduced; AUC unchanged	E
Cefamandole	disulfiram reaction with alcohol	*
Cefixime	slows rate of absorption; decreased side effects	N
Cefoperazone	disulfiram reaction with alcohol	*
Cefotetan	disulfiram reaction with alcohol	*
Cefpodoxime	increased absorption	F
Cefuroxime	increased absorption	F
Cephalexin	slows rate of absorption	N
Cephradine	slows rate of absorption; reduces side effects	N
Cetirizine	slows rate of absorption; increased sedation with alcohol	*
Charcoal, activated	reduced efficacy when mixed with dairy foods, marmalade, simple syrup or cocoa	*
Chloral hydrate	increased sedation with alcohol	*
Chlorambucil	decreases bioavailability by 10 to 20 percent	N
Chlordiazepoxide	increased sedation with alcohol	*

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DRUG	EFFECT	NOTE
Chloroquine	reduced side effects	F
Chlorpheniramine	slows rate of absorption; GI side effects decreased; increased sedation with alcohol	*
Chlorpromazine	increased sedation with alcohol	*
Chlorpropamide	disulfiram reaction with alcohol	*
Chlorothiazide	increased absorption	C
Choline magnesium salicylate	reduced side effects; excretion de termined by urine pH	F
Cimetidine	increased blood alcohol levels; reduced caffeine clearance	*
Ciprofloxacin	dairy products decrease absorption; food delays rate of absorption; AUC unchanged	*
Cisapride	increased absorption; take 30 minutes ac for best effect; increases blood alcohol levels	N *
Clarithromycin	slows rate of absorption; may reduce GI side effects	N
Clomipramine	increased sedation with alcohol; metabolism reduced by grapefruit juice	*
Clonazepam	increased sedation with alcohol‡	*
Clonidine	increased sedation with alcohol; reduces side effects	N
Clorazepate	increased sedation with alcohol	*
Cocaine	alcohol increases cardiac toxicity of cocaine	*
Codeine	reduced side effects with food; increased sedation with alcohol	*
Conjugated estrogens	reduced side effects	F
Cyclobenzaprine	increased sedation with alcohol	*
Cyclosporine	may increase or delay absorption; fruit juice reduces absorption; grapefruit juice increases AUC†	C *
Cyproheptadine	increased sedation with alcohol	*
D-xylose	interference with test outcome; fast overnight & 5 hrs post-test	E
Danazol	increased absorption	C
Dantrolene	increased sedation with alcohol	*
Delavirdine	increased absorption when taken with acidic juices	C
Demeclocycline	reduced absorption	E
Desipramine	increased sedation with alcohol	*
Dextroamphetamine	acidic juices reduce absorption; foods which acidify urine increase clearance	C
Diazepam	may increase absorption; increased sedation with alcohol	C
Diclofenac	reduced peak concentration but not extent of absorption; reduced side effects	F
Dicloxacillin	decreased absorption	E
Didanosine	decreased absorption	E
Diethylstilbestrol	reduced side effects	F
Diphenoxylate/ atropine	increased sedation with alcohol	*
Dipyridamole	caffeine reduces effect of drug	*
Digoxin	slows rate of absorption; decreased absorption with high-fiber foods	N *
Diltiazem	increased absorption	C
Dimenhydrinate	increased sedation with alcohol	*
Diphenhydramine	increased sedation with alcohol	*
Disulfiram	alcohol intolerance	*
Divalproex sodium	delayed absorption; reduced side effects with food; increased sedation with alcohol	F *
Doxepin	increased sedation with alcohol	*
Doxycycline	reduced side effects; reduced absorption with milk; reduced efficacy with alcohol	F *
Doxylamine	increased sedation with alcohol	*
Dronabinol	reduced rate of metabolism with alcohol	*
Enalapril	increased bioavailability with fats and grapefruit juice	C
Erythromycin	increased/decreased absorption depending on form; avoid high fat meals with P.C.E.	*
Erythromycin/ sulfisoxazole	reduced side effects	F
Ethinyl estradiol	reduced side effects	F
Ethionamide	reduced side effects	F
Etidronate	reduced absorption	E
Etretinate	increased absorption with high-fat foods	C
Felbamate	reduced side effects	F
Felodipine	bioavailability markedly increased by grapefruit juice and fatty meals	*

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DRUG	EFFECT	NOTE
Ferrous sulfate	maximal absorption on empty stomach; reduced side effects; ascorbic acid increases absorption; tea, coffee and cocoa reduce absorption	*
Flecainide	reduced side effects	F
Fludrocortisone	reduced side effects	F
Fluoxetine	reduces rate of absorption	N
Fluphenazine	increased sedation with alcohol	*
Flurazepam	increased sedation with alcohol	*
Fluvastatin	delayed absorption, reduced peak levels (not clinically significant)	N
Furazolidone	disulfiram reaction with alcohol; tyramine precautions	*
Furosemide	reduced absorption	C
Gabapentin	enhanced absorption with protein	C
Ganciclovir	increased absorption	F
Glipizide	delayed absorption; take 1/2 hour before meal; disulfiram reaction, prolonged hypoglycemia with alcohol	*
Glutethimide	increased sedation with alcohol	*
Glyburide	disulfiram reaction, prolonged hypoglycemia control with alcohol	*
Granisetron	increased peak levels, lower total systemic exposure	N
Griseofulvin	increased rate or extent of absorption with fats; reduced side effects with food; disulfiram reaction with alcohol	F *
Guanethidine	increased vasodilation with alcohol	*
Haloperidol	reduced side effects; increased sedation with alcohol	N *
Hydralazine	variable effects on absorption; reduced hypotensive effects with food in some patients	C *
Hydrochlorothiazide	reduced peak levels and AUC	C
Hydrocodone	increased sedation with alcohol	*
Hydrocortisone	slows rate of absorption; reduced peak levels; reduced side effects	F
Hydromorphone	increased sedation with alcohol	*
Hydroxychloroquine	reduced side effects	F
Hydroxyzine	increased sedation with alcohol	*
Ibuprofen	reduced side effects	F
Imipramine	increased sedation with alcohol	*
Indinavir	reduced absorption with fat, proteins; slightly decreased AUC with grape fruit juice	E *
Indomethacin	slows rate of absorption; reduced side effects	F
Insulin	prolonged hypoglycemia with alcohol	*
Iron preparations	see ferrous sulfate	F
Isocarboxazid	tyramine precautions; increased sedation with alcohol	*
Isoniazid	reduced absorption with food; disulfiram reaction, increased hepatotoxicity, and reduced INH levels with alcohol	E *
Isosorbide dinitrate	delayed absorption	E
Isotretinoin	increased absorption with food; disulfiram reaction with alcohol	F *
Isradipine	delayed absorption	N
Itraconazole capsules	increased absorption	F
Itraconazole solution	reduced bioavailability	E
Ketoconazole	delayed absorption with food; disulfiram reaction with alcohol	N *
Ketorolac (oral)	delayed absorption; reduced side effects	F
Labetalol	increased absorption	C
Lansoprazole	slows rate of absorption	E
Levamisole	disulfiram reaction with alcohol	*
Levodopa	see carbidopa/levodopa	C
Levofloxacin	di- and trivalent cations reduce absorption	*
Levorphanol	increased sedation with alcohol	*
Levothyroxine	reduced absorption; anionic exchange resins reduce absorption (Product information-Synthroid(R))	E *
Lithium	reduced side effects with food	F
Loracarbef	slows rate of absorption	N
Loratadine	delayed absorption, increased peak levels	C
Lorazepam	increased sedation with alcohol	*
Losartan	delayed absorption, AUC decreased somewhat	N
Lovastatin	increased absorption (except reduced absorption with high-fiber foods)	N *
Loxapine	increased sedation with alcohol	*

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DRUG	EFFECT	NOTE
Mag/Al/simethicone	high-protein foods decrease efficacy	*
Magnesium/ aluminum hydroxide	high-protein foods decrease efficacy	*
Mebendazole	increased absorption	F
Mecamylamine	delayed absorption with food (may permit more gradual onset of effects)	F *
Meclizine	increased sedation with alcohol	*
Meclofenamate	reduced absorption; reduced side effects	F
Mefloquine	reduced side effects	F
Melphalan	reduced absorption	E
Meperidine	reduced side effects; increased sedation with alcohol	F *
Meprobamate	increased sedation with alcohol	*
Mercaptopurine	reduced absorption; reduced side effects	C
Mesalamine	slows rate of absorption	N
Mesoridazine	reduced side effects; increased sedation with alcohol	F *
Metformin	decreases rate and extent of absorption; alcohol potentiates its effects on lactate metabolism; reduced side effect	C *
Methadone	reduced side effects; increased sedation with alcohol	F
Methenamine	foods which alkalize urine may reduce efficacy	*
Methocarbamol	increased sedation with alcohol	*
Methohexital	increased sedation with alcohol	*
Methotrexate	reduced absorption with food; increased hepatotoxicity with chronic alcohol use	E *
Methoxsalen	increased absorption; reduced side effects	F
Methylprednisolone	reduced side effects	F
Methysergide	reduced side effects	F
Metoclopramide	take 30 minutes ac for best effect; increases rate of absorption of alcohol	*
Metoprolol	increased absorption	C
Metronidazole	reduced side effects with food; disulfiram reaction with alcohol	F *
Mexiletine	reduced side effects; slows rate of absorption; reduces rate of caffeine clearance	F
Midazolam	increased sedation with alcohol; bioavailability increased by grapefruit juice	*
Minocycline	dairy products decrease absorption	*
Mirtazepine	increased sedation with alcohol	*
Misoprostol	delayed absorption; reduced side effects	F
Moexipril	reduced absorption	E
Molindone	increased sedation with alcohol	*
Morphine solution	increased absorption; increased sedation with alcohol	F *
Morphine sulfate	increased sedation with alcohol	*
Moxalactam	disulfiram reaction with alcohol	*
Mycophenolate	slows rate of absorption	C
Nabumetone	increased absorption; reduced side effects	F
Nafcillin (oral)	reduced absorption	E
Naproxen	reduced side effects	F
Nefazodone	reduced bioavailability, slows rate of absorption; may potentiate alcohol	C
Nelfinavir	greatly increases absorption and AUC	F
Niacin	reduced absorption; decreases side effects	F
Nicardipine	reduced absorption	E
Nicotine polacrilex	reduced absorption in presence of acidic substances such as coffee or cola	*
Nifedipine capsules	reduces rate of absorption reduced side effects; grapefruit juice increases AUC†	C *
Nifedipine ERT ***Adalat CC** ****Procardia XL**	depends on brand *delayed absorption **minimal effects; grapefruit juice increases AUC†	* E ** C *
Nisoldipine	reduced rate of absorption grapefruit juice inhibits metabolism	*
Nitrendipine	grapefruit juice greatly enhances bioavailability	*
Nitrofurantoin	increased absorption with food	F *
Norfloxacin	dairy products decrease absorption	*
Nortriptyline	increased sedation with alcohol	*
Olanzapine	increased sedation and orthostatic hypotension with alcohol	*
Olsalazine	increased efficiency of drug	F
Omeprazole	delayed absorption	E
Ondansetron	increased absorption	N

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DRUG	EFFECT	NOTE
Opium tincture	increased sedation with alcohol	*
Oxacillin	reduced absorption	E
Oxazepam	increased sedation with alcohol‡; low calorie diet may decrease metabolism	*
Oxybutynin	increased peak serum levels	C
Oxycodone	reduced side effects; increased sedation with alcohol	*
Oxytocin	reduced efficacy with alcohol	*
Pancreatin	alkaline foods dissolve enteric coating	*
Penicillamine	reduced absorption	E
Penicillin G	reduced absorption	E
Penicillin VK	reduces and prolongs peak serum level; extent of absorption unchanged	N
Pentazocine	increased sedation with alcohol	*
Pentobarbital	increased sedation with alcohol	*
Pentoxifylline	delayed absorption; reduced side effects	F
Pergolide	reduced side effects	F
Perphenazine	reduced GI side effects; increased sedation with alcohol	F
Phenelzine	tyramine precautions	*
Phenobarbital	increased sedation with alcohol	*
Phenytoin	increased absorption with food; increased phenytoin metabolism with chronic alcohol use	C *
Piroxicam	slows rate of absorption; reduced side effects	F
Potassium salts	reduced side effects	F
Prazosin	variable effects	C
Prednisolone	reduced side effects	F
Prednisone	reduced side effects	F
Primidone	increased sedation with alcohol	*
Procainamide	reduced side effects; increased absorption with fat	F
Procarbazine	tyramine precautions; disulfiram reaction and increased sedation with alcohol	*
Prochlorperazine	increased sedation with alcohol	*
Promethazine	increased sedation with alcohol	*
Propafenone	increased absorption	C
Propoxyphene	slows rate of absorption; increased toxicity of propoxyphene with alcohol	*
Propranolol	slows rate but increases extent of absorption; efficacy reduced by alcohol	F *
Propylthiouracil	variable effects	C
Protriptyline	increased sedation with alcohol	*
Pseudoephedrine	delayed absorption	N
Pyridostigmine	delays time to peak plasma level	N
Quazepam	increased sedation with alcohol	*
Quetiapine	increased peak concentration and AUC; potentiates the effects of alcohol	C *
Quinacrine	reduced side effects; disulfiram reaction with alcohol	F *
Quinapril	delayed absorption	N
Quinidine	variable effects; grapefruit juice reduces both absorption and metabolism; clinical significance unknown	C *
Quinine	reduced side effects	F
Raloxifene	increased absorption	N
Rescinnamine	reduced side effects	F
Reserpine	reduced side effects	F
Rifabutin	high-fat meal delays absorption; food reduces side effects	N
Rifampin	delayed absorption	E
Ritonavir capsules	increased absorption	F
Ritonavir liquid	slightly reduced absorption	N
Salsalate	delayed absorption; reduced side effects	F
Saquinavir	increased absorption; grapefruit juice increases bioavailability	F *
Secobarbital	increased sedation with alcohol	*
Selegilene	tyramine precautions	*
Sertraline	increased absorption; reduced side effects	N
Simvastatin	absorption may be reduced by high-fiber meal	*
Sodium chloride	reduced side effects	F
Sodium fluoride	foods, especially dairy foods, reduce bioavailability	*
Sotalol	reduced absorption	C
Spironolactone	increased absorption; reduced side effects	F
Sucralfate	reduced efficacy	E

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DRUG	EFFECT	NOTE
Sulfasalazine	reduced side effects	F
Sulfinpyrazone	reduced side effects	F
Sulfisoxazole	reduced side effects	F
Sulindac	reduced absorption; reduced side effects	F
Tacrolimus	reduced absorption; grapefruit juice reduces metabolism	E *
Temazepam	increased sedation with alcohol‡	*
Terbinafine	potentiates caffeine by reducing its clearance	*
Tetracycline	reduced absorption, especially when taken with antacids or dairy products	E
Theophylline	reduced absorption (increased absorption from SR products in children is possible);reduced side effects; high fat meal increases absorption; high carbohydrate diet reduces absorption; high caffeine intake inhibits metabolism	C
Thiopental	increased sedation with alcohol	*
Thioridazine	increased sedation with alcohol	*
Thyroid	reduced absorption	E
Ticlopidine	increased absorption; reduced side effects	F
Tolazamide	disulfiram reaction, prolonged hypoglycemia with alcohol	*
Tolazoline	disulfiram reaction with alcohol	*
Tolbutamide	disulfiram reaction, prolonged hypoglycemia with alcohol	*
Tolmetin	reduced absorption; reduced side effects	F
Topiramate	reduces rate of absorption; increased sedation with alcohol	N *
Tranylcypromine	tyramine precautions	*
Trazodone	delayed absorption; reduced side effects; increased sedation with alcohol	F *
Triamterene	high-potassium foods or salt substitutes may cause hyperkalemia	*
Triazolam	reduced rate of absorption with food; increased sedation with alcohol; AUC increased by 50% by grapefruit juice	E *
Trifluoperazine	increased sedation with alcohol	*
Trihexyphenidyl	increased sedation with alcohol	*
Trimethoprim	reduced absorption; reduced side effects	N
Trimipramine	increased sedation with alcohol	*
Troglitazone	increased absorption	F
Typhoid vaccine (oral)	reduced absorption	E
Ursodiol	may reduce side effects	F
Valproate sodium	reduced side effects; increased sedation with alcohol	F *
Valproic acid	delayed absorption, reduced side effects; increased sedation with alcohol	F *
Venlafaxine	reduced side effects; may potentiate effects of alcohol	F *
Verapamil	grapefruit juice increases AUC†; blood alcohol levels may be increased; prolongs half-life of caffeine	*
Warfarin	large amounts of vitamin K-containing foods may reduce efficacy; alcohol consumption may increase anticoagulation; garlic may increase anticoagulation	*
Zafirlukast	reduced absorption	E
Zalcitabine	reduced peak concentration and bioavailability	E
Zidovudine	reduced absorption when taken with high-fat foods	*
Zinc salts	reduced absorption, reduced side effects	N
Zolpidem	reduced absorption; reduced side effects	C

Sources:

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‡—Tatro DS, Olin BR, Hebel SK (eds): Drug Interaction Facts. Facts and Comparisons, St. Louis, Missouri, 1996.

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ACTION KEY: **C**—take with or without food, but be consistent; **E**—take on an empty stomach; **N**—no specific action necessary, but consistency may be advised; **F**—take with food; ***—specific action/precaution as in food effects column