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Oct 2005 "Food/Drug Interactions" 707-000-05-010-H01

DEADLINE FOR US TO RECEIVE QUIZZES & HAVE THEM COUNT FOR 2005 IS NOVEMBER 30, 2005.

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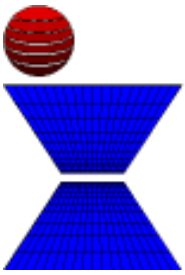

THIS MONTH
"Food/Drug Interactions"

QUIZ DEADLINE FOR THIS YEAR = NOVEMBER 30, 2005.

Food/drug, supplement/drug, and herb/drug interactions are significant. Our goal is to provide appropriate information that can be shared with patients. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings.

The program ID # for this lesson is 707-000-05-010-H01.
Pharmacists completing this lesson by October 31, 2008 may receive full credit.

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. List the mechanism of drug/food interactions.
2. Describe the role of cytochrome P450 in drug metabolism.
3. Identify the drugs that can interact with grapefruit.
4. Acknowledge the ingredients in grapefruit that may trigger interactions.
5. Relate common herd/drug interactions.

INTERACTIONS THAT MAY OCCUR BETWEEN DRUGS & FOOD; DRUGS & DIET SUPPLEMENTS; OR DRUGS & HERBAL PRODUCTS

Food and dietary supplements can influence the efficacy or safety of concurrently taken drugs due to potential for the occurrence of an interaction. Drug-food interactions have become increasingly important due to complexity of many therapeutic approaches, especially in the elderly. Awareness of potential drug-food interactions is essential in the prevention of potential problems that may occur. Patient counseling, labeling systems and the selection of the most appropriate time and frequency of administration are helpful in achieving optimal use of the medication.

The frequency of drug-food interactions is much higher in the elderly due to the number of drugs prescribed for these patients and age-related physiological changes that may affect the pharmacokinetic as well the thermodynamic properties of the administered drugs.

MECHANISMS OF DRUG-FOOD INTERACTIONS

These interactions can be classified into 2 categories: 1) pharmacokinetic; and, 2) pharmacodynamic interactions.

Pharmacokinetic Interactions

Pharmacokinetic interactions, the most common, are those that affect absorption, distribution, metabolism or excretion of drugs.

Drug Absorption: Changes in the rate of drug absorption may be due to **chelation, adsorption, changes in gastric acidity, gastrointestinal motility and urinary pH**. Even though these interactions are common, they are occasionally of clinical significance.

Chelation is the combining of metallic ions with certain heterocyclic ring structures, resulting in the formation of a complex whose ions are held by chemical bonds. Antibiotic absorption may be hindered as a result of chelation with dietary multivalent ions such as calcium, magnesium or iron. Such ions are found in fortified and unfortified diets. Calcium found in milk, dairy or non-dairy-fortified products might form complexes with tetracycline and fluoroquinolones, resulting in a decrease in the absorption of these drugs. The intake of milk with the laxative bisacodyl should be avoided because it may dissolve the outer enteric coating of the drug in the stomach, causing pain and gastritis. Absorption of ciprofloxacin may be significantly reduced if taken with dairy products or calcium-fortified orange juice alone; however, the drug may be taken with a meal that includes these products.

Adsorption is a phenomenon that occurs as a result of adhesion of a substance to the surface of another one without covalent bonding. For example, dietary fiber (i.e., bran) can diminish the absorption of penicillins. Ingestion of digoxin concurrently with high amounts of dietary fiber, such as that recommended for patients with hypercholesterolemia, can reduce the bioavailability of digoxin by 16% to 32%. This interaction is significant due to the narrow therapeutic index of digoxin. A dosage adjustment may be required. A number of drugs, that are insoluble in the GI tract, and possess a large surface area (i.e., kaolin, or activated charcoal) can adsorb other drugs onto their surface. Guar gum, a thickening agent utilized in foods such as low-fat sauces and salad dressings, may delay absorption of the antidiabetic drug, glucophage.

Changes in gastric pH can alter drug absorption. The concentration of drug solutions in the intestine available for absorption is governed by the dissolution rate of the drug. Weak basic drugs have a slow dissolution rate at a higher pH, whereas weakly acidic drugs dissolve rapidly in such an environment. In general, the intake of water with drugs has no detrimental effect on drug absorption. However, diminished absorption of drugs may occur

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if they are taken with acidic liquids such as fruit juice, vegetable juice or carbonated beverages. A meal rich in fat may cause a delay in the gastric emptying rate. Such meals resulted in reduction in blood concentration of indinavir by 84% when compared to low-fat meals. Conversely, similar meals caused an increase in the bioavailability of saquinavir.

Changes in urinary pH may affect the rate of urinary clearance of a drug. Acidic drugs may be eliminated at a faster rate in alkaline urine. Alkalinization of urine may be achieved by the intake of basic elements such as calcium or magnesium.

Drug Distribution: Factors such as ratio of lean body weight to body fat or binding of drugs by serum protein (i.e., albumin) can affect drug distribution. Higher body fat can increase the half-life of lipid-soluble drugs, and, therefore, increase duration of drug action.

Drug Metabolism: Drugs, nutrients, as well as dietary supplements, may alter the activity of a metabolic enzyme system (Cytochrome P450—abbreviated CYP) when taken concurrently with certain drugs, causing either an increase or a decrease in the metabolic process. Certain fruits, vegetables, minerals, vitamins, herbs, spices, and teas can result in induction (stimulation) or inhibition of the enzyme system that is responsible for metabolism. Cytochrome P450 constitutes a vast multigene family of hemeothiolate proteins widely distributed in the endoplasmic reticulum of cells throughout the body, especially in the liver and intestinal wall. These enzymes are involved in the oxidative biotransformation of a variety of endogenous and exogenous compounds such as drugs, environmental chemicals and other xenobiotics. There are approximately 1000 known cytochrome P450 enzymes, forty of which are active in human beings. These enzymes are divided into 17 families and numerous subfamilies. The most abundant and active subfamily of cytochrome P450 is CYP3A4. This subfamily represents approximately 30% of CYP contents in the liver and 70% in the intestinal tract. Cytochrome P450 (CYP)3A4, a metabolizing system, can be affected by diet and may result in a clinically significant interaction when food is taken with drugs that are substrate to the enzyme. For example, grapefruit juice, St. John's wort, and red wine are intestinal but not hepatic CYP3A4 inhibitors and may reduce the bioavailability of concurrently taken drugs. This interaction may require dosage adjustment to maintain a therapeutic blood concentration. Other drug-food interactions that result in alteration of metabolism (involve CYP1A2, CYP2E1 and glucuronosyltranferase) have been reported. Many of those interactions were clinically insignificant. Diets rich in protein and carbohydrates may stimulate hepatic metabolism of some drugs.

Drug excretion: The major portion of a drug dose is eliminated in the urine. Diets that alter the pH of the urine may affect the duration of the drug in the circulation.

Thermodynamic Interaction

Changes in drug action may occur as a result of food-drug interactions. Foods rich in vitamin K such as cabbage, brussel sprouts, asparagus, lettuce, spinach, avocado and liver, can antagonize the activity of warfarin and should be avoided. This interaction occurs as a result of the role of vitamin K in activating coagulation. Another example may occur because soybeans, peanuts and the above vegetables contain goitrogens that affect thyroid activity and can lead to goiter.

DRUG-DIETARY SUPPLEMENT INTERACTIONS

In 1997, over $17 billion dollars were spent in the USA on dietary supplements and $5 billion dollars on herbal products. With increased health awareness, the number of health food and nutritional supplement retail stores are on the rise. Food manufacturers not only list the nutrition facts of many of their products, but when possible, fortify the products with multivalent cationic minerals, such as calcium, iron, magnesium, and vitamins, such as C, A, D, E, and B complex. The percentage daily value (DV) of the US recommended daily allowance based on a 2000 caloric diet is usually listed. A review of listed percentages of fortified foods shows that supplements may include up to 100% of DV. For example, one cup (8 fl. oz.) of nonfat milk contains 30% DV of calcium, 25% of Vitamin D, 10% of vitamin A and 25% of phosphorus. One serving of breakfast cereal contains 100% DV of certain vitamins and minerals. Calcium-fortified soymilk contains 30% DV of calcium, 30% of vitamin D, 50% of riboflavin, 50% vitamin B-12, 6% folate, and 4% zinc. Calcium carbonate is the source of calcium in this product. Calcium fortified orange juice contains 35% DV of calcium. As indicated earlier, calcium tends to chelate antibiotics, especially

tetracycline, if taken concurrently. In addition to fortified-calcium products, consumers receive additional amounts of calcium from vegetables and other foods. A person who consumes a small glass of calcium-fortified orange juice for breakfast, along with one cup of breakfast cereal, and a cup of non-fat milk, will have taken 165% DV of calcium from that meal. This does not take into account that more than one serving of food is often consumed. The calcium contained in one meal is equivalent to the contents in 2 tablets of calcium carbonate used as an antacid. Additionally, foods such as vegetables, herbs, spices and teas, may contain phytochemicals that may induce or inhibit the activity of drug-metabolizing enzymes. Other dietary constituents such as fat, protein, carbohydrates and fiber may play roles in the absorption rate of drugs. A potentially serious interaction may result from the intake of herbal dietary supplements. Thus, the increased use of dietary supplements as well as the increased health awareness present a challenge to health professionals, since interactions between foods with dietary and herbal supplements can inadvertently intensify or diminish the effects of drugs, resulting in reduced therapeutic effects or increased toxicity.

DRUG-HERBAL DIETARY SUPPLEMENT INTERACTIONS

In a survey conducted recently, it was revealed that 49% of Americans used herbal dietary supplements occasionally, and 24% used these supplements regularly, often concurrently with prescription or OTC medications. These supplements are used by the elderly, by pregnant and nursing mothers and are administered to children. Even though the efficacy of such products is based on claims and anecdote, they are taken to treat anxiety, depression, memory loss, headache, weight-gain, prostate hyperplasia, and cancer. More importantly, patients often purchase these products outside the pharmacy and fail to inform their physician or pharmacist. About 20% of Americans take prescription medications concurrently with at least 1 herbal product, a multivitamin preparation, or both. The most widely used herbs are St. John's Wort, ginseng, ginkgo, echinacea and garlic.

St. John's Wort

St. John's Wort, which is often used to treat depression, is a CYP3A4 inducer and may increase the metabolism of certain concomitantly taken drugs. Reports have shown that St. John's Wort may cause a reduction in the blood level of indinavir, cyclosporine and digoxin. The interaction between St. John's Wort and oral contraceptives (ethinyl estradiol) resulted in incidences of breakthrough bleeding and pregnancies. When taken with selective serotonin reuptake inhibitors, St. John's Wort caused hypertension. St. John's Wort seems to reduce the effect of sildenafil (Viagra®). It apparently reduces the efficacy of warfarin.

Ginseng (Panax ginseng)

Ginseng was reported to have caused a reduction in international normalized ratio (INR) in a patient with established warfarin anticoagulation. Other reports indicated that bleeding episodes occurred in persons consuming ginseng, but not taking warfarin.

Ginkgo Biloba

Ginkgo is claimed to improve memory. An interaction of ginkgo and warfarin was reported in one case. A woman who was taking warfarin for five years suffered from an intracerebral hemorrhage two months after she began taking ginkgo.

Echinacea

Echinacea is a commonly used herbal product for treating cold symptoms. This has varying effects on the metabolizing enzymes CYP3A, CYP1A2, CYP2D6, and CYP2C9 in healthy persons. A study indicated that the administration of 400 mg of echinacea for 8 days resulted in the inhibition of CYP1A2 and intestinal CYP3A, while hepatic CYP3A was induced and no effect was observed on CYP2C9 and CYP2D6.

Garlic (Allium sativum)

The intended use of garlic is to treat blood presence or reduce blood cholesterol and thrombus formation. In vivo studies have shown that garlic inhibits CYP3A4, resulting in an increase in blood concentration of the metabolizing enzyme substrate drugs. The administration of garlic resulted in 50% decrease in the HIV protease, saquinavir. Garlic is reported to inhibit platelet aggregation and potentiate the effect of other platelet inhibitors. It may also increase the anticoagulant effect of warfarin.

DRUG-DIET INTERVENTION

Vegetables

As stated earlier, vegetables rich in vitamin K, such as cabbage, brussel spouts, asparagus, lettuce, spinach, and avocado, may antagonize the therapeutic action of warfarin. Carrots and celery may decrease the CYP1A2 activity. Fluvoxamine (an antidepressant) is an inhibitor of CYP1A2. Caffeine, found in coffee and carbonated beverages, is a substrate for this enzyme. The intake of fluvoxamine with caffeine may cause in intoxication of the drug.

Tyramine Containing Foods

The intake of tyramine-rich foods and monoamine oxidase inhibitors (MAOI) can result in a potentially fatal interaction that is characterized by palpitation, sweating, headache and hypertensive crises that could result in cerebral hemorrhage. Tyramine is a sympathomimetic agent, and inhibition of its metabolites by MAOI causes the interaction. Foods that contain tyramine include broad bean pods, yeast concentrate, salted, smoked or pickled fish, aged cheese (blue cheese, cheddar, Swiss or parmesan), over-ripe fruits, fermented beverages (wine or beer), tofu and soybeans.

Wine

It has been reported that the consumption of moderate amounts of red wine can be beneficial to the cardiovascular system due to the presence of antioxidants; however, it also contains flavonoids and other polyphenols that may inhibit CYP3A4. White wine, which lacks flavonoids and other antioxidants that are found in red wine, has no effect on CYP3A4.

Orange Juice

Most orange and tangerine juices have no effect on CYP3A4. However, it has been reported that orange juice obtained from Seville oranges has grapefruit-like effects. The intake of a glassful of this type of orange juice can produce a 76% increase in felodipine (Plendil®) exposure. This action is believed to be due to presence of dihydroxybergamottin, a bioflavonoid found in grapefruit, but not in the other types of oranges.

Grapefruit Juice

Grapefruit juice is a popular beverage that is consumed by 20% of the households in the USA. It has been found that grapefruit juice can markedly augment the bioavailability of certain drugs when concurrently ingested. This phenomenon was first observed when patients who ingested felodipine (Plendil®) with grapefruit experienced a lower blood pressure and a higher incidence of orthostatic hypotension compared to intake of the drug with a meal devoid of grapefruit juice. This chance observation took place during a study that was designed to investigate the potential for an interaction between felodipine and alcohol. To mask the taste of alcohol in the preparation, grapefruit juice was added. When the mixture of felodipine, alcohol and grapefruit was taken, the aforementioned adverse effects were noticed. The intake of the same preparation without grapefruit caused no adverse reactions. Subsequent studies confirmed that grapefruit juice was the culprit. It was revealed that while the plasma felodipine concentrations were not different between treatments, they were five-fold greater with grapefruit juice, compared to ingesting the drug without the juice. It was concluded that grapefruit juice significantly increased the oral availability of felodipine. The interaction between certain drugs and grapefruit juice appears to take place due to the inhibiting effects of grapefruit juice on one of the intestinal cytochrome enzymes, CYP3A4.

The effect of grapefruit juice appears to be limited to the CYP system in the intestinal mucosa, but has no effect on the liver enzyme system. When a medication that interacts with grapefruit juice is taken, it first undergoes metabolism by the enzyme CYP3A4 found in the intestine. Grapefruit juice has no effect on intravenously administered drugs. When grapefruit was ingested with felodipine, a marked elevation of plasma peak concentration (C_{max}) and plasma area under the curve (AUC) occurred. However, this combination did not affect systemic elimination. The fact that felodipine did not have an effect on the pharmacokinetics of intravenously administered drugs indicates that the pharmacokinetics that occurred have done so as a result of presystemic (first-pass) metabolism. It is recognized now that grapefruit juice selectively inhibits the CYP3A4 enzymes in the intestinal wall, but does not alter liver enzymes. It has been estimated that grapefruit juice intake for 5 days resulted in a mean 62% reduction of the intestinal wall contents of CYP3A4. Ingestion of the juice caused 47% reduction in the amount of this enzyme in the intestine within 4 hours, and its effect lasted up to 24 hours. Grapefruit juice acts as a CYP3A4 inhibitor in vitro, but not in vivo. The effect of certain drugs that inhibit CYP3A4 appears to decline with repeated administration. However,

this is not the case with grapefruit juice whose inhibitory action continued undiminished with recurrent ingestion. The extent of grapefruit juice-drug interaction varies from one individual to another, depending on factors inherent to the individual. In general, inhibition of CYP3A4 occurs following ingestion of 1 glass of fresh grapefruit juice. One glass of regular-strength juice has a similar effect on a concurrently administered drug as 2 to 3 glasses of double-strength grapefruit juice obtained from frozen juice reconstructed with half the recommended water. Recent reports indicate that daily intake of grapefruit juice over a few weeks may cause a slight reduction in its CYP3A4 inhibiting effect. Consumption of 6 to 8 glasses daily may lead to inhibition of CYP3A4 in the liver. Likewise, the intake of 1 glass of double-strength juice 3 times daily for 3 days may cause inhibition of hepatic CYPA34. Drinking of up to 3 glasses daily of regular-strength juice appears to have an inhibiting effect on intestinal CYP3A4 only.

The active constituent of grapefruit juice appears to consist of flavonoids and nonflavonoids. These constituents inhibit CYP3A4 in vitro, but have little or no effect in vivo. In addition, flavonoids in the form of glycosides are found in grapefruit juice and are hydrolyzed by the intestinal microbial flora to aglycons and sugar. Due to their polyphenolic and electron-rich nature, these components may potentially inhibit CYP enzymes. Naringenin is the most abundant flavonoid in grapefruit juice, and is present at a concentration of 450 mcg/ml of juice. This glycoside, which is responsible for the bitter taste and the distinctive smell of grapefruit juice, is not present in any other citrus juices. Naringenin appears to have no inhibiting effect on human CYP systems in vitro. However, a metabolite of naringenin exerts a strong inhibiting effort on both CYP3A4 and CYP1A2 in vitro, but weakly inhibits these enzymes in vivo. Most of CYP1A2 is located in the liver, and only slight amounts of oral naringenin reach the plasma. The fact that naringenin is incapable of markedly inhibiting intestinal CYP1A4 indicates that there must be other active ingredients in grapefruit juice that exert the inhibitory effect on CYP3A4. Other flavonoids produced similar results. The nonflavonoids, 6,7-dihyroxybergamottin and its parent compound bergamottin, have been recently proposed as the active ingredients in grapefruit juice. Bergamottin is found in grapefruit juice as well as in grapefruit segments, but in lesser quantities in peel extract. Studies have revealed that this active ingredient is not the one responsible for drug-grapefruit juice interaction. The active ingredients in grapefruit juice are found in various concentrations depending on how ripe the fruit is and the method of juice preparation and purification. It has been postulated that the inhibitory effect exerted on CYP3A4 occurs as a result of the combined action of flavonoid and nonflavonoid components, and that such activity does not occur in isolation. Furthermore, it has been suggested that the active compounds in the fruit are distributed in the juice, pulp, peel, and core, since blended grapefruit segments and extracts from grapefruit peel have caused identical drug interactions with felodipine as the fresh juice alone.

Calcium Channel Antagonists - Grapefruit Juice

As indicated earlier, the first case of drug-grapefruit juice interaction was noticed when grapefruit juice was used as a flavoring agent to mask the taste of alcohol used in a preparation containing felodipine, a dihydropyridine calcium channel antagonist. Calcium channel antagonists are lipid soluble, and are used mainly to treat essential hypertension and angina pectoris. They are metabolized in vivo by CPY3A4 enzymes found in the intestinal membrane. In addition to felodipine, these drugs include amolodipine, nifedipine, nimodipine, nisoldipine, nitrendipine, and pranidipine. These drugs have similar metabolic pathways, but the extent of metabolism by CYP3A4, as well as the resultant bioavailability, depends largely on presystemic drug elimination. The lower the oral bioavailability of these drugs, the higher the extent of the interaction with grapefruit juice. The bioavailability of felodipine increased by two-fold when taken with one glass of grapefruit juice. The magnitude of this interaction was highly variable among individuals. When taken with grapefruit juice, felodipine resulted in increased blood pressure and heart rate and in an increase in vasodilation effect. Nisoldipine and amolodipine have very low and very high innate oral bioavailability, respectively. When taken with grapefruit juice compared with water, the C_{max} for nisoldipine was 406% and for amolodipine was 115%. Thus, it would be expected that nisoldipine achieves a greater increase in plasma drug concentration compared to amolodipine. Furthermore, individual variability of the interaction with the juice was greater with nisoldipine. The non-dihydropyridine calcium channel antagonists such as diltiazem and verapamil appear to have no interaction with grapefruit juice, even though both drugs are metabolized in vivo by CYP3A4. Due to the variability of the effect of grapefruit juice on the dihydropyridine calcium channel antagonists in individuals, and in order to eliminate the potential for adverse effects, it is advisable that patients, who are taking such medications, in particular nisoldipine and felodipine, should avoid the intake of grapefruit juice.

Statins - Grapefruit Juice

The statins (lovastatin, simvastatin, cerivastatin, and atorvastatin) are widely used for treating hyperlipidemia. They act by inhibition of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, resulting in reduction in blood cholesterol. These medications are metabolized presystemically by intestinal CYP3A4, and consequently their metabolism may be augmented by the concurrent use of grapefruit juice. The bioavailability of lovastatin was increased by 15-fold when taken with a double-strength grapefruit juice, 3 times daily. The intake of one glass of regular strength juice taken at breakfast and a dose of lovastatin in the evening caused an increase in AUC of the drug by two-fold. It appears that the cause of rhabdomyolysis (disintegration or dissolution of muscle) may be related to high blood levels of HMG-CoA reductase inhibitors. This disease has been reported in patients taking simvastin or lovastatin with CYP3A4 inhibitors. Since grapefruit juice is a CYP3A4 inhibitor, patients should be advised not to take grapefruit juices with statins. It should be remembered that fluvastatin and pravastatin are mildly biotransformed by CYP3A4.

Protease Inhibitors - Grapefruit Juice

Saquinavir (Invirase®) is a protease inhibitor used in the treatment of immunodeficiency virus infection. The effectiveness of this drug is limited by low bioavailability because of its extensive first-phase intestinal metabolism. A significant increase in bioavailability occurred when grapefruit juice was taken with the drug.

Hormones - Grapefruit Juice

The estrogen ethinyl estradiol undergoes significant first-pass metabolism. It has been found that the consumption of up to four glasses of grapefruit juice daily caused a 30% increase in oral bioavailability of this hormone. Even though no studies have been conducted to evaluate the effect of the intake of grapefruit juice on progesterone, it seems that one could expect that such a combination may cause an increase in serum level of the hormone, since it is metabolized by CYP3A4.

Sildenafil - Grapefruit Juice

Sildenafil (Viagra®), a widely used drug for erectile dysfunction, is rapidly absorbed following oral administration, resulting in a 40% bioavailability. This drug undergoes extensive metabolism by CYP3A4. Due to the fact that erythromycin and itraconazole, potent inhibitors of CYP3A4, significantly increase sildenafil blood level, one could expect that grapefruit juice, which inhibits CYP3A4, may cause an increase in sildenafil blood levels. While this may improve efficacy, it also may increase the incidence of adverse effects of the drug.

Antianxiety - Grapefruit Juice

Midazolam (Versed®), triazolam (Halcion®), and diazepam are antianxiety medications that exhibit high presystemic drug metabolism. When midazolam was taken with grapefruit juice, the oral bioavailability of the drug was increased by 50%. Ingestion of grapefruit juice with triazolam caused an increase of the bioavailability, as well added in drowsiness. Consumption of one glass of grapefruit juice resulted in a significant increase in the bioavailability of diazepam. Other studies, however, contradicted these findings. As a result, it was concluded that grapefruit juice had no effect on the bioavailability of both midazolam and triazolam. In light of these contradictory findings, and since there is no benefit to be gained from drinking grapefruit juice with such drugs, it behooves the patient to avoid such coadministration. There is no definite data regarding alprazolam (Xanax®), chlordiazepoxide, clonazepam, flurazepam and lorazepam (Ativan®). However, it is doubtful that these medications interact with grapefruit juice because of their high bioavailability.

Sertraline (Zoloft®) - Grapefruit Juice

This selective serotonin reuptake inhibitor undergoes a first-pass metabolism by CYP3A4. It has been observed that the intake of a glass of grapefruit juice has caused a 1.5-fold increase in sertraline blood levels.

Cyclosporine - Grapefruit Juice

Cyclosporine is widely used as a T-cell immunosuppressant following transplantation. Because of its nephrotoxicity, blood concentration of the drug must be maintained within a narrow range in order to cause proper immunosuppression. Cyclosporine has a low and variable oral bioavailability ranging from 5% to 90% and is affected by both CYP liver enzyme systems and intestinal CYP3A4. The intake of grapefruit tends to cause an increase in the bioavailability. This absorption led some clinicians to recommend the intake of grapefruit juice along with cyclosporine. However, it was concluded that such an approach was limited, variable and could be hazardous. Consequently, this therapy was eliminated.

CONCLUSION

Drug interactions with food, diet supplements and herbal products are becoming increasingly important due to wide use of such products along with prescription and nonprescription drugs. The occurrence of interactions is more likely to occur among the elderly due to the number of drugs taken and due to physiological changes that accompany aging. Patients as well as health professionals need to be aware of such phenomena.

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REMAINING TOPICS FOR 2005

NOVEMBER/DECEMBER COMBINED LESSON

MS, ALS & HUNTINGTON'S CHOREA

(Please Note that we switched the October & November/December Topics).

Fill in the information below, answer questions and return **Quiz Only** for certification of participation to:
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NAME_____(ID # 1st line on label)_____

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LESSON EVALUATION

Please fill-out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

List the mechanism of drug/food interactions	Yes	No
Describe the role of cytochrome P450 in drug metabolism	Yes	No
Identify the drugs that can interact with grapefruit	Yes	No
Acknowledge the ingredients in grapefruit that may trigger interactions	Yes	No
Relate common herb/drug interactions.	Yes	No

2. Was the program independent & non-commercial? Yes No

	Poor			Average			Excellent
3. Relevance of topic to your practice	1	2	3	4	5	6	7
4. Author's ability to communicate	1	2	3	4	5	6	7

5. What did you like most about this lesson?_____

6. What did you like least about this lesson?_____

7. How would you improve this lesson?_____

8. Further comments or suggestions for future programs_____

(WATCH OUR WEBSITE FOR RESULTS OF PARTICIPANT EVALUATIONS)

Quiz—Please Select the Most Correct Answer

1. Naringenin appears to have no inhibiting effect on human CYP system in vitro.
   A. True
   B. False
2. Weak basic drugs have a slow dissolution rate at a higher pH in the intestines.
   A. True B. False
3. Increased body fat can decrease the half-life of lipid soluble drugs.
   A. True
   B. False
4. Dietary & herbal supplements, when taken concomitantly with a drug, may:
   A. Increase the risk of a food-drug interaction
   B. Counteract the formation of a food-drug interaction
   C. Result in a definite increase in therapeutic activity of the drug
   D. Cause increased drug excretion
5. St. John's Wort:
   A. May cause hypotension if taken with selective serotonin reuptake products
   B. May increase the efficacy of sildenafil
   C. Will diminish the metabolism rate of concurrently taken drugs
   D. May interact with ethinyl estradiol, resulting in pregnancies
6. Echinacea is commonly used to treat:
   A. Prostate cancer
   B. Common cold
   C. Obesity
   D. Depression
7. Which is a tyramine containing food?
   A. Cabbage
   B. Smoked fish
   C. Pecans
   D. Spinach
8. Which statement is correct?
   A. White wine lacks antioxidants
   B. Red wine lacks antioxidants
   C. White wine contains a high concentration of flavonoids
   D. Red wine & MAOIs is OK
9. Simvastatin taken with grapefruit juice:
   A. Raises simvastatin bioavailability
   B. Lowers simvastatin bioavailability
   C. Is recommended to reduce gastric irritation
   D. Should be avoided
10. Calcium may chelate with:
    A. Aspirin
    B. Vitamins
    C. Tetracycline
    D. Iron

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