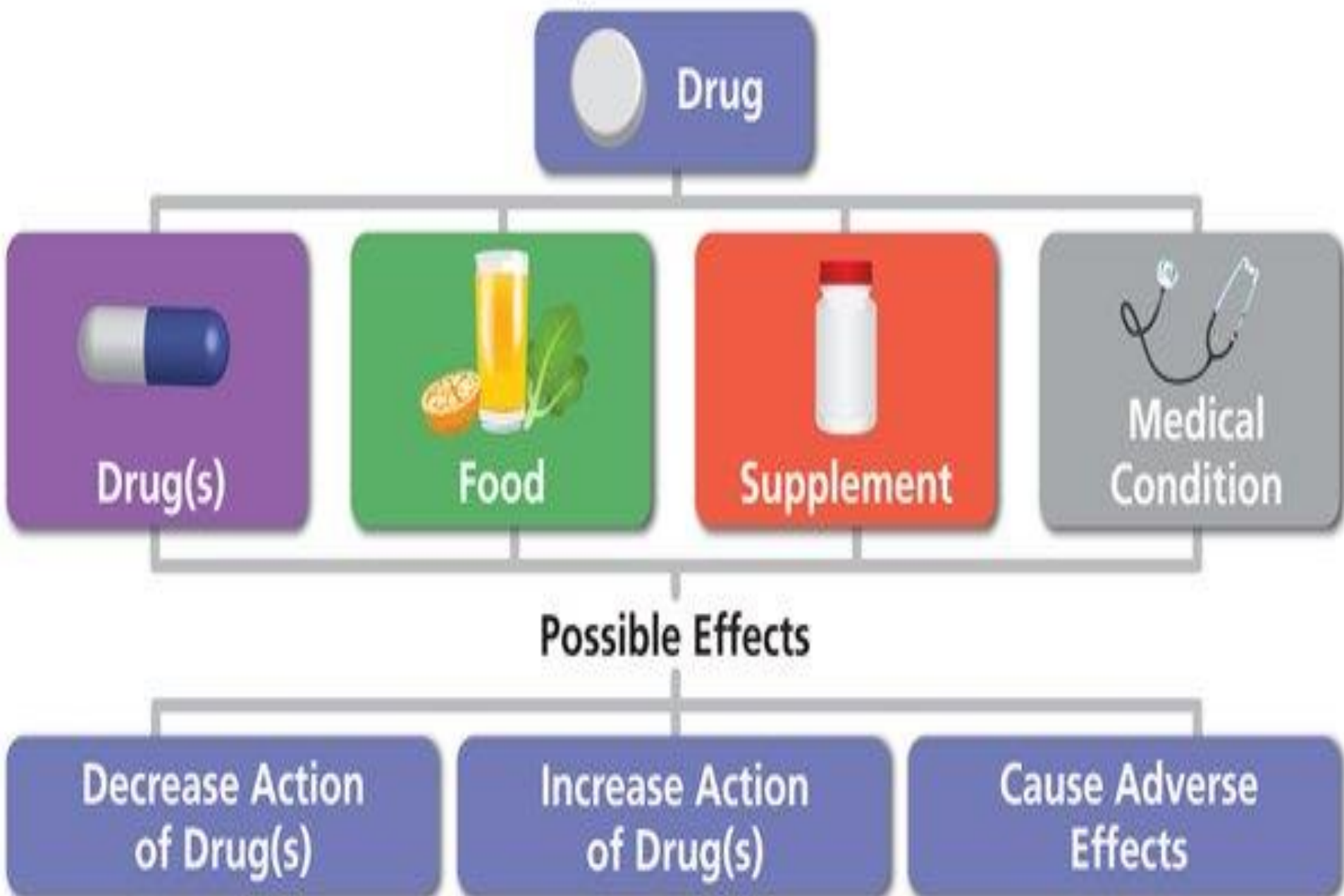


FOOD-DRUG INTERACTIONS



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Drug Interaction



DEFINITION OF TERMS

☞ **Drug-nutrient interaction: the result of the action between a drug and a nutrient that would not happen with the nutrient or the drug alone**

☞ **Food-drug interaction: a broad term that includes drug-nutrient interactions and the effect of a medication on nutritional status**

Food-Drug Interaction

For example, a drug that causes chronic nausea or mouth pain may result in poor intake and weight loss



Benefits of Minimizing Food Drug Interactions

- ① **Medications achieve their planned effects**
- ② **Improved compliance with medications**
- ③ **Less need for additional medication or higher dosages**
- ④ **Fewer caloric or nutrient supplements are required**
- ⑤ **Adverse side effects are avoided**

⑥ Optimal nutritional status is well-maintained

⑦ Accidents and injuries are avoided

⑧ Disease complications are minimized

⑨ The cost of health care services is reduced

Therapeutic Importance

Therapeutically important interactions are those that :

- * Change the planned response to the medication.**
- * Cause drug toxicity**
- * Change normal nutritional status**

Patients at risk for Food-Nutrient Interactions

- * Patient with chronic disease**
- * Elderly**
- * Fetus**
- * Infant**
- * Pregnant woman**
- * Malnourished patient**
- * Allergies or intolerances**

Food and Drug-Related Risk Factors

1-Special diets

2-Nutritional supplements

3-Tube feeding

4-Herbal or phytonutrient products

4- Alcohol intake

5-Polypharmacy

6-Drugs of abuse

7-Non-nutrients in foods

Malnutrition Effect on Drugs

Low albumin levels can make drugs more potent by increasing availability to tissues

--- Lower doses often recommended for persons with low albumin

☞ **Warfarin and phenytoin are highly protein bound in blood; ↓ albumin can result in poor seizure control (phenytoin) or hemorrhage (warfarin)**

☞ **Body composition: obese or elderly persons have a higher ratio of adipose tissue; fat soluble drugs may accumulate in the body ↑ risk of toxicity**

Food/ Nutrient Effects on Drugs

Absorption

Presence of food and nutrients in intestinal tract may affect absorption of drug

Antioosteoporosis drugs ,Fosamax or Actonel: absorption slight if given with food; ↓ 60% with coffee or orange juice

Food/Nutrient Effects on Drugs

Absorption

☞ **Absorption of iron from supplements**
↓↓ 50% when taken with food.

Best absorbed when taken with 8 oz. of water on empty stomach

Food may ↓↓ GI upset

If take with food, avoid bran, eggs, fiber supplements, tea, coffee, dairy products, calcium supplements

Ciprofloxacin and Tetracycline form insoluble complexes with calcium in dairy products or fortified foods; also zinc, calcium, magnesium, zinc or iron supplements; aluminum in antacids

Stop unnecessary supplements during drug therapy or give drug 2 hours before or 6 hours after the Mineral.

Presence of food enhances the absorption of some medications

Bioavailability of Axetil (Ceftin), an antibiotic, is 52% after a meal vs 37% in the fasting state

Absorption of the antiretroviral drug saquinavir is increased twofold by food

Food/ Nutrient Effects on Drugs

Adsorption: adhesion to a food or food component

High fiber diet may decrease the absorption of tricyclic antidepressants such as amitriptyline (Elavil)

Digoxin (Lanoxin) should not be taken with high phytate foods such as wheat bran or oatmeal

GI pH can affect drug absorption

Achlorhydria or hypochlorhydria can reduce absorption of ketoconazole

Antacid medications can result in reduced acidity in the stomach

Taking these meds with orange or cranberry juice can reduce stomach pH and increase absorption

Food/Nutrient Effects on Drugs

Metabolism

Changes in diet may alter drug action

☼ **Theophylline:** a high protein, low CHO diet can enhance clearance of this and other drugs

☼ **Grapefruit/juice:** inhibits the intestinal metabolism (cytochrome P-450 3A4 enzyme) of numerous drugs (calcium channel blockers, HMG CoA inhibitors, anti-anxiety agents) enhancing their effects and increasing risk of toxicity; may interfere with the absorption of other drugs

Foods that may Affects Medication You Taking



Dairy Products



Coffee



Grapefruit Juice



Cokes



Alcohols



Tea



Charcoal-Broiled foods



Green Leafy Vegetables



Licorice



Ginseng



Drug (use)	Food item	Reaction
Warfarin ⁱⁱ (blood thinning)	Cranberry juice	Can lead to bleeding problems
	Green Leafy Vegetables	Can lessen drug effectiveness
Statins ⁱⁱⁱ (cholesterol lowering)	Grapefruit juice	Muscle pain, Rhabdomyolysis
ramipril ^{iv} (anti-hypertensive)	Bananas	Irregular heartbeat, heart palpitations
isoniazid ^v (anti-tuberculosis)	Cheese, tuna and red wine	Palpitation, chills, diarrhea



Grapefruit Inhibits Metabolism of Many Drugs



→ Inactivates metabolizing intestinal enzyme resulting in enhanced activity and possible toxicity

Effect persists for 72 hours so it is not helpful to separate the drug and the grapefruit

Drugs known to interact with grapefruit juice



→ **Anti- hypertensive**
(**filodipine, nifedipine,**
nimodipine,
nicardipine, isradipine)

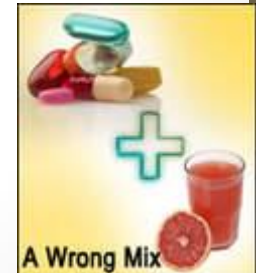
→ **Immuno**
suppressants
(**cyclosporine,**
tacrolimus)

→ **Antihistamines**
(**astemizole)**

→ **Protease inhibitors**
(**saquinavir)**

→ **Lipid-Lowering Drugs**
(**atorvastatin,**
lovastatin,
simvastatin)

→ **Anti-anxiety, anti-**
depressants
(**buspirone, diazepam,**
midazolam, triazolam,
zaleplon,
carbamazepine,
clomipramine,
trazodone



Food/Nutrient Effects on Drugs

Excretion

- **Patients on low sodium diets will reabsorb more lithium along with sodium; patients on high sodium diets will excrete more lithium and need higher doses**
- **Urinary pH: some diets, particularly extreme diets, may affect urinary pH, which affects resorption of acidic and basic medications**

Food/Nutrient Effects on Drug Action: MAOIs



Monoamine oxidase inhibitors (MAOI) interact with pressor agents in foods (tyramine, dopamine, histamine)

Pressors are generally deaminated rapidly by MAO; MAOIs prevent the breakdown of tyramine and other pressors

Significant intake of high- tyramine foods (aged cheeses, cured meats) by pts. on MAOIs can precipitate hypertensive crisis



Food/Nutrient Effects on Drug Action: Caffeine



Increases adverse effects of stimulants such as amphetamines, methylphenidate, theophylline, causing nervousness, tremor, insomnia
Counters the antianxiety effect of tranquilizers



Food/Nutrient Effects on Drug Action: Warfarin

Warfarin (anticoagulant) acts by preventing the conversion of vitamin K to a usable form

Ingestion of vitamin K in usable form will allow production of more clotting factors, making the drug less effective

Pts. must achieve a balance or steady state between dose of drug and consumption of vitamin K; recommend steady intake of K

Other foods with anticlotting qualities may also have an effect (garlic, onions, vitamin E in large amounts, and ginseng)

Food/Nutrient Effects on Drug Action: Alcohol

In combination with some drugs will produce additive toxicity

With CNS-suppressant drugs may produce excessive drowsiness, incoordination

Acts as gastric irritant; in combination with other irritants such as NSAIDs may increase chance of GI bleed

Should not be combined with other hepatotoxic drugs such as acetaminophen, amiodarone, methotrexate

Can inhibit gluconeogenesis when consumed in a fasting state; can prolong hypoglycemic episode caused by insulin or other diabetes meds.

Can produce life-threatening reaction when combined with disulfiram (Antabuse) which prevents the catabolism of ethanol by the liver

Causes nausea, headache, flushing, increased blood pressure

Metronidazole, Cefoperazone, chlorpropamide (Diabenese) and procarbazine cause similar symptoms

Drug Effects on Nutrition: Metabolism

Phenobarbital and phenytoin increase metabolism of vitamin D, vitamin K, and folic acid

Patients on chronic treatment may need supplements

Carbamazepine may affect metabolism of biotin, vitamin D, and folic acid, leading to possible depletion

Drug Effects on Nutrition: Metabolism

INH (anti-tuberculosis) blocks conversion of pyridoxine to active form

Patients with low intake at higher risk

May cause deficiency and peripheral neuropathy

Pts. on long term tx may need supplements

Hydralazine, penicillamine, levodopa and cycloserine are also pyridoxine antagonists

Drug Effects on Nutrition: Metabolism

Methotrexate (cancer and rheumatoid arthritis) and pyrimethamine (malaria, toxoplasmosis) are folic acid antagonists

May treat with folinic acid (reduced form of folic acid, does not need conversion to active form) or folic acid supplements

Drug Effects on Nutrition: **Excretion**

- **Loop diuretics (furosemide, bumetanide) increase excretion of potassium, magnesium, sodium, chloride, calcium**
- **Patients may need supplements with long term use, high dosages, poor diets**
- **Electrolytes should be monitored**

Drug Effects on Nutrition: Excretion

☺ **Thiazide diuretics (hydrochlorothiazide) increase the excretion of potassium and magnesium, but reduce excretion of calcium**

☺ **High doses plus calcium supplementation may result in hypercalcemia**

☺ **Potassium-sparing diuretics (spironolactone) increase excretion of sodium, chloride, calcium**

☺ **Potassium levels can rise to dangerous levels if pt. takes K⁺ supplements or has renal insufficiency**

Drug Effects on Nutrition: Excretion

☞ **Corticosteroids (prednisone) decrease sodium excretion, resulting in sodium and water retention; increase excretion of potassium and calcium**

☞ **Low sodium, high potassium diet is recommended**

☞ **Calcium and vitamin D supplements are recommended with long term steroid use (lupus, RA) to prevent osteoporosis**

☐ **Phenothiazine antipsychotic drugs (chlorpromazine) increase excretion of riboflavin**

Can lead to riboflavin deficiency in those with poor intakes

Cisplatin causes nephrotoxicity and renal magnesium wasting resulting in acute hypomagnesaemia in 90% of patients (also hypocalcaemia, hypokalemia, hypophosphatemia). 😊

May require intravenous mg supplementation or post-treatment hydration and oral mg supplementation
May persist for months or years after therapy is finished

Drug Effects on Nutrition: Absorption

***Drug-nutrient complexes: example, ciprofloxacin and tetracycline will complex with calcium, supplemental magnesium, iron, or zinc**

***Take minerals 2 to 6 hours apart from the drug**

***Decreased transit time: therapeutic agents, laxatives, drugs containing sorbitol, drugs that increase peristalsis**

Drug Effects on Nutrition; Absorption

Change GI environment

Proton pump inhibitors, H₂ receptor antagonists inhibit gastric acid secretion, raise gastric pH; cimetidine reduces intrinsic factor secretion; this impairs B12 absorption; ↑ pH may impair absorption of calcium, iron, zinc, folic acid, and B-carotene.

Drug Effects on Nutrition: Absorption

Damage GI Mucosa

ⓘ Chemotherapeutic agents, NSAIDs, antibiotic therapy

Alters ability to absorb minerals, especially iron and calcium

Affect Intestinal Transport

ⓘ Colchicine (gout) paraaminosalicylic acid (TB) sulfasalazine (ulcerative colitis) trimethoprim (antibiotic) and pyrimethamine (antiprotozoal)

Impair absorption of B12 or folate

Drug Effects on Nutrition: **Adsorption**

Cholestyramine (antihyperlipidemic bile acid sequestrant) also adsorbs fat-soluble vitamins A, D, E, K, possibly folic acid; may need supplements for long term therapy, especially if dosed several times a day

Mineral oil: (>2 tbsp./day) ↓ absorption of fat soluble vitamins

take vitamins at least 2 hours after mineral oil

Drug Side Effects that Affect Nutritional Status

- ◆ Appetite changes
- ◆ Oral taste and smell
 - ◆ Nausea
- ◆ Dry mouth
- ◆ Gastrointestinal effects
- ◆ Organ system toxicity
- ◆ Glucose levels



Examples of Drug Categories That May Decrease Appetite

Anti infective

Anti neoplastic

Bronchodilators

Cardiovascular drugs

Stimulants

Drugs That May Increase Appetite

Anticonvulsants

Hormones

Psychotropic drugs

—Antipsychotics

—Antidepressants, tricyclic, MAOIs

Drugs Affecting Oral Cavity, Taste and Smell

Taste changes: Cisplatin, captopril (anti-hypertensive) amprenavir (antiviral) phenytoin (anti-convulsive), clarithromycin (antibiotic)

Mucositis: antineoplastic drugs such as interleukin-2, paclitaxel, carboplatin

Dry mouth: Anticholinergic drugs (tricyclic antidepressants such as amitriptyline, antihistamines such as diphenhydramine, antispasmodics such as oxybutynin)

Drugs that Affect the GI Tract

- ✿ **Alendronate (Fosamax) anti-osteoporosis drug—patients must sit upright 30 minutes after taking it to avoid esophagitis**
- ✿ **Aspirin or other NSAIDs –can cause GI bleeding, gastritis**
- ✿ **Orlistat – blocks fat absorption, can cause oily spotting, fecal urgency, incontinence**
- ✿ **Narcotic agents cause constipation**

Examples of Drug Classes That Cause Diarrhea

Laxatives

Antiretroviral

Antibiotics

Antineoplastic

liquid medications in elixirs containing sugar alcohols

Drugs That May Lower Glucose Levels

***Antidiabetic drugs (acarbose, glimepiride, glipizide, glyburide, insulin, metformin, miglitol, neteglinide, pioglitazone, repaglinide, roiglitazone)**

***Drugs that can cause hypoglycemia: ethanol, quinine, disopyramide (antiarrhythmic) and pentamidine isethionate (antiprotozoal)**

Drugs That Raise Blood Glucose

- **Antiretroviral, protease inhibitors (amprenavir, nelfinavir, ritonavir, saquinavir)**
- **Diuretics, antihypertensive (furosemide, hydrochlorothiazide, indapamide)**
- **Hormones (corticosteroids, danazol, estrogen or estrogen/progesterone replacement therapy, megestrol acetate, oral contraceptives)**
- **Niacin (antihyperlipidemic) baclofen, caffeine, olanzapine, cyclosporine, interferon alfa-2a**

Nutrition Implications of Excipients in Drugs

Excipients: are inactive ingredients added to drugs as fillers, buffers, binders, disintegrate, flavoring, dye, preservative, suspending agent, coating

Approved by FDA for use in pharmaceuticals

Vary widely from brand to brand and formulation strengths of the same drug

Nutrition Effects of Excipients in Drugs

□ Excipients may cause allergic or health reactions in persons with celiac disease, dye sensitivity, other allergies, inborn errors of metabolism

Examples of excipients that might cause reactions are albumin, wheat products, alcohol, aspartame, lactose, sugar alcohols, starch, sulfites, tartrazine, vegetable oil

Some meds may contain sufficient CHO or protein to put a patient on a ketogenic diet out of ketosis

Some drugs at usual dosages may contain enough excipients to be nutritionally significant

Agenerase: (this drug, used in combination with at least 2 other medications, helps to control HIV infection), 1744 IU vitamin E

Accupril (is used to treat high blood pressure (hypertension)) : 50-200 mg magnesium

Fibercon/ Fiberlax : 600 mg ca⁺ in 6 tabs

Propofol (Diprivan) contains 10% soybean emulsion; may provide 1663 kcals/day for 70 kg person

Food/Nutrient Effects on Drugs – Enteral Feedings

Most medications should not be mixed with enteral feedings; physical incompatibilities can occur including granulation, gel formation, separation of the feeding leading to clogged tubes

Enteral feedings interfere with phenytoin absorption; window the feeding around drug dose (2 hours before and after)

MNT for Food-Drug Interactions

→ **Prospective: MNT offered when the patient first starts a drug**

→ **Retrospective: evaluation of symptoms to determine if medical problems might be the result of food-drug interactions**



Avoiding Food-Drug Interactions: Prospective

① When medications are initiated, patients should be provided with complete written and verbal drug education at an appropriate reading level including food-drug interaction information

② Patients should be encouraged to ask specific questions about their medications and whether they might interact with each other or with foods

③ Patients should read the drug label and accompanying materials provided by the pharmacist

4-In acute-care settings, patients receiving high risk medications should be identified and evaluated

5- Nurses should have information regarding drug-food interactions and drug administration guidelines available at the bedside

6- Med pass times should be evaluated in light of potential food-drug interactions

Avoiding Food-Drug Interactions: Prospective

Systems should be established so that pharmacists can communicate with food and nutrition staff regarding high risk patients



Avoiding Food-Drug Interactions: **Retrospective**

① Clinicians including dietitians should obtain a full drug and diet history including the use of OTC and dietary supplements and review potential drug-food interactions

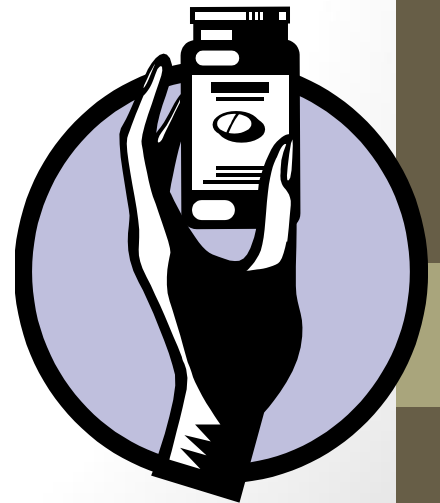
② A plan should be developed for dealing with potential drug-food interactions for short and long term drug therapy

③ When therapeutic goals are not met, clinicians should ask questions about how and when drugs are being taken in relation to foods and nutritional supplements

Avoiding Food-Drug Interactions: Retrospective

***Clinicians should evaluate whether medical problems could be the result of drug-food interactions**

***Often it may be the dietitian who is most aware of these issues**



Avoiding Food-Drug Interactions: Example

A 20-year-old disabled patient who was a long term resident of a nursing home was admitted to an acute care hospital for a workup to determine the cause of chronic diarrhea

The enteral feeding had been changed numerous times in an effort to normalize the patient's bowel function

The patient was currently receiving a defined formula feeding at a slow rate

The workup revealed no apparent medical reason for the impaired bowel function

After reviewing the pts., medications, the dietitian suggested that the patient's medications (given in liquid elixir forms containing sugar alcohols) might be causing the diarrhea

The patient's medications were changed, and the diarrhea resolved

The patient returned to the nursing home on a standard enteral feeding formula

Summary

***Most drugs have nutritional status side effects.**

***Always look for therapeutically significant interactions between food and drugs**

***Identify and monitor high risk patients, those on multiple medications and marginal diets**