hemorrhage. MAO inhibitors include the antidepressants isocarboxazid and phenelzine and the antineoplastic procarbazine. These drugs are infrequently used nowadays, partly because of this potentially serious interaction and partly because other effective drugs are available. Tyramine-rich foods to be avoided by clients taking MAO inhibitors include beer, wine, aged cheeses, yeast products, chicken livers, and pickled herring.

An interaction may occur between warfarin, a frequently used oral anticoagulant, and foods containing vitamin K. Because vitamin K antagonizes the action of warfarin, large amounts of spinach and other green leafy vegetables may offset the anticoagulant effects and predispose the person to thromboembolic disorders.

A third interaction occurs between tetracycline, an antibiotic, and dairy products, such as milk and cheese. The drug combines with the calcium in milk products to form an insoluble, unabsorbable compound that is excreted in the feces.

Drug–Drug Interactions

The action of a drug may be increased or decreased by its interaction with another drug in the body. Most interactions occur whenever the interacting drugs are present in the body; some, especially those affecting the absorption of oral drugs, occur when the interacting drugs are given at or near the same time. The basic cause of many drug–drug interactions is altered drug metabolism. For example, drugs metabolized by the same enzymes may compete for enzyme binding sites and there may not be enough binding sites for two or more drugs. Also, some drugs induce or inhibit the metabolism of other drugs. Protein binding is also the basis for some important drug–drug interactions. A drug with a strong attraction to protein-binding sites may displace a less tightly bound drug. The displaced drug then becomes pharmacologically active, and the overall effect is the same as taking a larger dose of the displaced drug.

Increased Drug Effects

Interactions that can increase the therapeutic or adverse effects of drugs are as follows:

1. *Additive effects* occur when two drugs with similar pharmacologic actions are taken.
   Example: ethanol + sedative drug → increased sedation
2. *Synergism* or *potentiation* occurs when two drugs with different sites or mechanisms of action produce greater effects when taken together than either does when taken alone.
   Example: acetaminophen (non-opioid analgesic) + codeine (opioid analgesic) → increased analgesia
3. *Interference* by one drug with the metabolism or elimination of a second drug may result in intensified effects of the second drug.
   Example: cimetidine inhibits CYP 1A, 2C, and 3A drug-metabolizing enzymes in the liver and therefore interferes with the metabolism of many drugs (eg, benzodiazepine antianxiety and hypnotic drugs, calcium channel blockers, tricyclic antidepressants, some antidysrhythmics, beta blockers and antiseizure drugs, theophylline, and warfarin). When these drugs are given concurrently with cimetidine, they are likely to cause adverse and toxic effects.
4. *Displacement* of one drug from plasma protein-binding sites by a second drug increases the effects of the displaced drug. This increase occurs because the molecules of the displaced drug, freed from their bound form, become pharmacologically active.
   Example: aspirin (an anti-inflammatory/analgesic/antipyretic agent) + warfarin (an anticoagulant) → increased anticoagulant effect

Decreased Drug Effects

Interactions in which drug effects are decreased are grouped under the term *antagonism.* Examples of such interactions are as follows:

1. In some situations, a drug that is a specific antidote is given to antagonize the toxic effects of another drug.
   Example: naloxone (a narcotic antagonist) + morphine (a narcotic or opioid analgesic) → relief of opioid-induced respiratory depression. Naloxone molecules displace morphine molecules from their receptor sites on nerve cells in the brain so that the morphine molecules cannot continue to exert their depressant effects.
2. Decreased intestinal absorption of oral drugs occurs when drugs combine to produce nonabsorbable compounds.
   Example: aluminum or magnesium hydroxide (antacids) + oral tetracycline (an antibiotic) → binding of tetracycline to aluminum or magnesium, causing decreased absorption and decreased antibiotic effect of tetracycline
3. Activation of drug-metabolizing enzymes in the liver increases the metabolism rate of any drug metabolized primarily by that group of enzymes. Several drugs (eg, phenytoin, rifampin), ethanol, and cigarette smoking are known *enzyme inducers.*
   Example: phenobarbital (a barbiturate) + warfarin (an anticoagulant) → decreased effects of warfarin
4. Increased excretion occurs when urinary pH is changed and renal reabsorption is blocked.
   Example: sodium bicarbonate + phenobarbital → increased excretion of phenobarbital. The sodium bicar-

How Can You Avoid This Medication Error?

Mrs. Beecher, a 76-year-old nursing home client, has just had a change in her antihypertension medications to felodipine 10 mg qd, a calcium channel blocker. Her blood pressure is 148/70. You give her the tablet with a large glass of grapefruit juice and caution her to swallow the tablet whole. Two days later Mrs. Beecher's blood pressure is 96/60.