"Nonprescription Drug Interactions with Prescription Drugs"
Illinois Council of Health System Pharmacists Conference
Drury Lane Conference Center
Oakbrook Terrace
September 12, 2015

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Session Objectives:

After participating in the session entitled, "Nonprescription Drug Interactions with Prescription Drugs," the pharmacy technician will be able to:

1. Define nonprescription drugs.
2. Describe the various ways nonprescription drugs interact with prescription drugs.
3. Provide typical examples of nonprescription drugs which interact with prescription drugs.
4. Provide typical prescription drugs which interact with nonprescription drugs.
5. Name an example of a nonprescription drug-prescription drug interaction for each way nonprescription drugs interact with prescription drugs

Format/Overview of this session:

Page 2 is for your convenience and note taking. It allows you to jot down some notes and any questions you have to clarify (a) point(s) you did not understand.

Pages 3-7 of this handout contain tables to illustrate the various ways nonprescription drugs can interact with prescription drugs and diagnostic tests.

Page 8 is for your personal assessment of the session.

1. What are the "take away" points which you can employ in my practice after this session?
2. If there was something in this presentation which "surprised me," it was.....

Page 9 demonstrates a glossary for your understanding and Page 10 provides 2 figures to clarify important points which will be made during the presentation.

Page 11 allows you to suggest how to improve future presentations of this topic.

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*The presenter is grateful to Ms. Clara Gary, Certified Pharmacy Technician II, CPhT, Ambulatory Pharmacy Services, PCC Pharmacy, University of Illinois at Chicago Hospital, for her guidance in creating this presentation.

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Notes:

Questions to ask:

Table I. Common mechanisms for drug-drug interactions with representative examples (R_X and OTC)

A. Drugs which act additively or synergistically when administered with other drugs

Drug (Category)	Interactant	Effect
Aspirin	Coumarin anticoagulants	Increased International Normalized Ratio [INR]. Oral warfarin and oral ASA increase the risk of side effects and cause bleeding or bruising. The need for simultaneous use of low-dose aspirin and warfarin are common for patients with cardiovascular disease; your doctor will monitor you closely.
	Nonsteroidal anti-inflammatory drugs (NSAIDs); e.g. Motrin, Naprosyn	Increased risk of gastroduodenal ulcers and bleeding; ASA should be taken at least 30 minutes before or 8 hours after ibuprofen;
Bulk Laxative (e.g., Psyllium Powder in Metamucil, Fiberall)	Anticholinergics (e.g. Pro-Banthine), Tricyclic Antidepressents [syn TCADs] (e.g., Elavil), and Phenothiazines (e.g., Thorazine)	Possible intestinal obstruction
Bismuth Subsalicylate (in Pepto-Bismol, KaoPectate)	Aspirin	Salicylate Toxicity (e.g., ringing, buzzing, or fullness in ears) if taken in high doses
Diphenhydramine HBr; Doxylamine succinate; in OTC Sleep Aids	Alcohol (as a beverage or a vehicle in medicinal products)	Additive CNS depression, e.g., sleepiness.
Fish Oils	Coumadin, e.g., Warfarin Sodium	Increased anticoagulant effect, i.e., ↑INR
Pseudoephedrine HCl in Cold-Decongestant Products, (e.g., Sudafed)	TCADs, Methyldopa	Increased blood pressure
Potassium chloride (salt substitutes, e.g. No-Salt)	Potassium Supplements (e.g., K-Lyte, Slow-K) Potassium-sparing diuretics (e.g. Aldactone, Midamor)	Possible hyperkalemia, i.e., increased serum potassium

B. Drugs which enhance or diminish the absorption of another drug from the GI tract.

Drug (category)	Interactant	Effect
Antacids	Anticoagulants, antidyskinetics, ketoconazole, antiretrovirals (e.g. atazanavir, indinavir)	Decreased absorption of interactant
Antacids, sucralfate, or large doses of zinc	Antibiotics (tetracyclines, oral quinolones [ciprofloxacin, norfloxacin, and ofloxacin], azithromycin)	Decreased absorption of interactant
Antacids or H_2 receptor antagonists (e.g., famotidine)	Ketoconazole, itraconazole, indinavir, iron salts	An acidic medium required for adequate dissolution and absorption. Thus, decreased absorption of the interactant.
Bismuth Subsalicylate (in Pepto-Bismol)	Tetracycline HCl and other tetracyclines	Decreased tetracycline absorption
Bulk Laxatives	Antibiotics, digoxin, salicylates	Decreased absorption of the interactants
Cholestryamine or Colestipol	Multiple interactants; check prescribing information	Decreased absorption of the interactants, administer 1 to 4 hours before or 4 to 6 hours after the drug
Iron Supplements (e.g., Feosol, Mol-Iron, Fergon)	Tetracycline antibiotics; oral quinolone antibiotics	Decreased antibiotic absorption
	Antacids, bulk laxatives	Decreased iron absorption
Magnesium-Aluminum Hydroxide Gel (e.g., Maalox, Kolantyl, Mylanta)	Tetracyclines, digoxin, phenytoin	Decreased absorption of interactants
Mineral Oil	Fat-soluble vitamins	Chronic mineral oil use can decrease the absorption of fat-soluble vitamins

C. Drugs which alter the distribution (e.g. plasma protein binding) of other drugs.

Drug (category)	Interactant	Effect
Aspirin (e.g. Bayer, Anacin)	Coumadin (Sodium Warfarin), Valproic Acid	Displacement of drug plasma binding sites resulting in an increased pharmacological response
Salicylates	Carbonic Anhydrase Inhibitors (e.g., Acetazolamide, methazolamide)	Displacement of CAIs from plasma protein binding sites resulting in lethargy, confusion, fatigue, anorexia, urinary incontinence, and hyperchloremic metabolic acidosis
Ibuprofen	Phenytoin	Displacement from protein-binding sites. Monitor free phenytoin levels; Adjust dosage or consider naproxen

D. Drugs which alter the renal excretion or effectiveness of another drug.

Drug (category)	Interactant	Effect
Ammonium Chloride (menstrual products, e.g., Aqua-Ban)	Weakly basic drugs dependent upon urinary excretion (e.g., TCAD's Quinidine)	Urinary acidification would enhance excretion of these drugs
Aspirin	Methotrexate	Competes for renal tubular secretion decreasing elimination of interactant
Sodium Bicarbonate (Antacid products, e.g., Alka Seltzer)	Weakly basic drugs dependent upon urinary excretion (e.g., amphetamine, quinidine)	Urinary alkalinization would diminish excretion of these interactants, possibly leading to toxicity
	Methenamine mandelate	Urinary alkalinization prevents conversion to methenamine to the active formaldehyde in urine
	Nitrofurantoin	Urinary alkalinization decreases the bactericidal effects of nitrofurantoin
	Pseudoephedrine HCl	Urinary alkalinization decreased renal excretion of psuedoephedrine
	Lithium	Sodium intake enhances lithium excretion
NSAIDs (e.g., Motrin)	Lithium	Serum lithium levels increase (N/V, diarrhea, anorexia, coarse tremor, slurred speech, confusion); Monitor for toxicity
	Methotrexate	Serum methotrexate levels increase (fever, mucosal ulcerations, severe nausea, diarrhea, gi bleeding); Monitor for toxicity

E. Drugs which decrease or increase the biotransformation of another drug resulting in increased toxicity or no therapeutic effect.

Drug (category)	Interactant	Effect
Phenylephrine HCl, Pseudoephedrine HCl (Decongestant products)	Monoamine Oxidase (MAO) Inhibitors, St. John's Wort	MAO Inhibitors decrease biotransformation causing possible hypertensive crisis
Cimetidine	Warfarin, Phenytoin, Propranolol, Theophylline, Diazepam	Cimetidine reduces hepatic metabolism of these drugs, thereby delaying elimination and increasing serum levels
Acetaminophen	Erythromycin, Azithromycin	Concurrent use of other hepatotoxic medications with erythromycin and azithromycin may increase the potential for hepatotoxicity
St John's Wort	Warfarin	The herbal may induce the Cytocrome P450 enzymes responsible for warfarin metabolism resulting in an altered International Normalized ratio (INR) or through an unknown mechanism decreases the absorption of the drug.
	SSRI	Concomitant ingestion may result in additive central serotonin excess (i.e., serotonin syndrome). Symptoms include grogginess, N/V, weakness, agitation, confusion, hypothermia, diaphoresis, hyperreflexia, and muscle rigidity
	Protease Inhibitor	The herbal caused a 28% decrease in the peak serum concentrations and AUC of indinavir (i.e., Crixivan) when administered concomitantly
Ginkgo biloba, feverfew, pure licorice, ginger	Warfarin (Sodium Warfarin), Clopidogrel (Plavix)	Should be used cautiously in patients on anticoagulant therapy, with known coagulopathy, or prior to some surgical or dental procedures

F. Drugs which interfere with or affect the desired effect of another drug/diagnostic test.

Drug (category)	Interactant	Effect
Alcohol (Vehicle e.g., Nyquil Nighttime Cold Liquid Medicine); 10% V/V. Mouthwashes, e.g., 20% V/V	Metronidazole, Chlorpropamide, Disulfiram (Antabuse)	Antabuse Effect, i.e., Elements of this reaction may include any of the following: flushing, throbbing in the head and neck, headache, nausea, vomiting, sweating, thirst, chest pain, palpitations, dyspnea, hyperventilation, tachycardia, confusion, arrhythmias, and convulsions. Avoid mouthwashes, antiperspirants, colognes, etc.
Ascorbic Acid	Fecal occult blood tests, urinary blood and Glucose Tests	False-Negative test results for blood; False-Negative for glucose in urine
Aspirin	Probenecid, Sulfinpyrazone	Inhibition of the uricosuric effect of the probenecid or sulfinpyrazone
Ephedrine SO_4	Inhalation Anesthetics, MAO Inhibitors, Sympathomimetics	May enhance the arrhythmogenic (capable of inducing a cardiac arrhythmias)/hypertensive effects of interactants
Milk of Mangesia	Aspirin, bisacodyl (Dulcolax)	Premature release of these drugs from their enteric-coated tablet in stomach could result in stomach distress for the patient.
	Methenamine Mandelate, Calcium Polystyrene Sulfonate	May increase adverse drug events of the interactant. Use in conjunction with magnesium containing laxatives may increase risk of metabolic acidosis
Pyridoxine (Vitamin B_6)	Levodopa	Levadopa's antiparkinsonian effects are reversed by as little as 5mg of oral pyridoxine
Salicylates, Iron Products, Ibuprofen	Fecal Occult Blood Tests	False-Positive Result

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1. What are the "take away" points which I can employ in my practice after this session?

2. If there was something in this presentation which "surprised me," it was.....

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Glossary

Page 3 OTC Drug, i.e., Fish Oils, can cause an increased anticoagulant effect. An anticoagulant effect is defined as acting to prevent or to retard coagulation of the blood.

Page 5 OTC Drug Class of Salicylates (e.g., aspirin, magnesium salicylate) can displace carbonic anhydrase inhibitors, such as acetazolamide, from plasma protein sites resulting in a number of adverse effects including hyperchloremic metabolic acidosis which is defined as a decrease in plasma bicarbonate concentration and an increase in the plasma chloride concentration. Note Figure 5.7 (Minimum Toxic Concentration).

Page #6 OTC Drug, i.e., phenylephrine, can cause a hypertensive crisis with some drugs. A hypertensive crisis is defined as a severe increase in blood pressure which can lead in some instances to a stroke

Page #6 OTC Drug, i.e., acetaminophen, which can cause liver damage, i.e., hepatotoxicity, when overused and/or if used with another drug which can cause liver damage, e.g., azithromycin.

Page #6 OTC Dietary Supplement, e.g., St. John's Wort, with protease inhibitors can increase serum concentrations and the area under the curve (AUC). Note Figure 5.4 and Figure 5.7. (Page 10)

Page #6 OTC Dietary Supplement, e.g., *Ginkgo biloba*, can cause coagulopathy. Coagulopathy (syn. clotting disorder, bleeding disorder) is a condition in which the blood's ability to clot (or coagulate) is impaired. This condition can cause prolonged or excessive bleeding which may occur spontaneously or following an injury or medical and/or dental procedures.

Page #7 A liquid product vehicle, i.e., Alcohol, can cause an antabuse effect when used concurrently with some medications, e.g., metronidazole. The Antabuse effect blocks the ability of the body to metabolize alcohol and can cause a bad reaction, e.g., flushing, fast heartbeats, nausea, thirst, chest pain, vertigo, and low blood pressure.

Page #7 OTC Drug, i.e., Aspirin, can inhibit the effectiveness of probenecid or sufinpyrazone to eliminate from the body uric acid. Uricosurics are often used in the treatment of gout, a disease in which uric acid crystals form deposits in the joints.

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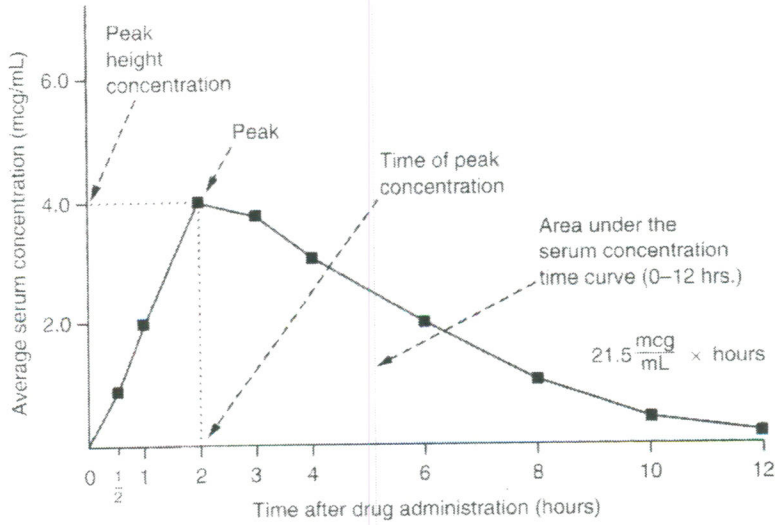

FIGURE 5.4 Serum concentration–time curve showing peak height concentration, time of peak concentration, and AUC. (Courtesy of D. J. Chodos and A. R. Disanto, Upjohn.)

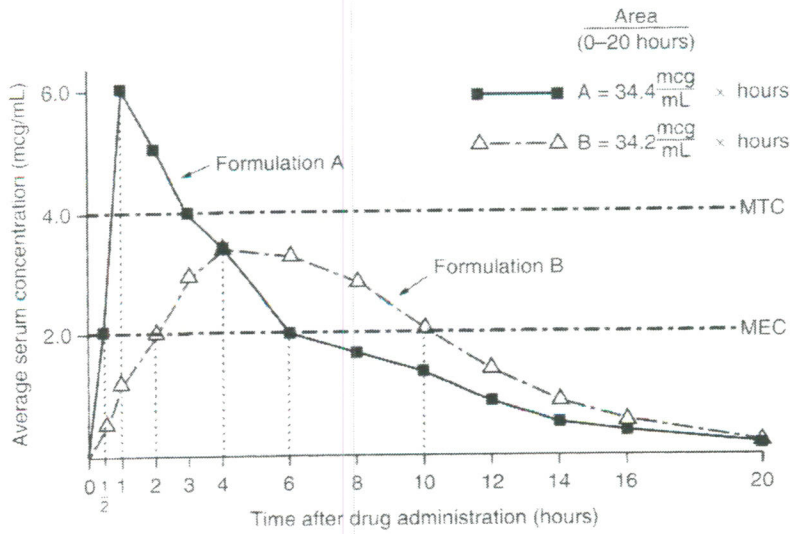

FIGURE 5.7 Serum concentration–time curve showing peak height concentrations, peak height times, times to reach MEC and areas under the curves for equal amounts of drug from two different formulations following oral administration. MEC, minimum effective concentration; MTC, minimum toxic concentration. (Courtesy of D. J. Chodos and A. R. Disanto, Upjohn.)

Allen LV, Popovich NG, Ansel HC. *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems*, 9th edition, 2011, Lippincott Williams and Wilkins, Philadelphia PA, p 153 and 156.

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Please answer the following question, remove this sheet from your handout, and turn this sheet into the session facilitator. Thank you very much.

My suggestion(s) to improve future presentations of this topic would include:

A. Drugs which act additively or synergistically when administered with other drugs

Drug (Category)	**Interactant**	**Effect**
Aspirin	Coumarin anticoagulants	Increased prothrombin time; bleeding
	Nonsteroidal anti-inflammatory drugs (NSAIDs); e.g. Motrin, Naprosyn	Increased potential lfor gastric upset; possible diminished activity for the NSAIDs
Bulk Laxative (e.g. Metamucil, Fiberall)	Anticholinergics (e.g. Pro-Banthine), Trricyclic Antidepressents (e.g. Elavil), and Phenothiazines (e.g. Thorazine)	Possible intestinal obstruction
Bismuth Subsalicylate (in Pepto-Bismol, KaoPectate)	Aspirin	Salicylate Toxicity (e.g. ringing, buzzing, or fullness in ears) if taken in high doses
Diphenhydramine (Sleep-Aid Products, e.g. Compoz, Nytol with DPH)	Alcohol (as a beverage or a vehicle in medicinal products)	Additive CNS depression
Fish Oils	Coumadin	Increased anticoagulant effect
Pseudoephedrine HCl in Cold-Decongestant Products, (e.g. Sudafed)	Theophylline	Monitor for increased CNS stimulation, e.g. restlessness, insomnia, irritablity
Potassium chloride (salt	Potassium Supplements (e.g. K-Lyte, Slow-K)	Possible hyperkalemia

substitutes, e.g. No-Salt)	Potassium-sparing diuretics (e.g. Aldactone, Midamor)	Possible hyperkalemia

B. Drugs which enhance or diminish the absorption of another drug from the GI tract.

Drug (category)	**Interactant**	**Effect**
Antacids	Anticoagulants, antidyskinetics, ketoconazole	Decreased absorption of interactant
Antacids, sucralfate, or large doses of zinc	Antibiotics (tetracyclines, oral quinolones [ciprofloxacin, norfloxacin, and ofloxacin])	Decreased absorption of interactant
Antacids or H2 receptor antagonist (e.g. cimetidine)	Ketoconazole	An acidic medium required for adequate ketoconazole dissolution and absorption. Thus, decreased absorption of ketoconazole
Bismuth Subsalicylate (in Pepto-Bismol)	Tetracycline HCl and other tetracyclines	Decreased tetracycline absorption
Bulk Laxatives	Antibiotics, digoxin, salicylates	Decreased absorption of the interactants
Cholestryamine or Colestipol	Multiple interactants; check prescribing information	Decreased absorption of the interactants, administer 1 to 4 hours before or 4 to 6 hours after the drug
Iron Supplements (e.g Feosol, Mol-Iron, Fergon)	Tetracycline antibiotics; oral quinolone antibiotics	Decreased antibiotic absorption
	Antacids, bulk laxatives	Decreased iron absorption

Magnesium-Aluminum Hydroxide Gel (e.g. Maalox, Kolantyl, Mylanta)	Tetracyclines, digoxin, phenytoin	decreased absorption of interactants
Mineral Oil	Fat-soluble vitamins	chronic mineral oil use can decrease the absorption of fat-soluble vitamins
C. Drugs which alter the distribution (e.g. plasma protein binding) of other drugs.		
Drug (category)	**Interactant**	**Effect**
Aspirin (e.g. Bayer, Anacin)	Coumadin, Diabinese, Valproic Acid	Displacement of drug plasma binding sites resultingin an increasedpharmacological response
Salicylates	Carbonic Anhydrase Inhibitors (e.g. Acetazolamide, methazolamide)	Displacement of CAIs from plasma protein binding sites resulting in lethargy, confusion, fatigue, anorexia, urinary incontinence, and hyperchloremic metabolic acidosis
D. Drugs which alter the renal excretion or effectiveness of another drug.		
Drug (category)	**Interactant**	**Effect**
Ammonium Chloride (menstrual products, e.g. Aqua-Ban)	Weakly basic drugs dependent upon urinary excretion (e.g. TCAD's Quinidine)	Urinary acidification would enhance excretion of these drugs
Aspirin (e.g Bayer, Anacin)	Methotrexate	Competes for renal tubular secretion decreasing elimination of interactant

Sodium Bicarbonate (Antacid products, e.g. Alka Seltzer)	Weakly basic drugs dependent upon urinary excretion (e.g amphetamine, quinidine)	urinary alkalinization would diminish excretion of these interactants, possibly leading to toxicity
	Methanamine mandelate	urinary alkalinization prevents conversion to methenamine to the active formaldehyde in urine
	Nitrofurantoin	Urinary alkalinization decreases the bactericidal effects of nitrofurantoin
	Lithium	sodium intake enhances lithium excretion
NSAIDs (e.g. Motrin)	Lithium	Serum lithium levels increase (N/V, diarrhea, anorexia, coarse tremor, slurred speech, confusion)
	Methotrexate	Serum Methotrexate levels increase (fever, mucosal ulcerations, severe nausea, diarrhea, gi bleeding)
E. Drugs which decrease or increase the biotransformation of another drug resulting in increased toxicity or no therapeutic e		
Drug (category)	**Interactant**	**Effect**
Phenylephrine, Pseudoephedrine HCL (Decongestant products)	Monoamine Oxidase (MAO) Inhibitors, St. John's Wort	MAO Inhibitors Decreae biotransformation with possible hypertensive crisis
Cimetidine	Warfarin, Phenytoin, Propranolol, Theophylline, Diazepam	Cimetidine reduces hepatic metabolism of these drugs, thereby delaying elimination and increasing serum levels
Acetaminophen	Erythromycin	Concurrent use of other hepatotoxic medications with erythromycin may increase the potential for hepatotoxicity

St John's Wort	Warfarin, SSRI, Protease Inhibitors	The herbal may induce the Cytocrome P450 enzymes responsible for warfarin metabolism resulting in an altered International Normalized ratio (INR) or through an unknown mechanism ecrease the absorption of the drug. Concomitant ingestion may result in additive central seratonin excess (i.e., serotonin syndrome). Symptoms inclue grogginess, N&V, weakness, agitation, confusion, hypothermia, diaphoresis, hyperreflexia, and muscle rigidity - The herbal caused a 28% decrease in the peak serum concentrations and AUC of indinavir (i.e., Crixivan) when administered concomitantly

F. Drugs which interfere with or affect the desired effect of another drug/diagnostic test.

Drug (category)	**Interactant**	**Effect**
Alcohol (Vehicle e.g., Nyquil Nighttime Cold Liquid Medicine)	Metronidazole, Chlorpropamide, Disulfiram	Antabuse Effect
Ascobic Acid	Fecal occult blood tests, urinary blood and Glucose Tests	False-Negative test results for blood; False-Negative for glucose in urine
Aspirin	Probenecid, Sulfinpyrazone	Inhibition of the uricosuric effect of the probenecid or sulfinpyrazone
Ephedrine SO4	Inhalation Anesthetics, MAO Inhibitors, Sympathomimetics	May enhance the arrhymogenic/hypertensive effects of interactants
Milk of Mangesia	Aspirin, Bisacodyl, Methenamine Mandelate, Calcium Polystyrene Sulfonate	Premature release of these drugs from their enteric-coated tablet in stomach coul result in stomach distress for the patient. --- Drug may increase adverse drug events of the interactant- Use in conjunction with magnesium containing laxatives may increase risk of metabolic acidosis

Pyridoxine (Vitamin B6)	Levodopa	Levadopa's antiparkinsonian effects are reversed by as little as 5mg of oral pyridoxine
Salicylates, Iron Products, Ibuprofen	Fecal Occult Blood Tests	False-Positive Result

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Assessment Questions

1. (Objective One) Define nonprescription drugs.

   All of the following are true about nonprescription drug products EXCEPT:

   A. Can be purchased over-the-counter at a pharmacy and/or retail outlet.
   B. These have a sufficient degree of safety for patient self care.
   C. With appropriate and clear directions can be used by the consuming public.
   D. Can be purchased without a doctor's prescription.
   E. Can be used to treat a long-term illness which can be self-diagnosed by the patient.

2. (Objective Two) Describe the various ways nonprescription drugs interact with prescription drugs.

   Intestinal obstruction can result when which of the following over-the-counter drugs is administered with a drug that slows down the gastrointestinal tract?

   A. Bismuth subsalicylate
   B. Calcium carbonate
   C. Famotidine
   D. Psyllium powder
   E. Zinc Ion

3. (Objective Three) Provide typical examples of nonprescription drugs which interact with prescription drugs.

   Antacids and H_2 receptor antagonists decrease the effectiveness of some drugs, e.g., antibiotics, digoxin, administered orally by:

   A. Displacing these drugs from plasma-protein binding sites.
   B. Causing increased metabolism of these drugs in the liver.
   C. By increasing stomach pH hinders prescription drug from dissolving.
   D. Altering the kidney excretion of these drugs.
   E. Adsorbing these drugs onto their surface.

4. (Objective Four) Provide typical prescription drugs which interact with nonprescription drugs.

   All prescription drugs have potential interactions with nonprescription drugs, but a few prescription drugs can lead to serious, life-threatening situations. An example of such a prescription drug would be:

   A. azithromycin
   B. metronidazole
   C. phenytoin
   D. propranolol
   E. sodium warfarin

5. (Objective Five) Name an example of a nonprescription drug-prescription drug interaction for each way nonprescription drugs interact with prescription drugs

   Which of the following combinations of a nonprescription drug administered with a prescription drug can cause organ damage?

   A. Acetaminophen-Azithromycin (Liver Toxicity)
   B. Ammonium chloride-Quinidine (Kidney Damage)
   C. Diphenyhydramine HBr-Alcohol (Brain Damage)
   D. Potassium chloride-Aldactone (Kidney Damage)
   E. Aspirin-Sodium Warfarin (Kidney Damage)
