Chapter 14: Detailed Summary

Medicinal Chemistry

Drugs are a broad class of chemicals that have some biological effect when taken into the body. A drug having therapeutic properties is also called a medicine. Governments regulate drugs based upon their safety and social acceptability. Chemists tend to classify drugs based upon their origins. A drug isolated from nature is called a *natural product*. A drug produced solely in the laboratory is referred to as *synthetic*. A natural product whose structure has been chemically modified in the laboratory is *semisynthetic*. The enhancing by one drug of the action of another is called the *synergistic effect*, and a synergistic effect is often more powerful than the sum of the activities of the two drugs taken separately.

How many drugs work can be understood by way of the *lock-and-key model*. The basis of this model is that there is a connection between a drug's chemical structure and its biological effect. According to the model, a drug functions by fitting into receptor sites on proteins in the body. When a drug molecule fits into a receptor site, the way a key fits into a lock, a particular biological event is triggered. Knowing the precise shape of a target receptor site allows chemists to design drugs that have an optimum fit and specific biological effect. The most talented designer of drugs is nature. Many drugs today, therefore, are still discovered in nature rather than created in the laboratory.

The use of drugs that destroy disease-causing agents without destroying the animal host is known as *chemotherapy*. Chemotherapeutics work by taking advantage of the different biochemistries of the disease-causing agent and the host. Many bacteria, for example, produce their own folic acid, which is a vital nutrient for practically all organisms. Humans, however, obtain folic acid through their diet. The first chemotherapeutics, sulfa drugs, developed in the 1930s, work by disrupting the production of folic acid. This is lethal for bacteria that need to produce their own folic acid. For humans, however, the sulfa drugs are well tolerated because humans obtain folic acid through their diet. After the sulfa drugs, other antibiotics, such as penicillins and cephalosporins, were soon discovered. Chemotherapy for viruses is difficult because viruses are not alive (they remain dormant) in between infections. Some successes, however, have been realized against certain viruses, such as those that cause herpes and AIDS.

Chemotherapy has found much success in treating various cancers, especially those detected in their early stages. The classic cancer chemotherapeutic works by being lethal to cells that are in the process of dividing. Selectivity against cancer occurs because cancer cells are dividing more often than normal cells. As scientists learn more about the pathology of different forms of cancer, they become better equipped to develop new and more effective cancer chemotherapeutics. An important example is the drug Gleevec, which was designed to bind to a receptor site found on an abnormal protein produced by certain cancers.

Most of the neurons of our nervous system are connected to each other by a small gap called the

synapse. A nerve impulse that reaches the terminal end of a neuron causes the release of *neurotransmitters* into the synapse. These neurotransmitters migrate across the synapse to the next neuron, where they bind to receptor sites. Once bound, the nerve signal is reinitiated within the second neuron. Drugs that affect our nervous system act by modifying the movement of nerve impulses. Stimulants such as cocaine cause a buildup of the neurotransmitter dopamine within the synapse. A depressant, such as alcohol, opens channels that allow chloride ions to migrate into the axon of the neuron. This depolarizes the neuron, which makes it less able to conduct the nerve impulse.

Pain relievers known as *anesthetics* prevent neurons from transmitting sensations to the brain. Local anesthetics, such as Novocain, cause a numbness that is localized to where the anesthetic is applied or injected. A general anesthetic, such as diethyl ether, renders the patient unconscious. Pain relievers known as *analgesics* enhance our ability to tolerate pain without abolishing nerve sensations. Over-the-counter analgesics, such as acetaminophen, inhibit the formation of prostaglandins, which the body produces to initiate inflammation after some form of injury. The more potent opioid analgesics, such as morphine, moderate the brain's perception of pain by mimicking the action of *endorphins*, which are a group of polypeptides produced by the body as a means of suppressing awareness of pain that would otherwise be incapacitating in life-threatening situations. Endorphins are implicated in the *placebo effect*, in which patients experience a reduction in pain after taking what they believe is a drug but is actually a sugar pill.

A common heart disease is *arteriosclerosis*, which is a buildup of plaque on the inside walls of arteries. This build up can be slowed and sometimes reversed by a class of compounds known as *statins*, which work by inhibiting the biosynthesis of cholesterol in the liver. Arteriosclerosis can be alleviated with *vasodilators*, such as nitroglycerine, which allows the muscles of the arterial walls to relax so that more blood can pass through the artery. To slow down an overworked heart, a physician may prescribe beta-blockers, which inhibit the binding of stimulatory neurotransmitters, such as norepinephrine.

On the whole, drugs have increased our life span and improved our quality of living. They are no substitute, however, for a healthy lifestyle and preventative approaches to medicine.

Summary of Terms

Agonist A molecule that binds to a receptor site and initiates a biological effect.

Analgesic A drug that enhances the ability to tolerate pain without abolishing nerve sensations.

Anesthetic A drug that prevents neurons from transmitting sensations to the brain.

Antagonist A molecule that binds to a receptor site and does not initiate a biological effect except for that it blocks other active molecules from binding to the receptor site.

Chemotherapy The use of drugs to destroy pathogens without destroying the animal host.

Combinatorial Chemistry A laboratory approach intended to mimic nature's chemical diversity that takes advantage of the many different ways in which a series of reacting chemicals can be combined.

Lock-And-Key Model A model based upon the idea that there is a connection between a drug's chemical structure and its biological effect.

Neuron A specialized cell capable of sending and receiving electrical impulses.

Neurotransmitter An organic compound released by a neuron and capable of activating receptor sites within an adjacent neuron.

Physical Dependence A dependence characterized by the need to continue taking a drug to avoid withdrawal symptoms.

Psychoactive Drug A drug that affects the mind or behavior.

Psychological Dependence A deep-rooted craving for a drug.

Re-Uptake A mechanism whereby a presynaptic neuron absorbs neurotransmitters from the synaptic cleft for reuse.

Synaptic Cleft A narrow gap across which neurotransmitters pass either from one neuron to the next or from a neuron to a muscle or gland.

Synergistic Effect One drug enhancing the effect of another.