



Chapter 14

Medicinal Chemistry

THE MAIN IDEA



Medicines are like keys that unlock various biological responses.

[14.1 Medicines Improve Health](#)

[14.2 The Lock-and-Key Model](#)

[14.3 Chemotherapy](#)

[14.4 The Nervous System](#)

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14.7 Medicines for the Heart

Heart disease is any condition that diminishes the heart's ability to pump blood. A common heart disease is *arteriosclerosis*, a buildup of plaque on the inside walls of arteries. As discussed in Section 13.8, plaque deposits are primarily an accumulation of low-density lipoproteins, which are high in cholesterol and saturated fats. Plaque-filled arteries are less elastic and have a decreased volume, as shown in **Figure 14.47**. Both of these effects make pumping blood more difficult, and the heart becomes overworked and weakens. Accumulated damage to heart muscle from arteriosclerosis or other stresses can result in abnormal heart rhythms, known as *arrhythmias*. Chest pains, known as *angina*, result from an insufficient oxygen supply to heart muscles. Ultimately, the weakened heart does not adequately circulate blood to the body. People with heart disease have decreased stamina and frequently need to pause to catch their breath during or after exercise.

As discussed in Section 13.8, another danger of arteriosclerosis is the potential for a blood clot around the site of plaque formation. Such a clot can break off and be carried through the bloodstream until it clogs a blood vessel, effectively cutting off the blood supply to tissue, which then begins to die.

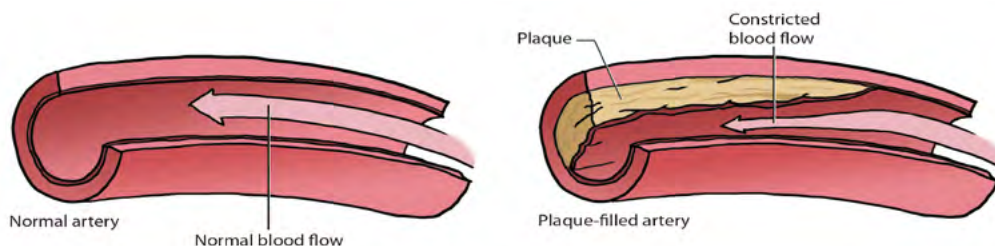


Figure 14.47

The heart has to work harder to push blood through vessels narrowed by plaque deposits. Furthermore, inflammation around the plaque can lead to the formation of heart-attack-causing blood clots.

A heart attack occurs when the dying tissue is heart muscle. Some heart attacks progress slowly, allowing the victim time to seek medical assistance, which may involve the administration of a quick-acting clot-dissolving enzyme. Other heart attacks are more rapid, killing the victim within minutes. Surviving a heart attack means living with a heart weakened by dead tissue.

The most effective way to treat heart disease is to do what can be done to prevent it from happening in the first place. This includes avoiding stress; exercising regularly; and eating a well-balanced, low-cholesterol diet. For many people, however, such a healthy lifestyle does little to lower their blood cholesterol levels, because their livers naturally produce more cholesterol than they obtain from their diet. For such people, physicians can prescribe what are known as statins, which are drugs that inhibit the synthesis of cholesterol. Two popular statins are atorvastatin (Lipitor[®]), which is a synthetic drug, and lovastatin (Mevacor[®]), which is a natural product isolated from the fungus *Aspergillus terreus*.

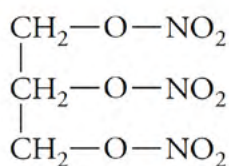


READING CHECK

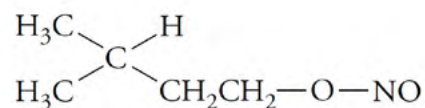
How do vasodilators increase blood supply?

Vasodilators are a class of drugs that increase the blood supply to the heart by expanding blood vessels. They are useful for treating angina. They also reduce the workload of the heart, because opening up the blood vessels makes pumping the blood easier. Traditional vasodilators include nitroglycerin and amyl nitrite, both shown in **Figure 14.48**. They can be administered by a number of routes: orally or sublingually (under the tongue) or as a transdermal (through the skin) patch. A benefit of the latter two approaches is that they allow the drug to enter the body slowly, in contrast to the effect of taking the drug orally or by injection. These organic nitrates are metabolized to nitric oxide, NO, which has been shown to relax muscles in blood vessels.

Drugs that relax the pumping action of the heart have also been developed. When bound to receptor sites called beta-adrenoceptors in heart muscle, the neurotransmitters norepinephrine and epinephrine stimulate the heart to beat faster. A series of drugs called *beta blockers* slow down and relax an overworked heart by blocking norepinephrine and epinephrine from binding to the beta-adrenoceptors. Propranolol (Inderal[®]), shown in **Figure 14.49**, was the first beta blocker developed and is useful for treating angina, arrhythmias, and high blood pressure.



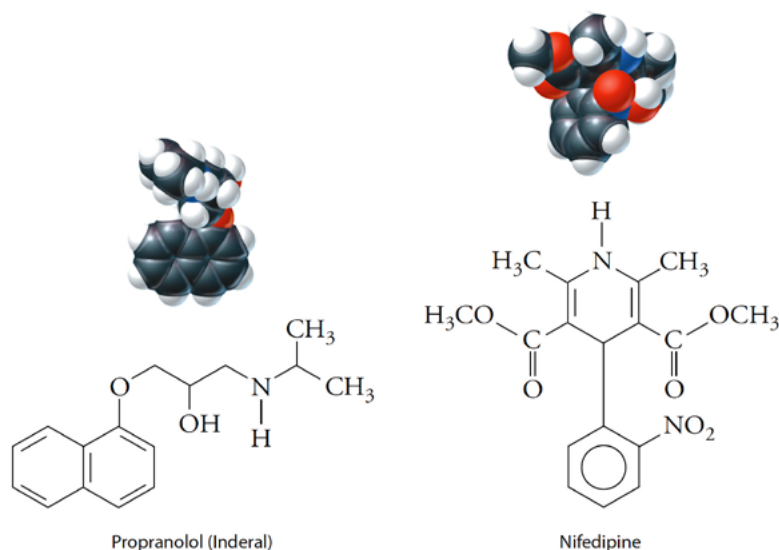
Nitroglycerin



Amyl nitrite

Figure 14.48 >

The vasodilators nitroglycerin and amyl nitrite.



< **Figure 14.49**

Propranolol is a beta blocker, and nifedipine is a calcium channel blocker.

Another group of drugs that relax heart muscle are the *calcium channel* blockers. One example is nifedipine, shown in Figure 14.49. Muscle contraction is initiated as a nerve impulse signals calcium ions to enter muscle cells. As their name implies, calcium channel blockers inhibit the flow of calcium ions into muscles, thereby inhibiting muscle contraction. This slows the heart rate, relaxing and dilating the muscles of blood vessels, which lowers blood pressure.

In the United States and in most other developed nations, heart disease is the number one cause of death for individuals over the age of 65. Because most people in these nations live past this age, heart disease is actually the leading cause of death for all age groups combined, as noted in **Table 14.3**.

TABLE 14.3 Causes of Death in 2020 within the United States (Source U.S. CDC)

AGE GROUP (YEARS)	CAUSE	TOP CAUSES, ALL AGES COMBINED
15–24	Accident	1. Heart disease: 690,882
25–44	Accident	2. Cancer: 598,932
45–64	Cancer	3. COVID-19: 345,323
>65	Heart disease	4. Accidents : 192,176
		5. Stroke: 159,050
		6. Lung diseases: 151,637
		7. Alzheimer's: 133,382
		8. Diabetes: 101,106
		9. Influenza/pneumonia: 53,495
		10. Kidney disease: 52,260
		11. Suicide: 44,834

Remember, seven days without exercise makes one weak!



Perhaps nowhere is the impact of chemistry on society more evident than in the development of drugs. On the whole, they have increased our life span and improved our quality of living. They have also presented us with a number of ethical and social questions. How do we care for an increasing elderly population? What drugs, if any, should be legally permissible for recreational use? How do we deal with addictive drug use—as a crime, as a disease, or both? As we continue to learn more about ourselves and our ills, we can be sure that more powerful drugs will become available. All drugs, however, carry certain risks that we should recognize. As most physicians would point out, drugs offer many benefits, but they are no substitute for a healthy lifestyle and preventive approaches to medicine.

CONCEPT CHECK

Why do long-time alcoholics require greater doses of a beta blocker in order to relax cardiac muscle?

CHECK YOUR ANSWER As discussed in Section 14.5, long-time excessive drinking leads to an increase in the number of receptor sites for stress neurotransmitters. With more of these receptor sites to block, alcoholics require a correspondingly greater dose of the beta blocker to achieve the desired degree of cardiac relaxation.

