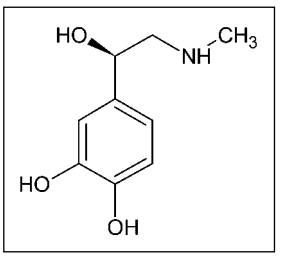
34. Epinephrine (Adrenaline)

CHEMICAL NAME = 4-(1-hydroxy-2-(methylamino)ethyl) benzene-1,2-diol
CAS NUMBER = 51–43–4
MOLECULAR FORMULA = $C_9H_{13}NO_3$
MOLAR MASS = 183.2 g/mol
COMPOSITION = C(59%) N(7.6%) H(7.2%) O(26.2%)
MELTING POINT = 211°C–212°C
BOILING POINT = decomposes at 215°C
DENSITY = 1.3 g/cm^3 (calculated)



Epinephrine, also known as adrenaline, is a hormone continually secreted by the medulla of the adrenal gland, which is located on the top of each kidney. Epinephrine comes from the Greek *epi nephros* meaning "on kidneys"; adrenaline is the English equivalent of epinephrine. Both epinephrine and adrenaline were named by original researchers without the "e" at the end and this "e" was added over time. Epinephrine is also secreted at nerve endings as a neurotransmitter. It was isolated by Jokichi Takamine (1854–1922) in 1900 and was the first hormone to be isolated in pure form. Takamine's success marked several years of efforts in attempting to obtain the compound from adrenal gland secretions of animals. English researchers George Oliver (1841–1915) and Edward Albert Sharpley-Schaffer (1850–1935) had injected adrenal secretions into animals in the mid-1890s, producing a rise in blood pressure; researchers believe adrenal compounds held promise for medical applications. In 1897, John Jacob Abel (1857–1938) and Albert C. Crawford (1869–1921), working at Johns Hopkins Medical School, isolated a compound they named epinephrin, but it turned out to be the monobenzoyl derivative of epinephrine. Takamine, who worked for the Parke, Davis & Company drug producer, visited Abel's laboratory in 1900. Takamine's assistant, Keizo Uenaka, successfully crystallized pure epinephrine in 1900. Takamine applied for a patent on a "Glandular Extractive Product" on November 5, which he called adrenalin; on April 16, 1901, Takamine was granted a trademark for Adrenalin. Takamine presented and published the first articles on epinephrine in 1901. Concurrently, another Parke-Davis chemist, Thomas Bell Aldrich

(1861–1938), also produced epinephrine and determined its correct formula. Parke, Davis began promoting Adrenalin soon after the discoveries of Takamine and Aldrich. It was promoted as a treatment for heart disease, goiter, deafness, and Addison's disease.

Epinephrine is synthesized in the body from the nonessential amino acid tyrosine. Tyrosine undergoes hydroxylation to produce DOPA (3,4-dihydroxyphenylalanine). DOPA decarboxylation produces dopamine, which is hydroxylated to norepinephrine. Norepinephrine, which is closely related to epinephrine, performs a number of similar functions in the body. The prefix "nor" associated with a compound is used to denote an alkylated nitrogen in the compound that has lost an alkyl group. It comes from the German *N-ohne-radical,* which means Nitrogen without the radical. Therefore norepinephrine is epinephrine minus the methyl, CH_3, radical on the nitrogen. The methylation of norepinephrine gives epinephrine. The synthesis is summarized in Figure 34.1.

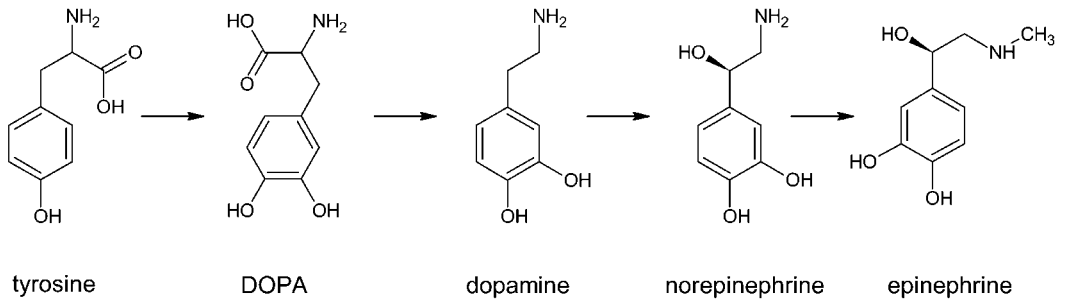


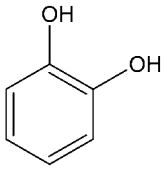
Figure 34.1 Synthesis of epinephrine.

Epinephrine has several important physiological functions in the body. Its effect is produced when it binds to receptors associated with different organs. Receptors are highly specialized, and the effect of a hormone such as epinephrine depends on the type of receptor to which it binds. For this reason, epinephrine can produce different effects in different organs, so it is important to realize that physiological effects produced by epinephrine are not absolute. The physiological effects of epinephrine are the same whether it is produced in the adrenal gland or at the nerve endings, but because the adrenal source delivers the hormone to organs via the bloodstream, its effect lasts considerably longer. In general, epinephrine in the blood produces an effect lasting several minutes, which is several times as long as when it is produced at nerve endings.

Epinephrine is vital for normal physiological function and maintaining homeostasis, but it is secreted in large quantities during times of stress (norepinephrine is also secreted and many of its effects are similar to those of epinephrine). The stress response, sometimes called the "fight or flight" response, highlights the effects of epinephrine on the body. Epinephrine increases heart rate and stroke volume, resulting in an increase of blood flow to muscles. It produces vasoconstriction in peripheral arteries and veins, but vasodilation in other organs such as muscles, liver, and the heart. Epinephrine's effect on blood vessels depends on the type of receptor it acts upon. When it acts on alpha receptors, it results in vasoconstriction; with beta receptors it produces vasodilation. There is evidence showing that vasoconstriction dominates at high epinephrine concentrations and vasodilation at low concentrations.

High epinephrine results in an increase in blood pressure because of vasoconstriction. High epinephrine increases lipid metabolism and the conversion of glycogen to glucose providing increased energy input to cells. During times of stress, epinephrine inhibits nonessential functions such as gastric secretions and insulin production.

Epinephrine belongs to a class of hormones called catecholamines, which are derived from tyrosine and have a structure related to catechol. It is used in drugs and medications, often in the salt form as epinephrine hydrochloride. It is best known for treating allergic reactions, a condition called anaphylaxis. Anaphylaxis is caused by insect bites, foods, medications, latex, and other causes. A common device familiar to many is the epi-pen, which is an autoinjector that delivers a single dose of epinephrine. EpiPen, the most popular pen, is a registered trademark of Dey Laboratories. Adult pens are designed to deliver 0.3 mg of epinephrine, and child pens deliver a 0.15 mg. dose. Injection of epinephrine almost immediately improves breathing, stimulates the heart, and reverses swelling to the face and lips. Epinephrine is also used for heart conditions, bronchitis, bronchial asthma, emphysema, and glaucoma. It is a heart stimulant. The use of epinephrine has recently been adopted in hair transplant surgeries to reduce bleeding.



catechol