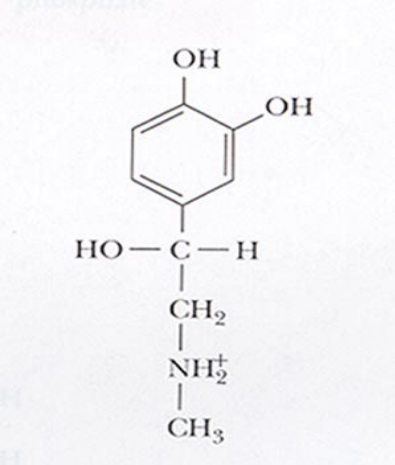
Epinephrine



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Epinephrine, more commonly known as adrenaline, is a hormone secreted by the medulla of the adrenal glands. Strong emotions such as fear or anger cause epinephrine to be released into the bloodstream, which causes an increase in heart rate, muscle strength, blood pressure, and sugar metabolism. This reaction, known as the "Flight or Fight Response" prepares the body for strenuous activity. In medicine epinephrine is used chiefly as a stimulant in cardiac arrest, as a vasoconstrictor in shock, and as a bronchodilator and antispasmodic in bronchial asthma. Epinephrine is found in small amounts in the body and is essential for maintaining cardiovascular homeostasis because of its ability to divert blood to tissues under stress.

During cardiac arrest the top priority is to maximize the amount of blood flow through the coronary artery. Epinephrine, when injected into an intravenous fluid solution, will increase the coronary artery pressure thereby promoting increased coronary blood flow. Increased doses of epinephrine quicken the response, but some studies have shown that brain and heart damage are some of the side effects.

Anaphylactic shock is caused whenever the heart is unable to pump enough blood throughout the body due to an allergic reaction, weakening of the heart muscle, or shrinking of the veins (vasodilation). Injection of epinephrine into the blood stream will cause an increase of blood flow throughout the body. The relief is only temporary due to the short half-life of adrenaline;

therefore, immediate hospitalization is required to ensure safety to the individual.

Individuals who are prone to asthma attacks have lung passages that are more susceptible to inflammation and swelling. The swelling causes constriction of the muscles around the airway tubes and an increase in mucus. The combination of these three leads to the shortness of breath, coughing, or wheezing common to those who suffer from asthma. When inhaled in small doses, epinephrine causes short-term relief from the symptoms by widening the bronchial tubes allowing air to pass through. Once again epinephrine is not the best cure, but a temporary relief when an asthma inhaler is not present.

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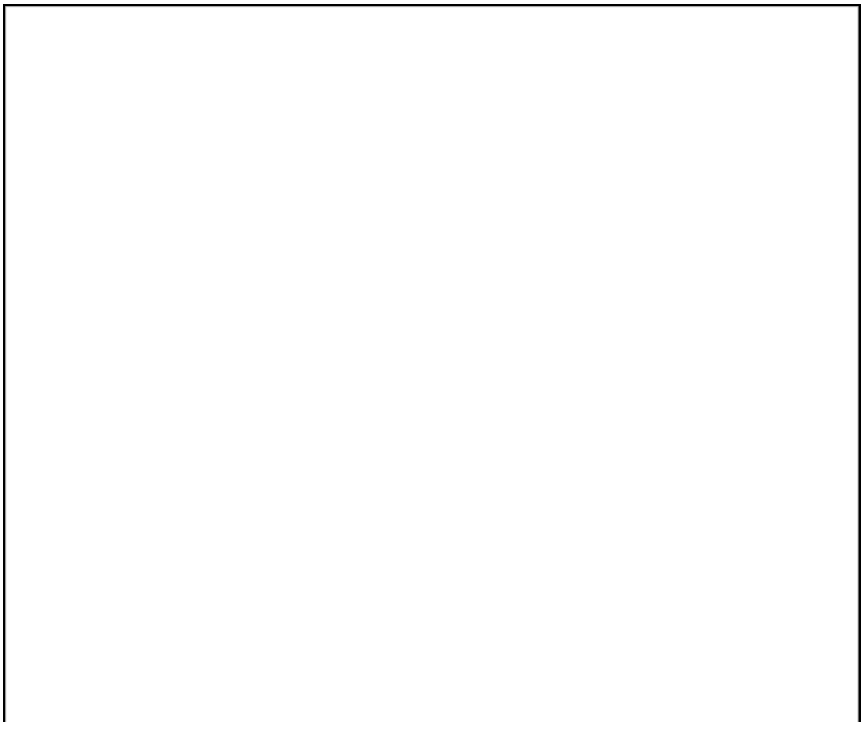
Formation of Epinephrine in the Body

Epinephrine is formed in the body from Tyrosine through a four-step process outlined below.
click to see on separate page



(1) Tyrosine is hydroxylated to L-DOPA by tyrosine hydroxylase.

(2) L-DOPA is decarboxylated to dopamine.

(3) A secondy hydroxylation yields norepinephrine.

(4) Methylation of norepinephrine's amino group produces epinephrine.

[1]Voet, Donald and Voet, Judith. Biochemistry. 2nd Edition. Pages 759-760

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Epinephrine and Its Effect on Smooth Muscle Cells

Relaxation and contraction of smooth muscle cells (i.e. heart, arteries, and veins) are controlled through epinephrine receptors. The click here to view the figure which represents the mechanism of this control.
Contraction occurs through binding of calmodulin to Calcium ions when the concentration is ten times larger than normal in the cell. The Calcium-Calmodulin complex then activates the myosin light chain kinase (MLCK), which in turn phosphorylates the LC2 causing contraction. Binding of epinephrine to the epinephrine receptors activates adenylyl cyclase producing cyclic AMP from ATP. Cyclic AMP activates a protein kinase thereby phosphorylating the MLCK. This has a lower affinity for Calcium-Calmodulin complex and is thus inactive; thereby, relaxing the smooth muscle tissue. For this reason epinephrine is used for cardiac arrests, asthma, and anaphylactic shock patients.

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Epinephrine and Its Effects in Liver Cells

Glycogen synthesis and degradation occurs in the liver cells. It is here that the hormone insulin (the primary hormone responsible for converting glucose to glycogen) acts to lower blood glucose concentration. Insulin stimulates glycogen synthesis; thereby, inhibiting glycogen degradation as shown in the figure (click here to view figure).

Epinephrine, on the other hand, is one of the two primary hormones (the other being glucagon) that breakdown glycogen. Epinephrine will bind to the receptor on the outside of a liver cell allowing a conformational change to occur. This receptor shape change allows G protein to bind, and become active. The activation G protein causes a conformational change on the molecule causing adenylate cyclase to bind. Once adenylate cyclase has been activated ATP binds to the complex. Adenylate Cyclase breaks down ATP into Cyclic AMP, which becomes the second messenger protein in this process. Cyclic AMP activates protein kinase, which activates phosphorylase catalyzing the breakdown of glycogen to glucose. For a better understanding of this process, a PowerPoint slide presentation is found here. (www.cabrillo.cc.ca.us/divisions/becho/bio/dscott/homeostasis/sld059.htm) (Note: Click on View Image to show the PowerPoint presentation.)

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Ephedra, Ephedrine, Ma Huang

Epinephrine exists as an extremely regulated hormone in the body. Medication containing this hormone must be prescribed by a doctor or administered in a hospital for severe cases of asthma, shock or cardiac arrest. Ephedrine is a protein extracted from a Chinese plant that acts similar to epinephrine and acts on the same receptors. Ephedra equisetina (also known as its 5000 year-old Chinese name Ma Huang) is this desert shrub from which ephedrine is extracted. It contains two substances, ephedrine and pseudoephedrine. The first helps to relieve asthma and stimulates the sympathetic nervous system, while pseudoephedrine acts as a nasal decongestant. Since epinephrine receptors will recognize ephedrine molecules, ephedrine can also cause the breakdown of glycogen in the liver. For this reason, Ma Huang is one of the more popular dietary herbal supplements on the market, which can be found at any pharmacy, grocery store or General Nutrition Center in the nation. For dieters it suppresses the appetite and stimulates the thyroid gland increasing thermogenic metabolism. Metabolism similar to that if one were exercising for a prolonged period of time, such as, during a cardiovascular routine. The adrenal glands dump epinephrine into the blood stream, which leads to an increase in body temperature thereby burning more calories. Although, ephedrine will not cure a poor diet, weight loss has only been proven in people in coordination with Calorie restriction.

For athletes ephedrine, in theory, could enhance athletic abilities by opening the lungs, enhancing muscle contractility, and increasing blood glucose levels during competition. Responses similar

to an “adrenaline rush” felt by athletes. If used at all for helping to improve athletic performance, the best situation would be in the gym. Ephedrine has fast acting effects that may tire an athlete on the playing field, but not during a shorter workout routine. However, long-term reliance on this compound to “energize” them for a particular workout is not a good idea and will eventually lead to negative effects on the playing field. Also, college athletes should be aware that the IOC, NCAA, and the Olympic committee all ban the use of this product. No high schools have placed any band on any herbal supplement.

Ma Huang does have several negative effects to it, which have warranted action by the FDA to attempt to ban this drug. Ephedrine can increase blood pressure and heart rate, while causing dizziness, insomnia, and headaches. The Food and Drug Administration proposed limits on ephedrine levels in supplements and to be taken for no longer than 7 day intervals. They should also contain a warning label indicating the overdosing (more than 25 mg/day) may cause heart attack, stroke, seizures, or death. Last year the FDA did not provide conclusive evidence needed to put restrictions on ephedra. One major reason that the FDA did not provide enough evidence is the fact that a 1994 law removed dietary supplements from control of the FDA, and as a result, they are not subjected to the strict clinical tests as prescription medication. Like any drug (prescribed, over-the-counter, or dietary supplement) the daily dosage should not be exceeded for risk of long-term affects on the body.

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