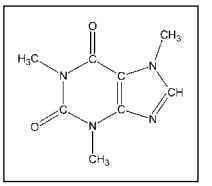
18. Caffeine

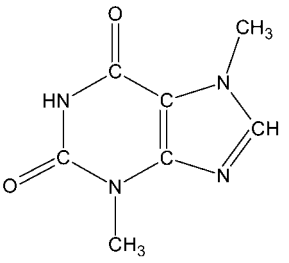
CHEMICAL NAME = 3,7-dihydro-1,3,7-trimethyl-1H-purine-2,6-dione
CAS NUMBER = 58–08–2
MOLECULAR FORMULA = $C_8H_{10}N_4O_2$
MOLAR MASS = 194.2 g/mol
COMPOSITION = C(49.5%) H(5.2%) N(28.9%) O(16.5%)
MELTING POINT = 237°C
BOILING POINT = sublimes
DENSITY = 1.2 g/cm^3



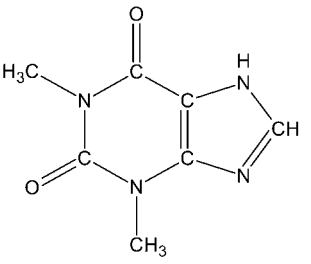
Caffeine is an alkaloid purine belonging to the group of organic compounds called methylxanthines. Pure caffeine is a white, crystalline, bitter-tasting compound. Caffeine is found in a number of plants, principally coffee and tea plants, as well as cola and cacao nuts. In plants, caffeine functions as a natural pesticide to deter insects. The consumption of caffeine dates back thousands of years. Tea was consumed in China several thousand years B.C.E. but quite possibly was used in India before that and introduced into China. Coffee consumption is believed to have started in the Kaffa region of Ethiopia around 800 c.e. and over time spread to Arabia, Turkey, and other parts of the Middle East. The port city of Mocha on the Red Sea in Yemen became a principal coffee-growing region and area of export in the Middle East. Rulers in coffee-growing areas imposed strict laws against the exportation of coffee plants to exercise their monopolies over the lucrative product. Coffee plants spread throughout the world from successful smuggling. Tea and coffee were introduced into Europe in the 17th century, well after its use in other parts of the world. Chocolate drinks from cacao beans (cocoa is often used for the drink or powder product made from the cacao beans) were being concocted by native populations in Central and South America several hundred years B.C.E. The Spanish explorer Hernando Cortés (1485–1587) brought cocoa back to Spain around 1528.

Only a small amount of caffeine is found in the cacao plant and chocolate. The principal alkaloid in the cacao plant is theobromine, which is almost identical to caffeine, but differs by having one less methyl group. Theobromine does not contain bromine but derives its name

from the genus *Theobroma* of the cacao tree. Theobroma's Greek translation is "food of the gods." Another compound almost identical to caffeine in tea is theophylline. It also contains one fewer methyl group.



theobromine



theophylline

The discovery of caffeine is attributed to Friedlieb Ferdinand Runge (1795–1867), a German physician and chemist. Runge was working in the laboratory of Johann Wolfgang Döbereiner (1780–1849), when Döbereiner's friend, Johann Wolfgang von Goethe (1749–1832), paid a visit. Runge performed an experiment for Goethe in which he dilated a cat's eye with an extract from a nightshade plant. Goethe awarded Runge with a sample of rare coffee beans and challenged him to determine the compound that gave coffee its stimulating effects. After several months, Runge isolated caffeine from coffee in 1819. Caffeine derives its name from the Kaffa region of Ethiopia. Caffeine comes from the German *kaffeine,* which in turn is derived from the German word for coffee, *kaffee.* In 1827, a compound isolated from tea was named theine, but this was eventually shown to be caffeine.

Caffeine is a stimulant to the central nervous system and cardiac muscle and is a mild diuretic. Caffeine's physiological effects are thought to be the result of caffeine's interference with adenosine in the brain and body. Adenosine moderates nerve transmissions. As adenosine builds up while a person is awake, it produces a self-regulating mechanism to inhibit nerve transmission. As adenosine receptors in the brain acquire more adenosine, the reduction in nerve transmission induces sleep. Caffeine competes with adenosine and interferes with the neural modulation function of adenosine. This is why coffee has a tendency to keep people awake. The effects of coffee and caffeinated drinks vary widely among individuals. Generally, moderate consumption leads to restlessness and tends to energize individuals. Caffeine increases blood pressure and has been indirectly associated with heart and pregnancy problems; it increases stomach acid, which can lead to ulcers. Regular users of caffeinated drinks can experience withdrawal side effects such as anxiety, nervousness, fatigue, and headaches. The effects of caffeine lasts several hours after consumption. It is carried by the blood to all parts of the body and is eliminated primarily through the urine after a half-life from 4 to 10 hours in most adults.

Health experts advise that moderated amounts of caffeine from 100 to 300 mg per day are acceptable. Adult Americans consume approximately 250 mg of caffeine per day. The LD_{50} (the lethal dose that kills 50% of a test population of individuals subjected to a substance) of caffeine for humans is estimated between 150 and 200 mg per kilogram of body weight. The amount of caffeine in some popular food items is given in Table 18.1.

Coffee beans are the primary source of caffeine. These beans are obtained from a variety of plants but can be broadly grouped into two classes: arabica and robusta. Arabica is obtained from the species *Coffea arabica* and robusta from the species *Coffea canephora.* Robusta, as the

Table 18.1 Approximate Caffeine Content of Selected Food and Medicine Items

	Caffeine in mg
Coffee	30–140 (8-oz cup)
Mountain Dew	54 (12 oz)
Coca-Cola	45 (12 oz)
Pepsi-Cola	37 (12 oz)
Tea (brewed)	20–100 (8 oz)
Red Bull	80 (8.2 oz)
Häagen-Dazs coffee ice cream	58 (1 cup)
Hot chocolate	5 (8 oz)
Excedrin	130 (2 tablets)
NoDoz	200 (1 tablet)
Anacin	64 (2 tablets)

name implies, is more robust than arabica coffee but produces an inferior taste. Arabica plants are grown globally, but robusta plants are grown only in the Eastern Hemisphere. Coffee beans contain 1–2% caffeine, with robusta varieties generally containing twice the content of arabica varieties. Other sources of caffeine contain various caffeine content: kola nut (1–3.5%), tea leaves (1.4–4.5%), and cacao (0.1–0.5%).

Some food processors add caffeine to their products (soft drinks), but others remove caffeine and advertise the product as decaffeinated. Coffee was first decaffeinated in 1906 in Germany through a process founded by the coffee merchant Ludwig Roselius (1874–1943). Roselius's team sought to decaffeinate coffee without destroying the aroma and flavor. Roselius fortuitously worked on beans that had been soaked with seawater during a storm and found a method to remove 97% of the caffeine in coffee beans without destroying the flavor. Roselius then marketed the product under different names in various European countries. In France, the name of the decaffeinated coffee was Sanka, which is derived from *sans* caffeine (*sans kaffee*). Sanka was introduced in the United States in 1923. The traditional method of decaffeinating coffee beans involved steaming the beans and then extracting the caffeine in an organic solvent such as Freon, chloroform, methylene chloride, or ethyl acetate. Because of the environmental problems and costs associated with organic solvents, green decaffeination techniques have been developed in recent years. One popular method is to use supercritical carbon dioxide to extract caffeine (see Carbon Dioxide).

Caffeine has widespread therapeutic use. It is widely used in headache (migraine) remedies such as aspirin and other analgesics. Caffeine is a mild vasoconstrictor and its ability to constrict blood vessels serving the brain explains its use to relieve headache. Individuals who consume caffeine regularly through medications and food are susceptible to what is known as a rebound headache or caffeine rebound. This occurs when regular caffeine intake is suddenly reduced and the vessels dilate. Caffeine is a common substance in medications to treat apnea in premature infants. Apparently, the area of the brain controlling respiration in premature infants is not fully developed and caffeine helps to stimulate this portion of the

brain. The combination of caffeine and ephedrine is used in dietary and athletic supplements, and their role as appetite suppressant and energy boosters has been extensively studied. Some individuals claim that a modest dose (200 mg) of caffeine can enhance athletic performance, but its exact effect is unclear. Caffeine is used for the treatment of attention deficit disorder/attention-deficit hyperactivity disorder, but health experts do not recommend its use for this condition.