

## 28. Cocaine

**CHEMICAL NAME** = 8-Azabicyclo[3.2.1]octane-2,2-carboxylic acid, 3-(benzoyloxy)-8-methyl-, methyl ester

**CAS NUMBER** = 50-36-2

**MOLECULAR FORMULA** =  $C_{17}H_{21}NO_4$

**MOLAR MASS** = 303.4 g/mol

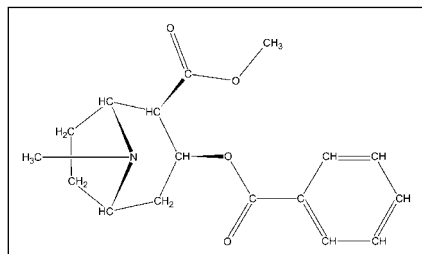
**COMPOSITION** = C(67.3%) H(7.0%)

N(4.6%) O(21.1%)

**MELTING POINT** = 98°C

**BOILING POINT** = 187°C

**DENSITY** = 1.22 g/cm<sup>3</sup> (calculated)



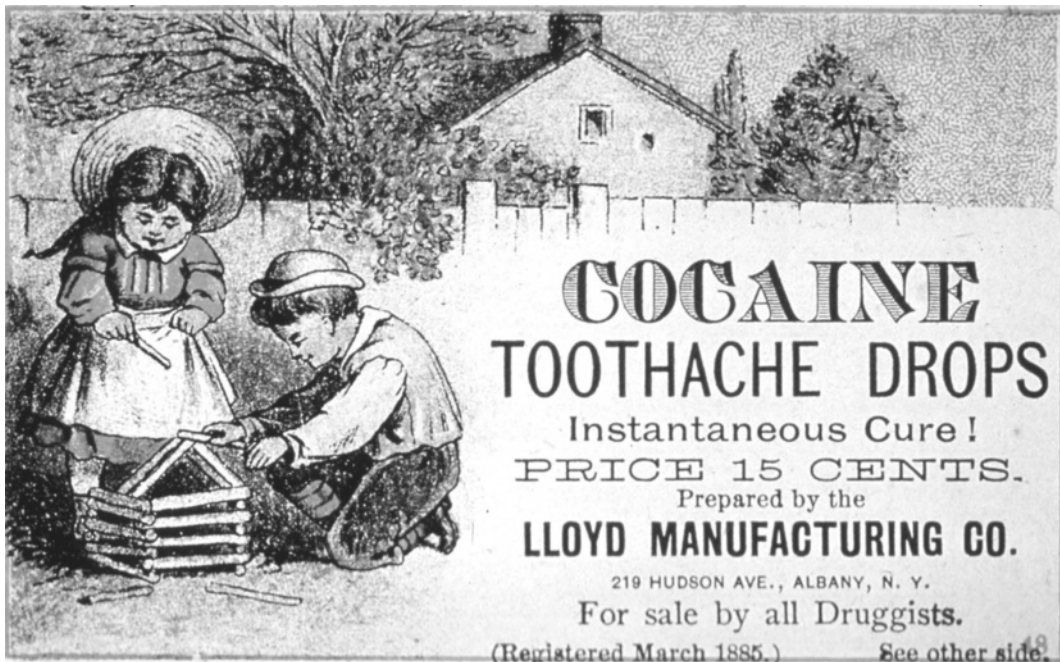
Cocaine is best known as an illegal drug that produces a euphoric “high” in individuals who use it. Cocaine is an alkaloid obtained from the leaves of the coca plant, *Erythroxylum coca*, which is native to northwestern South America and Central America. Native Indians in the Andes have chewed coca leaves for thousands of years, and early Spanish explorers noted the stimulating effect that chewing the leaves had on these people. Coca was traditionally reserved for royalty and religious ceremonies in many of these cultures. It was the most sacred plant for the Incas, and its use was reserved for priests and nobility. For many indigenous populations coca was an important food that provided nourishment and essential nutrients and was therefore widely cultivated. Natives carried pouches of coca leaves called *chuspas* and distances and time would be measured by the length of a chew. The time of a chew was called a *cocada*. Its traditional use among pre-Columbian cultures varied, but the subsequent conquest of these groups helped establish its general use among common people. This was related to the apparent ability of coca to provide stamina as well as induce insomnia to users.

Spanish conquistadors introduced coca to Europe and the original missionaries unsuccessfully attempted to ban its use. The Catholic Church viewed its use as an act of paganism and a remnant of native religious ceremonies. Despite this position and the Church’s destruction of cultured coca crops, coca’s widespread use among many isolated cultures prevented significant

elimination. As conquered native populations were enslaved, Europeans saw the utility of coca as a stimulant to induce greater work out of people. Furthermore, control of coca plants provided early European settlers a valuable economic commodity to obtain goods and labors from natives. Subsequently, King Philip II of Spain (1527–1598) lifted any ban on coca, gave land grants to establish coca plantations, and imposed a tax on it. Discovery of Andean silver further stimulated coca use, as Europeans used coca leaves to boost slave labor.

Coca was touted in Europe as a great elixir and its use increased between the 16th and 19th centuries. In 1855, the German chemist Friedrich Gaedcke (1828–1890) succeeded in isolating the active ingredient in coca leaves and called it erythroxyline. An improved process for isolating cocaine was discovered by Albert Niemann (1834–1861) during his dissertation work in 1860. Soon after Niemann's success, an explosion of cocaine in numerous therapeutic products ensued. It was widely used as a topical anesthetic in dentistry (Figure 28.1) and in ophthalmology; it also found use as an appetite suppressant, a drug used to treat morphine addiction, a stimulant, and a general elixir. Its popularity to treat depression was originally advanced by Sigmund Freud (1856–1939). In 1900, it was among the top five medicinal products in the United States.

Coca extracts were also added to common food items. A popular wine called Vin Mariani was concocted by the chemist Angelo Mariani (1832–1914) in 1863. Mariani's Bordeaux mixture used coca leaves. Cocaine from the coca leaves was extracted by the ethanol in the



**Figure 28.1. Advertisement for cocaine tooth medicine from 1885. Cocaine was extensively used in the latter part of the 19th century in medicines, as a stimulant, as an anesthetic, and to treat morphine addiction.** *Source:* National Library of Medicine of the National Institute of Health.

wine. After Mariani's success a number of other vintners used coca leaves to infuse cocaine into their wines. One of these was a druggist from Atlanta named John Stith Pemberton (1831–1888). Pemberton produced his own version of a coca wine, but he also added the cola nut, which was also believed to have therapeutic properties. Reacting to the temperance movement, Pemberton sought to produce a nonalcoholic version of his beverage. Pemberton obsessively worked to find a new formula using the coca leaf and cola nut ingredients. On May 8, 1886, the first coke was served at Jacobs Pharmacy in Atlanta. In establishing his new drink, which was to be marketed as an invigorating tonic, Pemberton sought a unique name. Frank Robinson was one of Pemberton's partners and his bookkeeper. Robinson, who was a keen marketer, joined the names of the two ingredients Coca and Cola together and designed the unique script of Coca-Cola. Coca-Cola was not an instant success. Pemberton, who suffered from morphine addiction, sold his company interests and Coca-Cola's formula during his last months and never realized the eventual success of the company. Although the cocaine extract of coca was eliminated from Coca-Cola in 1906 because of passage of the Pure Food and Drug Act, the formula still calls for other coca extracts for flavoring.

At the end of the 19th century, people started to become aware of the addictive and medical problems associated with cocaine. Cocaine is a stimulant and its use produces a euphoric high accompanied by increased motivation, energy, and libido. Concurrently, it has physiological effects that include increased pulse rate, breathing, and blood pressure (it is a vasoconstrictor); muscle tension; loss of appetite; and insomnia. Unfortunately, after the initial euphoric high, which may last several minutes to several hours, the user experiences a letdown. This state of depression leaves the user craving another dose and the vicious cycle of drug addiction has begun. One theory for cocaine's effect is related to its role in disrupting the neurotransmitter dopamine. Cocaine occupies receptor areas on nerve cells blocking dopamine from the cell. The dopamine in the cell discharges its signal in the synapse and leads to a prolonged and extended buildup of dopamine. Increased dopamine affects the pleasure center of the brain and the elevated dopamine produces the high. The neurons respond to cocaine use by reducing the number of dopamine receptors; therefore when the brain returns to normal conditions, the lack of receptors and decrease in dopamine results in depression.

The effects of cocaine vary according to how it is consumed, individual differences, dose, and frequency of use. The most common form is the crystalline salt cocaine hydrochloride. Cocaine in this form is water-soluble and can be pulverized into a fine powder and can be "snorted" or inhaled through the nose. Here it is adsorbed onto the mucous membranes and then absorbed into the bloodstream through mucous membranes. Cocaine can also be prepared as an aqueous solution and directly injected into the bloodstream. This method delivers cocaine quickly to the brain and the user can experience a high in a matter of minutes. Free base cocaine is cocaine in which the hydrochloride has been removed to produce a more pure product that can be used for smoking. Cocaine hydrochloride is not suitable for smoking because it vaporizes at too high a temperature. Free base is prepared by making an aqueous solution of cocaine hydrochloride with baking soda (sodium bicarbonate) or ammonia and then boiling the solution down to give the free base. Cracking sounds during the process led to the name "crack" for free-base cocaine.

Colombia is the world's leading producer of cocaine, with about 75% of the world's production. Coca is grown locally and is also imported from Peru and Bolivia. The processing of

coca involves mashing the leaves with a base, kerosene, and sulfuric acid to produce a paste containing between 40% and 70% cocaine. It can then be exported where it is dried and purified into cocaine hydrochloride. Estimates of global consumption of cocaine vary, but a reasonable approximation is roughly 750 tons. Of this amount, approximately one-third is imported into the United States, which is the leading consumer of cocaine.

Cocaine is used medicinally for local anesthesia and vasoconstriction, especially in surgery involving the ear, nose, and throat. It is the only naturally occurring anesthetic. Although it is still used in limited quantities for surgery, many surgeons and anesthesiologists have turned to safer alternatives such as lidocaine and benzocaine. Also, the use of alternatives eliminates the storage of a well-known addictive drug in clinics and hospital pharmacies.