# Idaho State Police
# Forensic Laboratory Training Manual
# Cocaine

## 1.0.0 HISTORY

Archaeological artifacts show that the use of coca was widely accepted in ancient cultures of South American Indians. Paintings on pottery, ornaments depicting pictures and symbols of the coca bush and its leaves, as well as sculptured wood and metal objects dating as far back as 3000 BC on the coast of Ecuador indicate the use of coca in both civil and religious rituals. Relatively recent studies of the antiquity of the use and cultivation of coca indicate that the coca plant is native to the eastern Andes Mountains. Until this day, the natives in the area continue the custom of chewing coca.

A French chemist, Angelo Mariani, introduced Europe to the coca leaf by importing tons of coca leaves and using an extract from them in many products such as his “Coca Wine.” Cocaine, as obtained from the coca leaves, was first discovered by Gaedecke in 1855 and rediscovered by Niemann in 1859, at which time he gave the compound the name cocaine. The local anesthetic properties of cocaine were demonstrated first by Wohler in 1860; however, it was not used medically until 1864 as a topical anesthetic in the eye.

## 2.0.0 TAXONOMY

The French botanist Joseph de Jussieu made the first taxonomical reference to coca[1] in 1750. He assigned the plants to the genus **Erythroxylum**. Later, Lamarck, another French botanist, published six new species, including the famous **Erythroxylum coca** Lamarck, in 1786. Today, the full taxonomical classification is:

| CATEGORY | TAXON |
|---|---|
| Division (phylum) | **Spermatophyta** |
| Class | **Dicotyledons** (shrubs and trees) |
| Order | **Geraniales** |
| Family | **Erythroxylaceae** |
| Genus | **Erythroxylum** |
| Species One | **Erythroxylum coca** Lamarck |

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[1] Note that other literature sources seem to credit Patrick Brown as the founder of the genus **Erythroxylum** (in 1756).

| | |
|---|---|
| Variety of Species One | **Erythroxylum coca var. ipadu** (Plowman) |
| Species Two | **Erythroxylum novogranatense** (Morris) Hieronymus |
| Variety of Species Two | **Erythroxylum novogranatense var. truxillense** (Rusby) Plowman |

The spelling of the genus name **Erythroxylum** is considered a hybrid of Greek and Latin. Linnaeus changed the spelling of the generic name to **Erythroxylon**, a pure Latin form. Nevertheless, botanists consider **Erythroxylum** as the proper spelling since it was derived in accordance with the rules of nomenclature.

Excluding the wild species of coca, all cultivated coca plants are currently considered to belong to two distinct species of **Erythroxylum** including one variety within each of the species. Specific areas of cultivation for each follows:

1. <u>**Erythroxylum Coca Lam. (**or **E. coca)**</u> -- This is the most important species from which almost all-commercial cocaine is derived. This species is native to the eastern Andes extending from Ecuador south to Bolivia. This was the first type of cultivated coca to be collected and studied by Europeans and was referred to as <u>Huanuco</u> or <u>Bolivian</u> coca after the main areas of cultivation. Like many plants that have been cultivated for thousands for years, E. coca is now rarely found in a truly wild state.

A particular variety of E. coca that warrants a brief mention since it has gained some recent notoriety is the coca of the Amazon Valley that, until today, continues to be cultivated on a very small scale by a number of Indian tribes. It belongs to the species of E. coca, but differs from the typical Andean species and is described as a variety, i.e., **Erythroxylum coca**, var. ipadu.

2. <u>**Erythroxylum novogranatense** (Morris) Hieronymus</u> -- This is the second species[2] of cultivated coca and is commonly known as <u>Colombian</u> coca. This species is cultivated throughout the mountains of Colombia. The species name "novogranatense" refers to the geographical origin of the plant, Nueva Grenad, the old colonial name for Colombia. There appears to be little cocaine production based upon this species.

During the early 1900s, the Europeans created a cocaine industry on one of the major islands of Indonesia (i.e., Java). Dutch farmers adapted the coca species **Erythroxylum novogranatense** to their soil and climate using modern agricultural techniques. Commonly referred to as "Java" coca, its total alkaloidal content was found to be higher than Colombian coca; however, its true cocaine content was found to be much lower than Colombian coca. This variation in alkaloidal content is attributed to changes in climate, soil, and possibly other

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[2] Older scientific publications (prior to 1976) refer to the studies of Morris who described this type of coca plant as a variety of E. coca. The German botanist Hieronymus was the first to recognize it as a distinct species.

environmental conditions. The Java coca industry practically collapsed just prior to World War II because of declining prices for coca leaves from other countries.

3. **Erythroxylum novogranatense var. truxillense** (Rusby) Plowman -- This is one recognized and distinct variety within the species **Erythroxylum novogranatense**. It is well known as Trujillo coca[3] since it is cultivated near the city of Trujillo in northern Peru on the slopes of the Andes (as well as the nearby desert coast of Peru). This variety of (Colombian) coca is particularly rich in methyl salicylate (oil of wintergreen) and other flavoring compounds that are used in the production of coca-flavored beverages. (Coca-Cola is a popular beverage that incorporates decocainzed extracts of Trujillo coca in its preparation.)

## 3.0.0 MORPHOLOGICAL AND ECOLOGICAL CHARACTERISTICS

Bolivian (or Huanuco) coca leaves are usually large and thick, broadly elliptic in shape, pointed at the apex, and dark green in color. The underside of the leaves has two lines (parallel) to the midrib. These leaves are not considered characteristic of this species since they are present to a degree in the other species of coca. The leaves are usually deciduous after the current season's growth. The plant grows as a small to medium size bush usually planted in rows on large, hillside plantations. This species thrives on moist, cool mountain climates.

Colombian coca can be distinguished from Bolivian coca by its smaller, narrower, thinner, bright yellowish-green leaves, which are usually rounded at the apex. Contrary to the Bolivian plant, the Colombian coca plant holds its leaves on the branches after a season's growth. This habit gives Colombian coca a larger, bushier, and robust appearance. In addition, Colombian coca prefers the hotter, drier climate and thrives at lower elevations. Dried Colombian leaves also have a more noticeable odor of methyl salicylate than Bolivian leaves.

Trujillo coca is morphologically similar to Colombian coca. Trujillo coca has smaller, narrower, and slightly thicker leaves that are darker green at maturity.

Refer to Table 1 for additional characteristics for both varieties of **Erythroxylum coca** and **Erythroxylum novogranatense**.

The genus **Erythroxylum** is the only natural source of the alkaloid cocaine and related compounds. Almost all commercial coca leaves and cocaine are derived from the species **Erythroxylum coca** Lam.; **Erythroxylum novogranatense** (Morris) Hieronymus, because of its quick adaptability to different climates, is most likely the dominant species that is illegally cultivated for the illicit drug trade.

## SPECIES OF COCA AND THEIR CHARACTERISTICS

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[3] Sometime referred to as Truxillo or Peruvian coca.

| **Genus, Species** | **ERYTHROXYLUM COCA** | | **ERYTHROXYLUM NOVOGRANATENSE** | |
|---|---|---|---|---|
| Varieties | **coca** | **ipadu** | **novogranatense** | **truxillense** |
| Origin | montaña region of eastern Andes; Ecuador, Peru, and Bolivia, mainly between 500 - 1500m | western Amazon of Brazil, Colombia, and Peru | Colombia, Venezuela and Central America, Sierra Nevada de Santa Marta and rugged mountains of Cauca and Hucha | desert coast of Peru and in adjacent arid valley of the Rio Maranon, Truxillo region on the north coast of Peru |
| Description of plant and/or leaves | pointed leaves, parallel longitudinal lines on leaf undersides | tall, spindly shrub with long weak branches and relatively large elliptical leaves which are blunt or rounded at the apex; flowers have a shorter flusher pedicel and a markedly denticulate staminal tube only short styled morphs | large bush plant with small, narrow, thin, and bright yellow-green leaves which are rounded | up to 3m tall with multiple trunks reaching 4 cm in diameter; branches are dense erect and spread leaves narrowly elliptical to oblong-lanceolate 20-65 mm long; medium to light green above pale green to glossy green beneath and midrib fluted with slight medial ridge |
| Odor | grassy or haylike | | wintergreen | wintergreen |
| Climate | favorable tropical environment with high rainfall, moderate temperatures and well drained mineral rich soils; moist cool | does not like intense heat or poorly drained soils, short-lived | hot, seasonably dry habitat resistant to drought | has been cultivated in arid, desert climate and wet montaña habitat of Colombia; even more tolerant to drought; prefers desert conditions |
| Adaptability | very little | very little | will survive under a wide range of environmental conditions; Resistant to drought | |
| Means of propagation | seeds | cuttings | seeds | seeds |
| Commercial uses | most important commercial species providing by far the largest supply of coca leaves and cocaine; 95% of Peru's crop | used for chewing | illegal in Colombia; grown illegally for coca chewing and cocaine production | principal variety used in beverage industry owing to its high content of essential oils and flavors-several hundred tons exported to N.Y. for preparation of extracts, used in making Coca-Cola |
| % Alkaloids | 0.5 - 1.0 | unknown | 1.0 - 2.5 | 1.0 - 2.5 |
| % Cocaine of Total alkaloid content | 70 - 90 | very little | 20 - 50 | 20 - 50 |

**Table 1**

Note that the genus **Erythroxylum** also includes a number of wild species of coca (reportedly about 200), most of which contain minimal quantities of cocaine and some of which contain no detectable quantities of cocaine.

## 4.4.0 CHEMISTRY

4.1.0 Coca leaves contain three basic groups of alkaloids, most of which are present in the form of esters. The content of these alkaloids will vary depending on the particular species of coca used, age of the plant, where it is grown, how it was cultivated, and when the leaves were picked. A higher total alkaloid content but with a smaller cocaine content reportedly occurs when the leaves are picked at an early stage of development; the reverse occurs when the leaves are picked when fully developed. Another important factor affecting the variation of an alkaloidal extract is the manner in which the alkaloids were refined from the leaves. Listed in specific groups are some of the popular alkaloids found in coca leaves:

Derivatives of Ecgonine

a. *l*-Cocaine (Methylbenzoylecgonine)
b. cis- and/or trans-Cinnamoylcocaine[4] (cis- and/or trans-Methylcinnamoylecgonine)
c. α and/or β-Truxillenes (Methyl α and/or β-truxilloylecgonine or α and/or β-cocaine)
d. Methylecgonine (Ecgonine methyl ester)
e. Methylecgonidine

Derivatives of Tropine (and ψ-Tropine)[5]

a. Tropococaine (Benzoyl-ψ-tropeine or ψ-tropine benzoate)

Derivatives of Hygrine

a. Cuscohygrine
b. Hygroline
c. Hygrine

In addition to *l*-cocaine, cinnamoylcocaine and the truxillenes are considered the most important coca alkaloids for pharmaceutical use. Hygrine and its related alkaloids are reported to be present in significantly large quantities in both varieties of **E. novogranatense** (i.e., Colombian and Trujillo coca). Hygrine is a tertiary aminoketone, hygroline is the secondary alcohol related to hygrine, and cuscohygrine is a diaminoketone containing two N-methyl groups.

The pharmaceutical industry produces pure cocaine semi-synthetically. The ecgonine conversion process employed eliminates the need to separate cocaine from related ecgonine alkaloids and produces a much greater yield of cocaine. Briefly, the procedure involves:

1. Extracting the coca alkaloids previously mentioned from dried coca leaves and isolating the mixture of ecgonine alkaloids.

2. Converting the group of alkaloids to ecgonine via hydrolysis with dilute hydrochloric acid:

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[4] Cinnamylcocaine and cinnamoylcocaine have been used interchangeably in the literature.

[5] Esters of tripine are called tropeines. ψ is the Greek symbol for pseudo.

Cocaine → *l*-Ecgonine•HCl + MeOH + Benzoic Acid

Cinnamoylcocaine → *l*-Ecgonine•HCl + MeOH + Cinnamic Acid

Truxillene → *l*-Ecgonine•HCl + MeOH + Truxillic Acid

(Tropococaine is excluded since it would hydrolyze to pseudotropin and not ecgonine.)

3. Isolating and purifying the ecgonine and converting it to its free base.

4. Converting the ecgonine to *l*-cocaine by benzoylating the ecgonine with benzoic anhydride to benzoylecgonine followed by methylation with methyl iodide.

An alternate commercial process converts the isolated alkaloids to ecgonine methyl ester (or methyl ecgonine) by hydrolyzing the alkaloids in methyl alcohol-hydrogen chloride. The ester is isolated and benzoylated directly to *l*-cocaine. Either industrial process provides the following approximate yield:

Dried Coca Leaves → Cocaine HCl
145 kgs → 1 kg

In clandestine cocaine laboratories in South America, the crude cocaine process also seeks to eliminate most of the coca alkaloids except cocaine. The cured process is an extensive operation. It generally consists of:

1. a “pasta” laboratory where all the coca alkaloids are extracted from a batch of coca leaves and converted to a water soluble (sulfate salt) pasty material called “pasta” or “sulfate” or coca paste;

2. a “base” laboratory (optional) where the coca paste is treated to remove most undesirable substances and to provide cocaine base;

3. a “crystal” laboratory where the cocaine base is converted to cocaine hydrochloride.

Very often, however, the illicit laboratory “cook” abbreviates or overlooks a critical step of the process and causes other alkaloids, impurities, and cocaine decomposition products to become part of the final product. The approximate yield from this illicit process can be summarized as follows:

Dried Coca Leaves → Coca Paste → Coca Base → Cocaine HCl
240 kgs → 1.4 kg → 0.9 kg → 1 kg

If chemical conditions become too acidic or basic, cocaine can degrade, as illustrated in Figures 1 and 2, and the degradation products may recombine to form new products. For example, benzoic acid and methyl alcohol will combine to yield methyl benzoate, a sweet smelling, volatile liquid. Similarly, cinnamoylcocaine and truxilline can decompose, producing products that can recombine to form new products, such as

## CHEMICAL STRUCTURE OF COCAINE

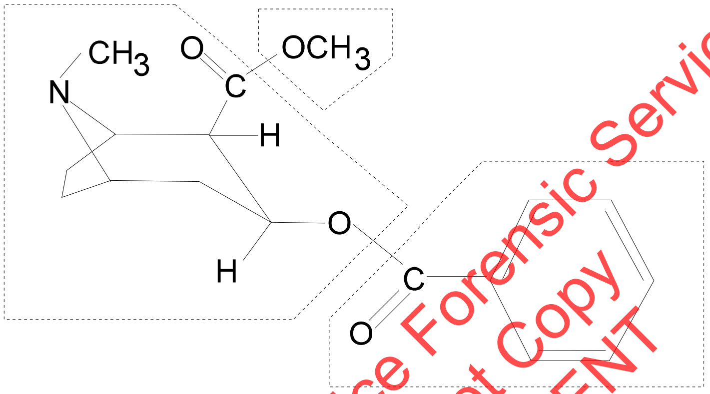


**Figure 1**

The cocaine molecule is made up of three building blocks. If chemical conditions become too acidic or too basic the cocaine molecule readily breaks down into these three pieces.

## DECOMPOSITION OF COCAINE

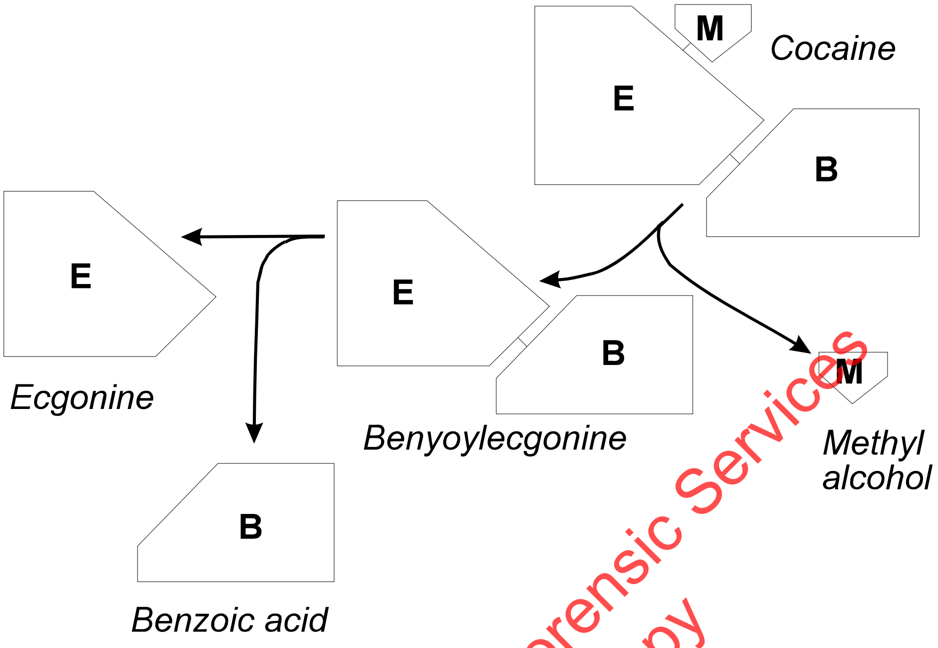


**Figure 2**

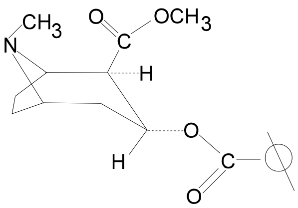
methyl cinnamate and methyl truxillate. Contrary to earlier studies, benzoylecgonine, ecgonine, pseudococaine, and cocaethylene are believed to be produced during the refining process and are not naturally occurring in the coca plant.

### 4.2.0 SYNTHESIS OF COCAINE

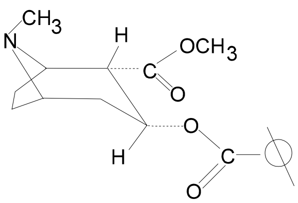
In 1923, using 2-carbomethoxytropanone as an intermediate, Willstatter prepared (±) cocaine along with pseudococaine. At least four synthetic methods have been reported for the synthesis of 2-carbomethoxytropanone. These syntheses range from the difficult cyclization of 1-methyl-2,5-dicarboethoxypyrrolidine, to the simplest, at least in principle, reaction of succindialdehyde, methylamine, and β-ketoglutaric acid to yield the target compound 2-carbomethoxytropanone. Willstatter's synthesis in 1923 involved the formation of the dipotassium salt of monomethyl-β-ketoglutarate, which was then reacted with methylamine and succinaldehyde to obtain the 2-carbomethoxytropanone. The methyl esters of (±) pseudoecgonine and (±) ecgonine are formed by the reduction of 2-carbomethoxytropanone using a sodium-mercury amalgam; fractional crystallization can be used to separate the two ecgonine methyl esters. The final step in the reaction scheme is between the (±) ecgonine methyl ester and benzoyl chloride to yield (±) cocaine.

### 4.3.0 STEREOCHEMISTRY

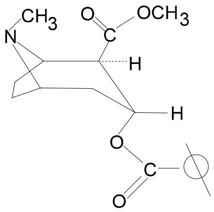
During the period 1898 to 1923, Willstatter and his collaborators were able to obtain pseudococaine by transformation of (-) cocaine and by total synthesis. At the time of this early work, stereochemistry was in its infancy. Based on chemical studies regarding ecgonine and tropine, Willstatter incorrectly assigned pseudococaine a structure that has both the C-2 carbomethoxy group and the C-3 benzoyloxy group axial. Instead, later studies show that pseudococaine has both the carbomethoxy group at C-2 and the benzoyloxy group at C-3 in equatorial position.



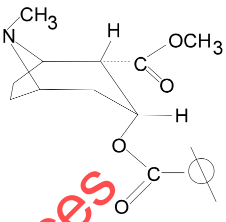
COCAINE



ψ-COCAINE



ALLOCOCAINE



ψ-ALLOCOCAINE

Two other cocaines, allococaine and allopseudococaine, were synthesized and characterized by Findley in the 1950s. Again, problems arose with the nomenclature used in representing the stereochemistry of these compounds. Using Findley's assignments, the carbomethoxy group at C-2 and the benzoyloxy group at C-3 were equatorial-axial, respectively, for allococaine and axial-axial for allopseudococaine. More recent nomenclature places allococaine and cocaine with the same stereochemistry at the C-2 position, that is, the carbomethoxy group is axial. Pseudococaine and allopseudococaine have the same spatial relationship at the C-2 position; viz., the carbomethoxy group is equatorial. Thus, the cocaine molecule has four asymmetrical centers which give rise to eight stereoisomers arranged as four diastereoisomeric pairs -- *d*,*l*-cocaine, *d*,*l*-pseudococaine, *d*,*l*-allococaine, and *d*,*l*-allopseudococaine.

## 5.0.0 SAMPLE ANALYSIS

The detection and identification of cocaine through acceptable analytical methods generally presents no problems; however, in most instances, pure cocaine is not presented for analysis. Even when diluents and adulterants have not been added to the cocaine, the sample usually contains impurities resulting from the original isolation of the alkaloid. For example, cis- and trans-cinnamoylcocaine are usually present in illicit cocaine samples. Benzoylecgonine may be present in many cocaine samples and should be eliminated by a basic extraction since its UV is similar to that of cocaine. Note that the detection of benzoyl ecgonine (as well as ecgonine) by UV, GLC, or TLC can be difficult because of the polar nature of the acid group at C-2.

A second complication in the analysis of cocaine samples results from the presence of adulterants. Many of the "caines," such as benzocaine, lidocaine, procaine, and tetracaine, are commonly encountered.

From a practical standpoint most of the analyses conducted at the ISP Laboratory will utilize capillary GC/MS for the identification of cocaine. The high resolution capabilities of capillary GC will easily separate cocaine from most common adulterants and diluents.

## 6.0.0 EXERCISES

1. Prepare a sample of "crack" cocaine from cocaine hydrochloride.

2. Obtain a sample of procaine base mixed with cocaine base. Via Infrared analysis, prove that the sample contains cocaine base. (In other words, separate the cocaine from the procaine without converting either to its salt.

## 7.0.0 DISCUSSION QUESTIONS

1. Is cocaine a stimulant or a narcotic?

2. Name the two countries that produce the majority of cocaine.

3. Name one country prominent in the smuggling of cocaine.

4. Draw the structure of the four cocaine isomers and show the equatorial/axial relationship for the carbomethoxy group and the benzoyloxy group for each isomer.

5. Draw the structures of procaine, lidocaine, tetracaine, and benzocaine. Are they related to cocaine?

6. Describe the process of preparing "crack" cocaine.

7. Draw the cocaine molecule and indicate what portion of the molecule the 82, 182, and 272 ions arise from.

8. Describe the process by which Colombian chemists convert the crude cocaine base to refined cocaine hydrochloride.

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## 9.0.0 HISTORY

Prior to revision 3 modules in the training manual did not have individual history pages.

| Revision # | Issue or review date | History | Author or Reviewer |
|---|---|---|---|
| 3 | 7/08/11 | Added 9.0.0, dropped some references | David Sincerbeaux |