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Cutting Agent

Adulterants (cutting agents or substances that either mimic or enhance the effects of controlled substances) or diluents (substances used to add weight to the sample) can crystallize with the reagent or hinder the crystallization of the drug and reagent complex (Schaeffer, 1953).

From: Encyclopedia of Forensic Sciences, Third Edition, 2023

Related terms:

Paracetamol, Lidocaine, Mass Spectrum, Patient, Sunscreen, Levamisole, Diamorphine, Illicit Drug, Chemotherapeutic Agent

Narcotics and Drugs

Peter W. Pfefferli, in Forensic Evidence Field Guide, 2015

Evidence of trafficking

- Narcotics (powders, cutting agents, tablets, pills, plants)
- Utensils (needles, filter paper, aluminum foil, containment, disinfectants, equipment for sterilization, glassware, flatware, spoons, balance)
- IT and communication (PC, cell phone)
- Documents and data
- Trace evidence: stains and residues on facilities (table, sink, toilet, ventilation)
- Biological (chemical) evidence of intake in: urine, blood, hair, saliva
- Trace evidence of illegal substances: clothing, hair, fingernails

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URL: https://www.sciencedirect.com/science/article/pii/B9780124201989000078

Cocaine

Morgan Alonzo, Shanlin Fu, in Encyclopedia of Forensic Sciences, Third Edition, 2023

Mixtures: Cutting Agents and Other Drugs

The reported purity of seized cocaine is highly variable and has been found to contain many different cutting agents, from pharmacologically inactive and readily available diluents such as sucrose, to pharmacologically active and more expensive adulterants, such as caffeine. The identity of cutting agents found in cocaine samples has shown variation between countries, as well as over time (Broséus *et al.*, 2016). Cocaine adulterants are often added to enhance or mimic the effect of cocaine, for example, lidocaine has similar anesthetic properties as cocaine and thus when taken gives the impression of higher quality cocaine. A list of common adulterants and diluents found in seized cocaine samples is provided in Table 2.

Table 2. Common cutting agents found in seized cocaine samples, classified as adulterants or diluents

Adulterants	Diluents
atropine	boric acid
benzocaine	carbonates

Adulterants	Diluents
caffeine	dextrose
codeine	fructose
diltiazem	glucose
ephedrine	inositol
hydroxyzine	lactose
ibuprofen	laundry detergent
levamisole	mannitol
lidocaine	starch
paracetamol	sucrose
phenacetin	talc
phenytoin	
prilocaine	
procaine	

A mixture of cocaine and heroin, referred to as a "speedball", is a dangerous drug combination taken intravenously and sometimes intranasally for the intense and longer lasting high. More recently, fentanyl and other potent synthetic opioids have been found in cocaine samples.

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2,3,7,8-Tetrachlorodibenzo-p-dioxin/Polychlorinated Biphenyls

Yukiko Ogino, ... Taisen Iguchi, in Handbook of Hormones, 2016

Biological and Pathophysiological Implications

Applications

The only present use for TCDD is in scientific research. Formerly, PCBs were widely used as electric fluids in transformers and capacitors, as pesticide extenders, adhesives, dedusting agents, cutting oils, flame retardants, heat transfer fluids, hydraulic lubricants, sealants, and paints, and in carbonless copy paper, due to their non-flammability, chemical stability, high boiling point, and electrical insulating properties.

Receptors

The aryl hydrocarbon receptor (AhR) plays a role in the toxicity of TCDD and its congeners, such as PCBs. [1] AhR repressor (AhRR) inhibits AhR function by competing with AhR for dimerizing with AhR nuclear translocator (Arnt) and binding to the xenobiotic responsive element (XRE) sequence [1].

Structure and Subtype

AhR, AhRR, and Arnt belong to a superfamily of the basic helix–loop–helix (bHLH)–Per–AhR/Arnt–Sim homology sequence (PAS) transcription factor superfamily (Figure 101G.2) [1]. Recently, the crystal structure of the PAS-A domain of AhR was reported [2].

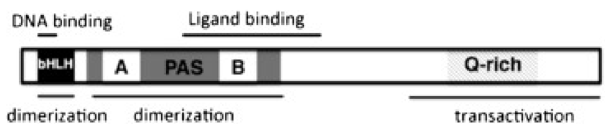

Figure 101G.2. The domain structure of AhR.

Signal Transduction Pathway

AhR is activated by ligand binding. The liganded AhR is translocated from the cytoplasm to the nucleus, and then the complex switches its partner protein from Hsp90 to Arnt. AhR/Arnt heterodimer binds to XRE/DRE (dioxin response element) sequences in the promoter and enhances transcription of the target genes [3].

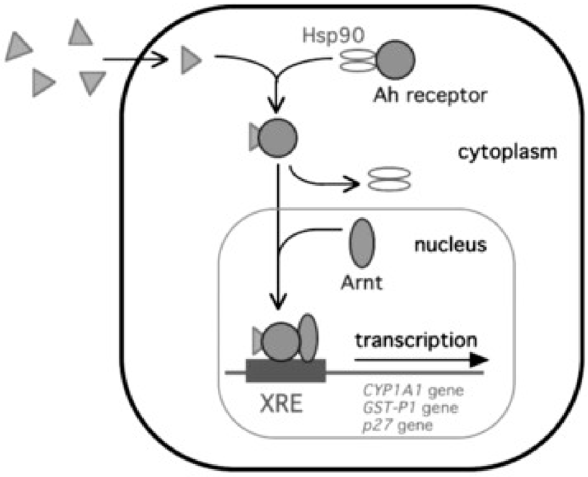

Figure 101G.3. Activation of the AhR pathway.

Health and Environmental Hazards

TCDD and PCBs have been demonstrated to alter endocrine, immune, and nervous system functions, and to have adverse effects on the reproduction and development of animals, including humans. The most characteristic symptoms of severe acute TCDD toxicity are chloracne and porphyria [4]. Acute exposure to TCDD may also cause transient hepatotoxicity, peripheral and central neurotoxicity, vomiting, and diarrhea. Because of the long-term persistence of TCDD in the human body, chronic effects appear as atherosclerosis, hypertension, diabetes, tumor promotion, and signs of neural system damage, including neuropsychological impairment [5]. PCBs have properties similar to those of TCDD if they can exist in a planar configuration (dioxin-like PCBs). After maternal exposure to PCBs, decreased embryonic growth, delayed implantation, and increased abortion rates have been observed [6]. AhR knockout mice are resistant to TCDD-induced teratogenesis such as cleft palate and hydronephrosis, and thymic atrophy [7].

Hormonal Effects

The biological activities of TCDD and PCBs have been reported to include both estrogenic and anti-estrogenic effects, and therefore pose a risk to the perinatal development of the female reproductive tract [8,9]. A relationship between these toxicities and the developing reproductive system of male offspring has been suggested.

Species Differences

Marked interspecies variability exists in the acute toxicity of TCDD, with the guinea pig having an oral LD_{50} dose (0.6 μg/kg body weight) about 10,000-fold greater than that of the hamster (5 mg/kg body weight) [10], and even among rat strains there may be a 1,000-fold difference.

Safety Standards and Regulatory Compliance

The production of PCBs was banned towards the end of the 1970s in most countries. The US Environmental Protection Agency prohibited PCB production in 1977. PCB production, use, and importation were banned in Japan in 1972.

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URL: https://www.sciencedirect.com/science/article/pii/B9780128010280002452

2,3,7,8-Tetrachlorodibenzo-p-dioxin/polychlorinated biphenyls

Yukiko Ogino, ... Taisen Iguchi, in Handbook of Hormones (Second Edition), 2021

Biological and pathophysiological implications

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Receptors

The aryl hydrocarbon receptor (AhR) plays a role in the toxicity of TCDD and its congeners, such as PCBs.[1] The AhR repressor (AhRR) inhibits AhR function by competing with AhR for dimerizing with the AhR nuclear translocator (Arnt) and binding to the xenobiotic responsive element (XRE) sequence.[1]

Structure and subtype

AhR, AhRR, and Arnt belong to a superfamily of the basic helix-loop-helix (bHLH) Per-AhR/Arnt-Sim homology sequence (PAS) transcription factor superfamily (Fig. 129G.2).[1] Recently, the crystal structure of the PAS-A domain of AhR was reported.[2] Species and strain differences in sensitivity to TCDD are caused by differences in the ligand-binding affinity of their polymorphic AhR variants.[3] The dissociation constant (K_d) of C57BL AhR for TCDD is 0.27 nM while that of DBA AhR is elevated up to six times that high. Human AhR shares key mutations with the DBA mouse strain that result in human AhR with low binding affinity.[4]

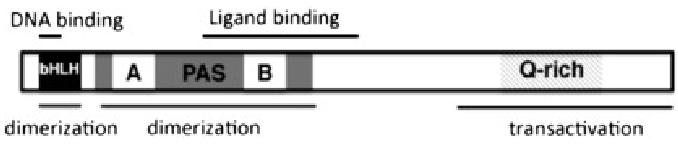

Fig. 129G.2. The domain structure of AhR.

Signal transduction pathway

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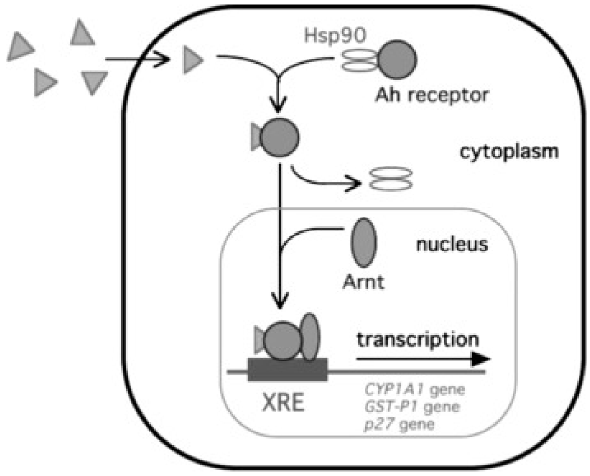

Fig. 129G.3. Activation of the AhR pathway.

Health and environmental hazards (Table 129G.1)

TCDD and PCBs have been demonstrated to alter endocrine, immune, and nervous system functions, and to have adverse effects on the reproduction and development of animals, including humans. The most characteristic symptoms of severe acute TCDD toxicity are chloracne and porphyria.[6] Acute exposure to TCDD may also cause transient hepatotoxicity, peripheral and central neurotoxicity, vomiting, and diarrhea. Once dioxins enter the body, they last a long time because of their chemical stability and their ability to be absorbed by fat tissue. Their half-life in the body is estimated to be 7–11 years.[7,8] Because of the long-term persistence of TCDD in the human body, chronic effects appear as atherosclerosis, hypertension, diabetes, tumor promotion, and signs of neural system damage, including neuropsychological impairment.[9] In the environment, dioxins tend to accumulate in the food chain. PCBs have properties similar to those of TCDD if they can exist in a planar configuration (dioxin-like PCBs). After maternal exposure to PCBs, decreased embryonic growth, delayed implantation, and increased abortion rates have been observed.[10] AhR knockout mice are resistant to TCDD-induced teratogenesis such as cleft palate, hydronephrosis, and thymic atrophy.[11] Environmental exposure to TCDD results in reproductive toxicities such as decreases in spermatogenesis and the ability to conceive and carry a pregnancy in mammals. It also leads to reductions in egg production and decreases in the hatchability of eggs produced in birds[12] as well as impairment of ovarian development and egg release in fish.[13]

Table 129G.1. Functions of TCDD and PCBs.

Species	Function	Reference
Human	Induction of chloracne and porphyria	6
Human	Induction of atherosclerosis, hypertension, diabetes, tumor promotion, and signs of neural system damage	9
Rodent	Induction of decreased embryonic growth, delayed implantation, and increased abortion rates	10
Rodent	Development of impaired prostate, hydronephrosis, kidney malformations, thymic atrophy, and cleft palate	11
Mammal	Development of reproductive toxicity by decreasing spermatogenesis and the ability to conceive and carry a pregnancy	12
Bird	Development of reproductive toxicity by reducing egg production and decreasing the hatchability of eggs	12
Fish	Development of reproductive toxicity by impairment of ovarian development and egg release	13

Hormonal effects

The biological activities of TCDD and PCBs have been reported to include both estrogenic and antiestrogenic effects; therefore, they pose a risk to the perinatal development of the female reproductive tract.[14,15] A relationship between these toxicities and the developing reproductive system of male offspring has been suggested.

Species differences

Marked interspecies variability exists in the acute toxicity of TCDD, with the guinea pig having an oral LD_{50} dose (0.6 μg/kg body weight) about 10,000-fold greater than that of the hamster (5 mg/kg body weight),[16] and even among rat strains there may be a 1000-fold difference.

Safety standards and regulatory compliance

The production of PCBs was banned toward the end of the 1970s in most countries. The US Environmental Protection Agency prohibited PCB production in 1977. PCB production, use, and importation were banned in Japan in 1972.

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URL: https://www.sciencedirect.com/science/article/pii/B9780128206492002813

Promoting Harm Reduction Personal Strategies by Means of Drugs Checking: Its Use in CAARUD

Nina Tissot, in Psychotropic Drugs, Prevention and Harm Reduction, 2017

8.2.3 Drugs checking in inquiry dynamics: initially, there was doubt

Let us move on more specifically to drugs checking, the reason why users turn to it, and what is at stake here in the exchanges between users and professionals.

To illustrate our point, we will share here with you some situations experienced by users regarding drugs checking in the CAARUD.

We want to clarify that in this institution, the collection of drugs in order to send them to an analytical laboratory is available to all the users, whether they are met inside the institution or in an informal environment. It concerns two different devices:

– the TLC analysis, managed by *Médecins du Monde*, which makes it possible to qualitatively analyze most drugs and common cutting agents, as well as some new synthetic drugs, but with no quantification possible;

–

and the analysis through the SINTES (National Identification System for Drugs and Toxic Substances) device of the OFDT, which can quantify nearly all the drugs present, but which limits the access to the device to drugs subject to health monitoring (new drugs or special dosage, unexpected or serious side effects), and with also longer periods to get results.

Amélie brought back a small parachute of purple crystals from a festival sold as MDMA. Even though she really doubted that MDMA could look like this, she still chose to take some, considering that the crystals were more significant than the color. The effect was not very clear, thus she could not accurately describe it during the analysis collection interview. The analysis revealed the absence of MDMA and the presence of chloroquine, an anti-malaria medicine. The professional informed her then about the risks of chloroquine, its toxicity, and the unknown hazards when mixed with other drugs. But the absence of effect took care of the rest, Amélie got rid of what was left of her stock…

A little while later, Laurianne wanted to get the ecstasy tablets that she consumed at a party analyzed as they caused unusual nausea and a "weird" sensation during the rush. However, as she had also consumed heroin, alcohol and opium at this party, it was hard to identify the causes of what she felt. She made several hypotheses with the professionals: the possibility that MDMA did not mix well with the rest, that it was too highly dosed, or that it was not MDMA. The analysis revealed the absence of MDMA and the presence of a psychoactive product of the cathinone family. Here again, mixing with other drugs results in different specific risks, even if they are little known regarding cathinones.

The analysis of a piece of ecstasy pill brought by José, whose effects (stomach cramps and sweating) he had found strange, showed here that it was indeed MDMA and only MDMA. No quantification was carried out, and José wondered with the professionals what other reasons could explain how he had felt. The professionals reminded him that common side effects of MDMA can be close to what he experienced, especially if the pill was highly dosed or if he was not hydrated enough.

These three examples show that, without analyzing the product, it is difficult to know to what should be linked to the sensations described by the users, and how to then adjust harm reduction strategies (not consuming the product, being careful with interactions, or reducing the dose and hydrating more).

One morning in the centre, Tatiana talks about the heroin she just bought, whose texture was particularly compact, but mainly which "made her totally go into withdrawal" over the last two days, she wondered what was this product that could cause such a withdrawal syndrome… An analysis of the product was offered to her and we mentioned the potential cutting agents, interactions, or heroin content, in order to explain what she felt. The result was indeed final: there was no trace of heroin in her rock or of any other psychoactive product.

Here, it is interesting for professionals to discuss the user's perception of a product that "makes one go into withdrawal", whereas it simply does not satisfy the craving inherent to the absence of opiates on which she is dependent…

We can identify three different stages during the exchanges between users and professionals concerning drugs checking: the discussion that leads to a request from the user – or an offer from the professional – the discussion during collection, and the one when the result is given.

During each one, we can note most of the criteria mentioned earlier regarding user inquiry dynamics: regarding the aspect of the product before consumption (color, texture, smell), regarding the effects experienced if it was consumed (where the user becomes a *metrological entity*), and finally regarding the body's symptoms that occur after consumption.

From these elements, the user then *makes a hypothesis* concerning the nature of the product, its concentration and the estimated cutting agents, about which they are more or less certain. We can consider it as a form of intuitive knowledge, proximity knowledge linked both to experimentation (what is felt during consumption) and experience ("the bottle").

We will then be able to identify the drugs checking request taking place here as the search for a scientific validation of this form of knowledge, *with which the user is usually satisfied.*

However, we can also see it as a new inquiry method, when actually *this knowledge at the disposal of the user allows them to doubt* what is really in their product, but not to solve the riddle raised. The situation is unclear, undetermined…

It is then the knowledge of the user that allows them to closely – but also approximately – perceive an anomaly, a break from the usual and expected. Reference points can vary from one user to another as we saw (texture rather than color, smell rather than effect, etc.), and when doubt is established from the effects experienced, users then also turn to drugs checking because a lot of them consider themselves as “metrologically reliable”, and thus the unusual feeling will necessarily be explained by the nature of the product consumed: “*I know myself, if that happens, it is because of the product*”. A disruption that triggers alarm, raises doubts, makes areas of uncertainty appear amid a usual experience.

We then will be able to perceive the drugs checking request (or its offer by the professional) as a response to the inquiry need, as a direct part of this inquiry movement by extending it from new criteria. This time, it is the criteria of the chemical, molecular knowledge or identification that are going to be a complement where there is still a lack of information.

Part of the professionals’ work is to discuss – before the analysis, and then from it – the experience of the user and its potential reasons, and to consider adjusting harm reduction strategies accordingly.

We offer two last examples to illustrate these elements:

– *Francis brought back a little heroin that he described as being “super strong”, to a point that it left him with a nearly traumatic souvenir of his last shoot. The analysis revealed, on top of the usual paracetamol and caffeine, a heroin rate of 10%… Is it small? Still, twice more than the usual 5% heroin available on the street market. So be careful about overdosing…*

Let us note that quantification is interesting because it makes it possible to compare even more the link between the effects sought and what causes them, a relationship which is not obvious and which always depends on the individual in question (and on the context).

Thus, a highly dosed heroin can seem like “*great stuff*” as well as a dangerous product, and the users themselves prefer to sometimes cut it again for their own consumption.

However, a very low-dosed heroin will require the questioning of cutting agents which are then present in great quantities and which will play a significant part in the experienced effects, and also the risks taken, which can sometimes be more noxious than those caused by the product initially sought.

– Joseph requested an analysis for his heroin, with which he had however no problem, which had the expected effects, had the “usual” aspect and came from his usual dealer. He simply wanted to know the cutting agents.

During the discussion, his inquiry, even worry, was then revealed at the idea of consuming a great quantity of cutting agents that could be dangerous, especially paracetamol, but also inactive drugs that were not detected then by the analysis, such as talc. Professionals talked about the noxious nature of some drugs according to the consumption method, and the possibility of adapting the consumption method to the product composition (especially to avoid injection if such or such product was present, while its absorption would be far less toxic), deploring the fact that inert drugs were far too expensive to analyze.

The analysis result revealed heroin, paracetamol and caffeine, as well as a non-identified cutting agent. He had to wait several weeks to know the final composition.

As the specificity of the cutting agents is often to “mimic” the characteristics of the product to which it is added, they can then “deceive” the user and their sensory experience and their metrological verdict. They will in turn copy the effect sought (caffeine for the stimulating effect of cocaine), reinforce it (caffeine in heroin to potentiate the effect if the latter is smoked), imitate the related effects (chloroquine for bitterness, lidocaine for anesthesia), or even copy the aspect of the product (caffeine for the color, texture, and other drugs for smell).

New synthetic drugs are often described from more common drugs that they are supposed to imitate, and coined with the suffix “like”: MDMA-like for mephedrone and nowadays 3MMC, LSD-like for DOB or NBOMe, etc. We could thus classify lidocaine as a cocaine-like texture or a cocaine-like drip…

Whether it is the cutting agents or the new synthetic molecules, users can never be certain of the reasons of what they feel, and there is still always the possibility of being scammed, whatever their level of experience.

It is what prompts some of them to actually consume medicines rather than drugs, whose content they can never be sure of. In addition, regarding the uncertainties linked to the concentration of the molecule sought, medicine will always be more reliable; there is no doubt about its composition, or the effects’ consistency. It is especially the case with Skenan, a morphine sulfate, which widely replaces – poor quality – heroin consumption among CAARUD users in some cities.

The examples showed us how the aim of the professionals, even before the analysis and verdict on the molecules present, is to discuss the possibilities of certainties of the nature of the product, and to question the experience from it.

It is this discussion in particular that will be the basis of the CAARUD professionals' intervention.

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URL: https://www.sciencedirect.com/science/article/pii/B9781785482724500081

Separation Methods

Max M. Houck PhD, FRSC, Jay A. Siegel PhD, in Fundamentals of Forensic Science (Third Edition), 2015

pH

Another property of certain chemical compounds is their acidity or alkalinity relative to water. An acidic substance is the one that releases hydrogen ions H^+ (they become hydrated in the presence of water, so they are in the form of H_2O. H^+ or H_3O^+ called hydronium ions) when dissolved in water. The amount of H_3O^+ in an aqueous solution is measured by its pH. This is the negative logarithm of the H_3O^+ concentration in moles per liter. Acids have pH values between 0 and 7. An alkaline or basic substance is the one that releases hydroxide (OH^-) ions when dissolved in water. Its pH is between 7 and 14. A neutral substance is the one that releases neither H_3O^+ nor OH^- ions when dissolved. Its pH is 7. Drugs, for example, can be classified as acidic, basic, or neutral. Cocaine is a basic drug. When it is dissolved in water or an aqueous solvent, it attracts H^+ from the solvent leaving OH^- behind. On the other hand, barbiturates are acidic drugs. They attract hydroxide ions leaving behind excess hydrogen ions. Caffeine is an example of a neutral drug. Sugars and carbohydrates (common cutting agents in street drugs) are also neutral. Figure 6.3 is an example of the reaction of a basic compound, in this case, cocaine in water making it an acidic salt.

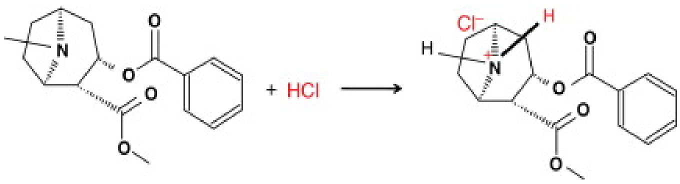

Figure 6.3. Cocaine hydrochloride. If cocaine is dissolved in an acidic solution, an extra proton (H^+) attaches itself to the amine group (NH_2R) on the cocaine. This makes the cocaine much more polar than it is in its free form.

In the Laboratory: Separation of a Drug Mixture by Liquid Phase Extraction

Both the properties of polarity and pH can be used to advantage when trying to purify a drug. Suppose that a forensic scientist receives a drug sample that turns out to be 50% cocaine hydrochloride and 50% sucrose, a sugar used as a cutting agent or diluent. Cocaine hydrochloride is a salt form of cocaine that is much more polar than cocaine free base, the naturally occurring form of cocaine. Sucrose is a neutral, nonpolar substance. The task is to separate the cocaine from the sucrose, saving the cocaine and getting rid of the sucrose. Two immiscible solvents will be employed in this process. This is an example of a liquid phase extraction. A diagram of how this works is shown in Figure 6.4.

1. The mixture is dissolved in water and filtered. All of the cocaine hydrochloride will dissolve. It is fairly polar and water is a polar solvent (remember: like dissolves like). Some of the sucrose will dissolve. The filtration step removes the sucrose that doesn't dissolve.
2. The filtered liquid (the filtrate) is then put into a glass **separatory** funnel. Then some weakly alkaline liquid such as ammonium hydroxide is added to the water. This gives the solution a high pH. The H^+ and Cl^- that are attached to the cocaine hydrochloride react with the ammonium hydroxide to form ammonium chloride and the cocaine hydrochloride is converted to the free base form of cocaine, which is much less polar than cocaine hydrochloride and much less soluble in water, causing it to precipitate out. The sucrose that originally dissolved in the water remains in solution.

3. Now an equal volume of a nonpolar solvent such as chloroform ($CHCl_3$) is added to the separatory funnel. The nonpolar cocaine free base dissolves readily in the chloroform, but the somewhat polar sucrose stays in the water.
4. The chloroform and water layers are separated. The chloroform can then be evaporated, leaving the purified cocaine free base.

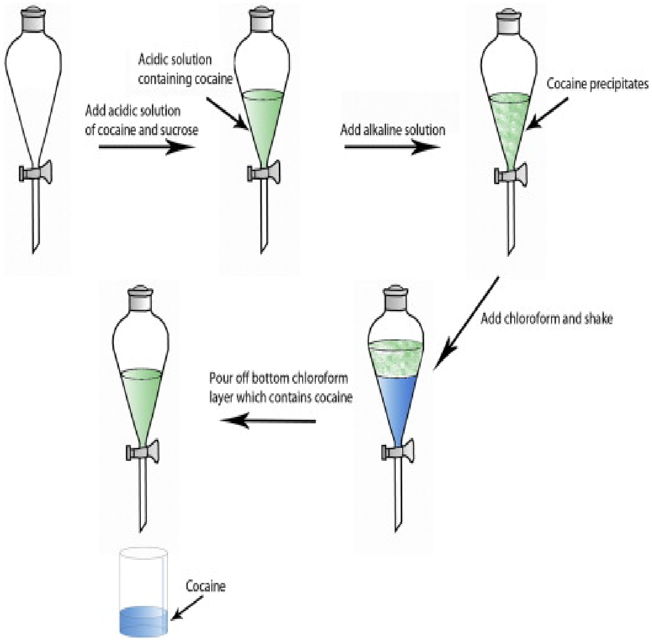

Figure 6.4. A liquid extraction process. Making use of a separatory funnel, this process takes advantage of the tendency of polar solutes to dissolve in polar solvents. The same holds true for nonpolar solutes and solvents.

Courtesy: Meredith Haddon.

The foregoing is called a basic extraction. The solvent containing the dissolved analyte is made basic and then extracted with a nonpolar solvent. An acidic extraction can be used on mixtures containing an acidic drug.

Note that in Figure 6.3 above, the cocaine has been converted to a salt form. The cocaine molecule has obtained a positive charge and the chloride ion from the hydrochloric acid (HCl) has a negative charge. This form of cocaine is much more polar than free cocaine. This property can be exploited in separating cocaine from a mixture.

Liquid phase extractions are commonly used to separate mixtures of solids. They are ideal for separating substances where one is much more soluble than the rest or if they are of different polarity and pH. If, however, the mixture contains two substances of similar polarity and both are acidic or basic, such as cocaine and heroin, then a liquid phase extraction would likely fail to achieve a good separation. A different type of separation process would be required for such mixtures.

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URL: https://www.sciencedirect.com/science/article/pii/B9780128000373000066

Presumptive Chemical Tests

Raychelle Burks, Agnes Winokur, in

Encyclopedia of Forensic Sciences, Third Edition, 2023

Drugs

SWGDRUG recommendations describe microcrystalline tests as a Category B, which offer selectivity through chemical properties. With high specificity, these fast and inexpensive tests can quickly provide information to guide the next steps in the analytical drug identification scheme. Accompanied with a high level of experience, microcrystalline tests can be used to help identify and even quantitate substances in a seized drug sample. Microcrystalline tests also provide a non-destructive method of analysis as a drug of interest can be extracted from a complex matrix with the application of a solvent, recovered, quantified, and retained.

Adulterants (cutting agents or substances that either mimic or enhance the effects of controlled substances) or diluents (substances used to add weight to the sample) can crystallize with the reagent or hinder the crystallization of the drug and reagent complex (Schaeffer, 1953). The effects of common adulterants to the morphology of the crystals has been explored (Nelson *et al*., 2011; Elie *et al*., 2012). Nelson *et al*. investigated trends in crystal morphology of cocaine mixed with caffeine and lidocaine at various concentrations when applying the gold chloride microcrystal test. Elie *et al*. described a microcrystalline test for the detection of mephedrone, benzylpiperazine, and 5,6-methylenedioxy-2-aminoindane using aqueous solutions of mercury and the effect of caffeine at various concentrations. Such studies provide crucial information to assist in the detection of drugs of interest – including the ratio of drug concentration to that of adulterant that impacts an expected observation.

Microcrystalline tests are also commonly used for the differentiation of enantiomers and the racemic mixture, such d-, l-, and d,l- methamphetamine samples (Laboratory and Scientific Section of the United Nations Office on Drugs and Crime, 2006; Brinsko *et al*., 2015). Just as critically, structurally similar substances (analogues) can be differentiated with specific microcrystalline tests (Brinsko *et al*., 2015; Quinn *et al*., 2020). Quinn *et al*. (2020) demonstrated how gold chloride microcrystalline tests can differentiate PCP from four PCP analogues. Table 4 depicts several of the most common microcrystalline tests used for the analysis of drugs. Several of these tests have been expanded into standards by organizations such as ASTM International (ASTM International, 2019a,b,c).

Table 4. Select microcrystalline tests for drugs

Test	Reagent	Response
Amphetamine and methamphetamine		
Gold Chloride ($HAuCl_4$)	5% of gold chloride in reagent grade water (or concentrated phosphoric acid)	Development of yellow rods/blades with d- or l-amphetamine, while d,l-amphetamine yields blades with serrated edges. Individual enantiomers of methamphetamine (d- or l-) will generate blade jointed crystals that will transform into clothespin shape rods, while with d,l-methamphetamine, the blade jointed crystals will transform into X shape rods.
Platinum Chloride (H_2PtCl_6)	5% of platinum chloride in reagent grade water (or concentrated phosphoric acid)	Development of long, bent needles transform into long rectangular blades with d- or l-amphetamine, while d,l-amphetamine yields irregular blades/needles that transform into irregular arms of blades. Individual enantiomers of methamphetamine (d- or l-) will generate the same crystal formation as with gold chloride, while with d,l-methamphetamine, sharp grains with fern shape and straight ends will form.
Cocaine		
Gold Chloride ($HAuCl_4$)	5% of gold chloride in reagent grade water (or concentrated phosphoric acid)	Development of long rods with many short arms at right angles.
Platinum Chloride (H_2PtCl_6)	5% of platinum chloride in reagent grade water (or concentrated phosphoric acid)	Development of feathery, pale yellow crystals

Test	Reagent	Response
Phencyclidine (PCP) and Its Derivatives		
Potassium Permanganate	2% w-v potassium permanganate in 0.5% v-v phosphoric acid	Purple razor blade crystals are observed in the presence of PCP
Gold Bromide	0.55 g of gold bromide in 42 mL reagent grade water, along with 37 mL of concentrated perchloric acid and 21 mL glacial acetic acid	In the presence of PCP, red-gold squares birefringent are developed, while PCPy generates rods and X-shaped birefringent. Oily drops to plates can be observed with PCPM and TCP yields X-shaped birefringent.
Gold Chloride ($HAuCl_4$)	2 g $HAuCl_4$, 20 mL glacial acetic acid, 40 mL concentrated sulfuric acid, 40 mL distilled water	While the presence of PCP generates unremarkable crystal formations, PCPy generates X-shaped crystals , PCPM generates H-shaped plates, and TCP generates yellow needles.
Heroin		
Gold Chloride ($HAuCl_4$)	5% of gold chloride in reagent grade water (or concentrated phosphoric acid)	Large, yellow needles develop
Mercuric Chloride/Iodide	1% mercuric chloride (or 1% mercuric iodide) in distilled water	Small dendrites with branches form with mercuric chloride, while dendritic stems form
Ketamine		
Platinic Iodide	5% of platinum iodide in reagent grade water (or concentrated phosphoric acid)	Rhomboidal plates develop in the presence of Ketamine.

Note: Test information was collected from Fulton, C.C., 1969. Modern Microcrystal Tests for Drugs: The Identification of Organic Compounds by Microcrystalloscopic Chemistry. Wiley-Interscience; ASTM International, 2019a. Standard practice for microcrystal testing in forensic analysis for cocaine. E1968–19. Available at: https://www.astm.org/e1968-19.html (accessed 13.05.22); ASTM International, 2019b. Standard practice for microcrystal testing in forensic analysis for methamphetamine and amphetamine. E1969–19. Available at: https://www.astm.org/e1969-19.html (accessed 13.05.22); ASTM International, 2019c. Standard practice for microcrystal testing in forensic analysis for phencyclidine and its analogues. E2125–19. Available at: https://www.astm.org/e2125-19.html (accessed 13.05.22).

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Street Level Heroin, an Overview on Its Components and Adulterants

Maryam Akhgari, ... Farzaneh Jokar, in
Neuropathology of Drug Addictions and Substance Misuse, 2016

Neurological Effects and Neuropathology of Adulterants and Diluents in Street Heroin

A broad spectrum of morphofunctional and neuropathologic changes has been reported in the brain of heroin abusers (Neri et al., 2013). These lesions are caused by the active ingredient, heroin, and other substances added as adulterants (Büttner, Mall, Penning, & Weis, 2000). Postmortem investigations on the brains of drug-addicted individuals show biochemical and ultrastructural abnormalities. Neuropathologic changes in the brain can be precipitated by direct effects of heroin such as respiratory depression or by other reasons (infections and adulterants) (Büttner et al., 2000).

Cerebral edema with increased brain weight, decreased neuronal densities in the globus pallidus, bilateral and symmetric ischemic lesions, and hypodensities in the basal ganglia are caused by hypoxia related to heroin abuse (Andersen & Skullerud, 1999). As indicated by Niehaus and Meyer (1998) heroin abuse has caused focal neurological deficits and stroke. Flaccid paraparesis and paraplegia along with sensory loss in the legs are clinical presentations of heroin addiction-induced myelopathy. Neurotoxic effects of heroin and its adulterants, allergic reaction to "cutting agents," and adulterants, and embolism are some causes of myelopathy in heroin abusers (Büttner et al., 2000). Inhalation of preheated heroin can cause spongiform leukoencephalopathy due to a lipophilic toxin-induced process by contaminants or cerebral hypoxia (Büttner et al., 2000).

Bacterial infections are a common problem among injecting drug users (Cole et al., 2010). Unsterile preparation and distribution processes in combination with poor health conditions and use of contaminated injection equipment contribute to inducing bacterial, fungal, and viral infections (McLauchlin et al., 2002). Septic foci in the brain can be produced as a result of bacterial or fungal endocarditis. Other studies have described intracranial mycotic aneurysms and development of subarachnoid hemorrhage in drug abusers with endocarditis (Gilroy, Andaya, & Thomas, 1973).

Direct toxic effects of heroin together with the action of adulterants have been hypothesized in the production of neurologic complications in drug abusers. Embolism from heroin adulterants has been proposed in some studies (Büttner et al., 2000).

There is a case report concerning Brown–Séquard syndrome, characterized by right-sided hemiparalysis with a contralateral sensory loss of touch and pain and vasculitis in the cervical region following quinine-adulterated heroin ingestion. Toxic effects of heroin and quinine caused vasculitis, cellulitis, and arachnoiditis in this heroin abuser (Krause, 1983).

Some lesions in the peripheral nervous system have been attributed to heavy metal adulterants such as lead in heroin. These include polyradiculopathy, brachial and lumbosacral plexitis, Guillain–Barré syndrome, and mononeuropathy (Antonini, Palmieri, Spagnoli, & Millefiorini, 1989).

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DRUGS OF ABUSE | Classification, including Commercial Drugs

L.A. King, in Encyclopedia of Forensic Sciences, 2000

Synthetic drugs

Amphetamine was first synthesized over 100 years ago, but its stimulant properties were not recognized until much later. It is now rarely prescribed as a medicine, where one of its few uses is in the treatment of narcolepsy. In Europe, amphetamine is the second most commonly abused drug after cannabis. Most amphetamine syntheses continue to start with phenyl-2-propanone (benzyl methyl ketone). Despite international trade controls deriving from the United Nations (UN) 1988 Convention, illicit supplies of this and other precursors appear to be readily available on the black market. In North America and the Far East, methamphetamine is more common. This has traditionally been made from ephedrine, but trade controls have caused a shift to pseudoephedrine. More recently, phenylpropanolamine has been used in the USA to produce amphetamine. Both amphetamine and methamphetamine are found as white or off-white powders. Typical cutting agents are caffeine and sugars such as glucose. In Europe, amphetamine is occasionally seen in tableted form.

The ring-substituted amphetamines are commonly known as the 'Ecstasy' drugs. The prototypical member of this family is 3,4-methylenedioxymethamphetamine (MDMA). First synthesized in the early part of the twentieth century, abuse did not become widespread until the 1980s. Both amphetamine and MDMA are derived from the phenethylamine molecule. In the past 10 years, dozens of designer drugs based on variously substituted phenethylamine have appeared in Europe and the USA. These drugs are invariably produced in the form of white well-made tablets, often bearing a characteristic design (logo) and usually around 10 mm in diameter. The MDMA content of tablets is typically 80–90 mg. Lactose is a common excipient (filler) in tablets.

Lysergide (LSD) is generally thought of as a purely synthetic material, but routes of manufacture usually start from ergotamine, a natural substance produced by the microorganism *Claviceps purpurea*. Until the mid-1970s, LSD was produced in small (approximately 2 × 2 mm) tablets known as microdots. For the past 20 years, paper squares of around 7 × 7 mm have been the common dosage form. These squares are usually printed with a coloured design featuring cartoon characters, symbols or drug-related motifs; the lysergide content averages 50 μg.

Apart from lysergide and dimethyltryptamine (DMT), few synthetic drugs based on the tryptamine molecule have become popular, even though the synthesis and properties of many have been described in recent popular literature. A factor that is likely to limit the wider abuse of hallucinogenic tryptamines is their inactivity when taken orally. Most need to be smoked, injected or mixed with an 'activator' to inhibit metabolic destruction.

Methaqualone, a drug formerly used as a hypnotic, but now produced illicitly, has remained a popular drug of abuse in South Africa. It is often smoked mixed with cannabis.

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