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Evolution of Forensic Toxicology

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Abstract

The field of science dealing with criminal investigation is known as forensic science. Throughout history, evidence has been used to condemn criminals of the crimes that they have committed. Over the past twenty-five years, the forensic sciences have made huge scientific breakthroughs with the application of modern techniques, physical evidence databases, and new scientific instrumentation. Forensic toxicology is a category of forensic science which deals with examination of chemicals, drugs and their fatal effects on the body. This report on forensic toxicology deals with classification of drugs and chemicals along with the modes of action of some poisons - Cocaine, Cannabis, Cyanide, Chloroform, and Aspirin. Various types of samples and classical and modern testing methods are discussed. Postmortem findings in case of death due to suspected chemical poisoning based on external and internal examination has been reviewed.

Keywords: Aspirin, Cocaine, Chloroform, Cannabis, Cyanide, Forensic Toxicology

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Forensic Toxicology

Toxicology is the study of fatal effects of chemicals on biological systems. Forensic toxicology is the application of toxicology to cases and matters where those adverse effects have medicolegal consequences, and where the outcomes are likely to be used in court. It deals with investigations in causes of death, poisoning and drug abuse. A forensic toxicologist must examine the context of an investigation, in particular if any physical symptoms were recorded, and any clue collected at a crime scene that may narrow the search, such as pill bottles, injections, powders, trace residue, and any chemicals. Provided with the information and samples, the forensic toxicologist must figure out the toxic substances present, their concentrations, and the probable effects of those chemicals on the individual.

Milestones in evolution of Forensic Toxicology

Table 1. Important events in Forensic Toxicology[1]

Timeline	Important Events
5000 BC	Early humans used poisonous plants and animals for hunting and as warfare agents
1500 BC	Written evidence proved that hemlock, opium, curare, and certain metals were used for poisoning
1700s	Convictions related with homicidal poisoning were based only on circumstantial evidence instead of the identification of the actual toxicant within the victim
1781	Joseph Plenic demonstrated that the detection, identification and estimation of the poison in the organs of the deceased was the only true sign of poisoning
1813	Mathieiv Orfila (considered the father of toxicology) published "Traite Des Poisons" the first full and complete work on the subject of poisons and legal medicine
1836	- James M. Marsh developed a test to determine the presence of arsenic in tissue - Albert Swaine published a textbook called "Elements of Medical Jurisprudence" which was the first textbook about the theory of Forensic Toxicology

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1839	Orfila successfully used Marsh's test to analyse arsenic extracted from human tissues
1900s	The Arsenic Act of 1851 and the Pure Food and Drugs Act of 1906 was passed
1918	The Medical Examiner's Office and Toxicology Laboratory was established in New York where the chief forensic toxicologist was Alexander O. Gettler (the father of American toxicology)
1931	Frances Glessner Lee established Harvard University's Department of Legal Medicine– the first of its kind in North America.

Classification of drugs and chemicals:

(a) Local Mode of Action

Table 2. Substances based on local mode of action

Class	Sub-class	Types
Corrosive	Strong Acid	Mineral acids and organic acids
	Strong Alkali	
	Metal salts	Mercuric chloride
Chemical	Inorganic	Weak acid, weak alkalies, Inorganic metals and non- metals
	Organic	Chemical preparations with animal and/or vegetable origin
Irritant	Mechanical	Glass powder

(b) Remote Action

Modes of action of some important poisons- Cocaine, Cannabis, Cyanide, Chloroform, and Aspirin

- **Cocaine**

Cocaine has a psychomotor stimulant effect. It crosses the blood brain barrier and is distributed within the body. In large and repeated doses, it is possibly accumulated in the central nervous system and adipose tissue, as a result of its lipid solubility. It produces euphoria, tachycardia, hypertension and appetite suppression similar to amphetamine, which is also a stimulant.

Cocaine has a strong boosting action and causes a rapid psychological dependence. The main metabolites are ecgonine, ecgonine methyl ester and benzoylecgonine,

Table 3. Substances based on remote action[2]

Class	Sub-class	Category	Examples
Neurotics	C.N.S. Poisons	Sleep inducers	Opium and its alkaloids, Barbiturates
		Intoxicants	Alcohol, Ether, Chloroform
		Stimulants	Cocaine, Amphetamines
		Deliriants	Dhatura, Belladonna, Hyocyamus, Cannabis
		Stupefacients	Chloral hybrate
		Hallucinogens	LSD (lysergic acid diethylamide), PCP(phencyclidine), magic mushrooms (psilocybin)
		Convulsants	Cyclothiazide, Gabazine
	Spinal	Convulsants	*Strychnos nux-vomica*
	Peripheral Nerves	Local Anaesthetics	Cocaine, Procaine
		Relaxants	Valium, Cyclobenzaprine
Cardiac Poisons			KCN, NaCN, Digitalis, Aconite, Nicotine, Quinine, Oleander
		Asphyxiants	Carbon Dioxide, Carbon Monoxide, Hydrogen Sulphide
		Nephrotoxic	Mercury, Oxalic Acid, Cantherides
		Hepatotoxic	Carbon tetrachloride, Chloroform, Phosphorus
		Miscellaneous	Food Poisons

all of which are inactive. When consumed with alcohol, it also produces the metabolite, cocaethylene. The plasma half-life is 0.7–1.5 hours and is dependent on dose. The predicted minimal lethal dose is 1.2 g, but prone individuals have died from as little as even 30 mg applied to mucous membranes, whereas addicts may tolerate large amounts up to 5 g daily. [3]

Possible side effects include aches, insomnia, insatiable hunger, lethargy, and persistent runny nose. With excessive or prolonged use, the drug can cause fast heart rate, hallucinations, and paranoid delusions. With excessive dosage, convulsions, tremors, and increased body temperature are observed. Severe adverse cardiac events, particularly sudden cardiac death, become a serious risk at high doses due to blocking effect of cocaine on cardiac sodium channels. [4]

- **Cannabis**

Cannabis is one of the most abused substances throughout the world. The primary psychoactive constituent of cannabis, delta 9-tetrahydrocannabinol (▵9_THC), produces a number of pharmacological effects. Although it is used as a recreational drug, it can likely lead to dependence and behavioral problems and its heavy use may increase the risk for psychotic disorders. [5] THC, the principal and psychoactive ingredient of the cannabis plant, has low toxicity. Acute effects may include anxiety, panic, impaired attention, and memory, an increased risk of psychotic symptoms, and possibly an increased risk of accidents if a person drives a vehicle while intoxicated. [6]

THC firstly enters the blood stream, reaches the brain, and binds to cannabinoid receptors. The internal ligand of these receptors is anandamide, whose effects THC imitates. This agonism of the cannabinoid receptors results in modification in the levels of neurotransmitters, especially dopamine and norepinephrine which are closely linked with the acute effects of cannabis ingestion, such as anxiety and euphoria. [7]

- **Cyanide**

Cyanides are deadly toxic. The cyanide anion is an inhibitor of the enzyme cytochrome c oxidase in the electron transport chain (present in the membrane of the mitochondria of eukaryotic cells). Within the protein, it attaches to the iron. The binding of cyanide to the enzyme prevents transport of electrons from cytochrome c to oxygen. As a result of which the electron transport chain is disrupted, such that the cell can no longer produce ATP aerobically for energy. [8] Tissues that depend greatly on aerobic respiration, such as the central nervous system and the heart, are especially affected. This is an example of histotoxic hypoxia. The most deadly compound is hydrogen cyanide, which is a gas at atmospheric temperature and pressure and can therefore be inhaled. Average lethal dose of HCN taken by mouth is between 60 and 90 mg (adult).

- **Chloroform**

Chloroform is the classic narcotic with a distinctive odour. It was previously used as an analgesic in medical practice in 1847. However, because of its narrow therapeutic range, severe respiratory depression, negative inotropic effects and liver toxicity which it caused, it was replaced by other anaesthetics. In animal studies, chloroform has been shown to be carcinogenic. Uptake of chloroform is commonly by inhalation of the vapour, rarely by ingestion. Depending on the concentration and exposure time, initially local irritation is detected followed by central nervous excitation or intoxication, then relaxation and paralysis follows. After an overdose of chloroform, death is caused by heart failure and accompanied by specific damage to the parenchymal organs. [9] Chloroform is metabolized primarily in the liver, but its metabolism also occurs in other tissues such as the kidney.

- **Aspirin**

Aspirin, acetylsalicylic acid, is classified among the non-steroidal anti-inflammatory drugs. The agent reduces the signs and symptoms of inflammation and shows a broad range of pharmacological activities, including analgesic, antipyretic, and antiplatelet properties. [10]

Aspirin causes reduction of inflammation and fever because of decreased synthesis of prostaglandins and thromboxane. Prostaglandins or thromboxane A2 play a direct role in the exposure of platelet fibrinogen receptors which is a prerequisite for platelet aggregation. Aspirin's ability to suppress the production of prostaglandins and thromboxanes is as a result of its irreversible inactivation of the cyclooxygenase (COX) enzyme. Cyclooxygenase is required for prostaglandin and thromboxane production. [11] Acute ingestion of > 150 mg/kg can cause severe toxicity. Salicylate tablets may form bezoars, toxicity and prolonging absorption. Chronic toxicity can occur after several days or more of high therapeutic doses.

Types of specimens collected in forensics

Table 4. Specimens and samples collected in post-mortem cases[12]

Type of death case	Recommended specimens
Suicides, motor vehicle crashes, industrial accidents	Blood, urine, liver, vitreous humour
Homicides	Blood, urine, gastric contents, vitreous humour, bile,liver, hair
Drug-related	Blood, urine, gastric contents, bile, vitreous humour, liver, hair
Volatile substance abuse	Blood, urine, lung fluid, vitreous humour, liver
Heavy metal poisoning and exposure to other kinds of poisons	Blood, urine, liver, vitreous humour, hair, kidney

Classical toxicity testing methods

The typical practice in toxicological examination begins with the prior identification of alcohol and screening of a wide spectrum of acidic, neutral and basic organic drugs or poisons. If a toxin is detected, confirmatory and, if needed, quantitative testing has to be done. In general, a positive identification is achieved using at least two independent analyses and preferably using different testing methods.

- **Immunoassays** - Immunoassays are highly sensitive and specific chemical tests used to identify or quantify a specific substance, the analyte, in a blood or body fluid sample, by using an immunological reaction. Immunoassay screening tests are devised to detect whether a sample is positive or negative for the targeted drug.
- **Chromatographic techniques** - Chromatographic detection is an analytical procedure used for separation of compounds/drugs and is mostly based on either high performance liquid chromatography (HPLC) or gas chromatography (GC) coupled with MS. This is the conclusive technique used in toxicology to establish proof of structure of unknown substances. [12]

Modern methods for testing

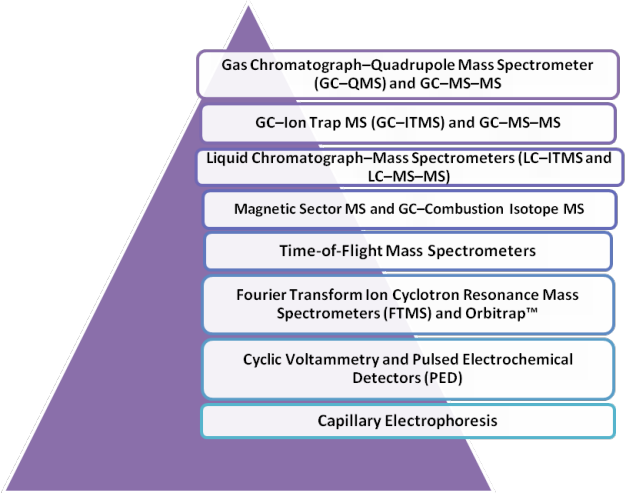


Figure 1. Modern detection methods.

Postmortem findings data in case of death due to suspected poisoning

- **External Examination**

Table 5. Observations and causes related to external examination

	Observations	Causes
1	Postmortem staining- Deep blue	Asphyxiant poisons and aniline
2	Postmortem staining- Bright red	CO and HCN
3	Deep cyanosis	Opium and cardiac poisons
4	Early rigor mortis	Strychnine
5	Early appearance of the signs of decomposition	H2S gas
6	Detectable smell	Volatile poisons, opium and HCN, KCN or NaCN
7	Hemorrhagic spots under the skin and mucus membrane	Phosphorus
8	Ulceration on lips and near the edges of mouth	Corrosive poisons
9	Stain near mouth and on hands	Copper sulphate and nitric acid

10	White froth from mouth, nose	Opium and its alkaloids
11	Blood tinged froth from mouth, nose	Organophosphorus compounds
12	Alopecia, hyperpigmentation and hyperkeratosis	Chronic arsenic poisoning
13	Staining, ulceration and erosion near the female external genitalia	Abortifacient agents or torturing agents
14	Injection marks	Injection of poisons, sign of treatment

- **Internal Examination**

The gastrointestinal tract should be examined very carefully for the signs of corrosive or irritant poisons as the poisons are likely to be find therein. These signs are softening, hyperemia, ulceration and perforation. Other internal findings are:

Table 6. Parts, observations and causes related to internal examination[2]

	Parts	Observations	Causes
1	Lips, mouth and tongue	Corrosion, ulceration and desquamation of interior portions of lips, mucus membrane of mouth and tongue	Corrosive agents
		Soft, swollen, sodden, translucent, and bleached tongue and mucus membrane of mouth	Corrosive alkali
		Discoloration and staining of inner portions of mouth	Coloured poisons
2	Teeth and Gums	Chalky appearance and consistency of teeth	Sulphuric acid
		Blue lining in the gums	Chronic lead poisoning
		Swollen gum, loose teeth, foetid smell	Chronic phosphorus poisoning, acute mercuric chloride poisoning
3	Oesophagus	Corrosion, irritation, desquamation and hemorrhage of the inner wall of the oesophagus	Corrosive and irritant poisons
		Hardening, whitish discolouration	Carbolic acid
		Oesophageal stricture	Sulphuric acid
4	Stomach	Softening and thickening of the stomach wall	Corrosive and irritant poisons
		Hard wall	Carbolic acid
		Leathery and hard wall	Formaldehyde
		Hyperemia hemorrhage and desquamation of mucus membrane	Irritant poisons
		Sloughing and laceration	Corrosive poison
		Perforation	Sulphuric and nitric acid
		Yellowish discolouration of mucus membrane	Nitric acid
		Bluish discolouration of mucus membrane	Copper sulphate
		Slaty grey discolouration of mucus membrane	Mercuric chloride
		Hardening of mucus membrane	Phenol
		Carbonization and charring of mucus membrane	Conc. Sulphuric acid
5	Stomach content	Blood	Corrosive and irritant
		Yellowish	Nitric acid
		Bluish	Copper sulphate
		Luminous in dark	Phosphorus
		Powder	Oxalic acid
		Detectable tablet	Soneryl
		White	Arsenic
		Detectable smell	Alcohol, kerosene, chloroform, chlorinated hydrocarbons, organophosphorus compounds, opium, formaldehyde, cyanogens, phosphorus
		Detectable liquid	Kerosene

6	Small intestine	May show irruption, sometimes show presence of poisonous remains	
7	Large intestine	Ulcerations (similar in appearance with ulcers of bacillary dysentery)	Mercuric chloride
8	Liver	Different degenerative changes (The extent and type of the degenerative changes depends on the type of poison, dose, duration of the exposure and the physical condition of patient.)	Phosphorus, chloroform, carbon tetra-chloride, tetrachlorethylene and many other poisons.
9	Kidneys	Swollen, soft, reddish, sometimes greasy in touch with hemorrhage in calyces and other degenerative changes	Mercury, carbolic acid, oxalic acid, phosphorus, cantherides, viper snake venom and many others.
10	Urinary bladder	Hemorrhage	Abrus precatorius or cantheride poisoning, viper snake bite
11	Larynx and trachea	Hyperaemic, inflamed	Inhalation of irritating gases
		Froth in the lumen of trachea and larynx	Organophosphorus
12	Chest cavity		Smell of volatile poisons cyanogens, opium etc. can be detected
13	Lungs	Voluminous, congested, presence of Tardieu's spots	Asphyxiants and other inhaled poisons
		Cut sections give blood stained frothy-fluid	Opium and other asphyxiants
14	Heart	Presence of subendocardial hemorrhagic spots	Arsenic, phosphorus, mercuric chloride
15	Brain and spinal cord	Congestion and edema	Cerebral and spinal poison(e.g. strychnine)
16	Uterus and vagina	Staining, congestion hemorrhage, ulceration	Attempted abortion by use of local abortifacient agents

Factors affecting the actions of a poison in the body

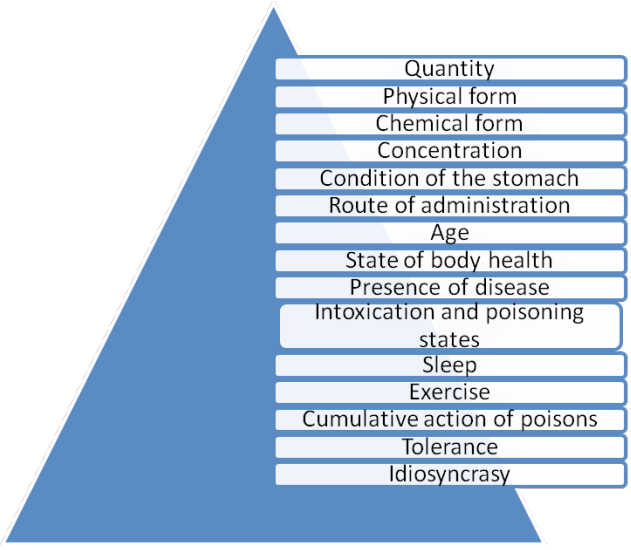


Figure 2. Factors affecting actions of poisons

Conflict of Interest: None Declared

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