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## Toxicological Investigation of Acute Cyanide Poisoning Cases: Report of Four Cases

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### Abstract

Cyanide is a deadly poison. Acute cyanide poisoning in humans is rare and is predominantly caused by smoke inhalation from fires and much more rarely by intentional ingestion of cyanide salts as in suicide or homicide attempts. The main objective of this report is to emphasize the need to consider cyanide poisoning, even if it is rare, in differential diagnosis while evaluating cases of sudden death and the significance of gastric content analysis in acute poisoning cases.

The authors reported four cases of lethal cyanide poisoning. Autopsy specimens were submitted to the author's laboratory for analysis. A presumptive test for cyanide using Vitamin B12 indicated the presence of cyanide. Confirmation and quantification of cyanide was performed using headspace gas chromatograph coupled to flame ionization detector technique. The toxicological analysis revealed lethal hydrogen cyanide concentrations in all postmortem specimens

ranging from 24 to 2600 mg/L in gastric contents, 70 to 282 mg/kg in liver specimens, 11 to 12 mg/kg in a mixture of viscera (liver, spleen, kidney) and 15 mg/L in blood. The cause of deaths in the reported cases was acute respiratory failure and cardiac arrest following cyanide intoxication.

الفضوصات السمية لأربع حالات تسمم حاد بالسيانيد، تقرير حالة

### المستخلص

بعد سم السيانيد من السموم القاتلة. وتعتبر التسممات الحادة بالسيانيد نادرة الحدوث عند الانسان، ويكون سببها في الغالب استنشاق الدخان المنبعث من الحرائق أو عن طريق الابتلاع المتعمد لأملح السيانيد كما هو الحال في محاولات الانتحار أو القتل.

إن الهدف الرئيسي لهذه الدراسة هو تأكيد ضرورة أخذ التسمم بالسيانيد بعين الاعتبار في التشخيص التفريقي حتى وإن كانت تلك الحالات نادرة، وذلك في أثناء التحقيق في حالات الموت المفاجئ، والتأكد على أهمية تحليل محتويات المعدة في حالات التسمم الحاد.

عرض المؤلفون أربع حالات من التسمم بالسيانيد أدت الى الوفاة، حيث تم طلب تحليل عينات المشرحة في مختبر المؤلفين. أشارت الاختبارات الافتراضية للسيانيد باستخدام فيتامين ب 12 الى وجود السيانيد، وتم التأكد من وجود كمية السيانيد باستخدام تقنية الرأس الفراغي المرتبط مع الكروماتوغرافيا الغازية المقترنة بكاشف التأين باللهب. كشفت الفحوصات السمية عن تراكيز قاتلة لسيانيد الهيدروجين في جميع العينات بعد الوفاة تتراوح بين 24-2600 mg/L في محتويات المعدة

**Key words:** Cyanide, Poisoning, Sudden Death, Gastric Contents, Gas chromatography, Flame Ionization Detector.

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وبين 70-282 mg/Kg في الكبد وبين 11-12 mg/Kg في مزيج الأحشاء (الكبد، الطحال، الكلى) و 15 mg/L. إن سبب الوفاة في الحالات التي وردت في هذه الورقة العلمية هو فشل تنفسي حاد والسكتة القلبية التالية للتسمم بالسيانيد.

الكلمات المفتاحية: السيانيد، التسمم، الموت المفاجئ، محتويات المعدة، كروماتوغرافيا الغاز المقترنة بكاشف التأين باللهب.

## Introduction

Cyanide is a very potent, rapidly acting, extremely lethal and deadly substance which has been used as a poison for thousands of years. Cyanide poisoning is almost always fatal because of its low fatal dose and the rapidity with which it acts. Cyanide is toxic to all living beings except bacteria. It has been used as a chemical warfare agent and for many military purposes, mainly in the form of volatile liquids like hydrocyanic acid (HCN). It is notoriously used in executions, homicides, and suicides. In civilian life, poisoning with cyanide and its compounds can occur from its use in chemical syntheses, electroplating, plastics processing, tanning, metallurgy, and as a fumigant [1]. Magnesium cyanide and cyanogen chloride are used as insecticides. It is also used as a part of a gold polishing chemical which is available in powdered form. Combustion of synthetic products that contain carbon and nitrogen (such as plastics, synthetic fibres) and cigarette smoke release gaseous HCN. In food products, like bitter almonds, apricot pits, lima beans and cassava beans, cyanide is present in the form of cyanogenic glycosides [1]. The release of HCN and cyanogenic compounds from combustion of such products is the most common source of human exposure to cyanide [1-3]. The pure hydrocyanic acid is a colourless, transparent, volatile liquid with an odour resembling that of bitter almonds. It decomposes rapidly on exposure to light. About 20 - 40% of the population cannot smell the gas, and the ability to detect it is a sex-linked recessive trait.

## Mechanism of Action

The cyanide anion is an inhibitor of the enzymes cytochrome c oxidase (also known as aa3) in the

fourth complex of the electron transport chain and carbonic anhydrase. It attaches to the ferric iron atom of intracellular cytochrome oxidase. The binding of cyanide to this enzyme prevents transport of electrons from cytochrome c to oxygen. As a result, the electron chain is disrupted meaning that the cell no longer aerobically produces ATP for energy. Tissues that depend highly on aerobic respiration, such as the central nervous system and the heart, are particularly affected. There is an interference with the intracellular oxidative processes in the tissues and it kills by creating histotoxic anoxia, although the blood may contain normal oxygen content [16].

## Analytical Method

An Agilent 7890A Gas Chromatograph coupled to a Flame Ionization Detector with a split injector and Agilent G1888 Headspace auto-sampler was used for the analysis. The loop, oven and transfer line temperatures of the headspace auto-sampler were set to 80°C, 70°C and 90°C respectively. Injection time and oven stabilization time were 1.0 min with a loop equilibration time of 5 seconds. The separation in the Gas chromatograph was accomplished on an HP-Innovax (PEG) capillary column (30m Length, 320µm internal diameter, 0.5µm film thickness). Injections were made in the split mode with the split ratio of 0.1:1. The injector was held at 200°C and at a pressure of 4.7543 psi (32779.7432 Pa). An Agilent split liner without glass wool was used. The Nitrogen carrier gas (99.999% pure, Noor Chemicals Private Limited, Pakistan) flow to the column was set to 1.4 mL/min. The initial GC Oven temperature was 50°C which was then ramped at a rate of 10°C/min to 70°C and held for 6.7 minutes. Maximum oven temperature was set to 265°C with an equilibration time of 0.5min. The FID heater temperature was set to 250°C. The Hydrogen gas (fuel gas in FID produced from HydroGen PH200 H2 generator by Peak Scientific, Scotland UK) and air flow rates were set to 30 mL/min and 400 mL/min, respectively, with a make-up flow of 25 mL/min. Cyanide in blood or other matrices was liberated by conversion of Potassium cyanide to the volatile Hydrogen cyanide



(HCN) through addition of 5N Sulphuric acid in the headspace vial. HCN gas diffuses into the headspace above the specimen in a sealed vial based on Henry's Law of partial pressure. The method showed good linearity ( $r^2 = 0.999$ ), 95-102% accuracy and a relative standard deviation (% CV) ranging from 1.3% to 3.8% [17].

### Sample Preparation:

In a 20 mL headspace vial, 1mL of the case sample (blood, gastric contents, liver homogenate or homogenized mixture of liver, spleen and kidney) was added. The vial was quickly sealed by crimping the aluminium vial cap after the addition of 1mL of 5N sulphuric acid.

### Case Reports

In this section, we present suicidal and homicidal cases of cyanide poisoning submitted to our laboratory for forensic toxicological analysis. There were no autopsy findings that were diagnostic of cyanide intoxication. The classical description of autopsy findings in cases of cyanide ingestion include: pink lividity, an odour of "bitter almonds", gastritis, and oral/peri-oral erosions, which were not observed in any of the four cases.

#### Case 1:

A young newly married couple, a 22 year old male and an 18 year old female, were found dead in their house. Police collected crime scene evidences, including an empty jar and bottle. The dead bodies were sent for postmortem analysis. Autopsy findings showed that bloody froth was coming out of their mouths and nostrils. All viscera including lungs, oesophagus, pharynx, kidney, stomach, liver and spleen were congested. Gastric contents and a mixture of liver, spleen and kidney samples of both husband and wife were sent in addition to the empty jar and bottle recovered from the crime scene to the author's laboratory for chemical analysis.

#### Case 2:

A man, aged 30, committed suicide in his house

by ingesting poison due to a failed love affair. The autopsy showed that there were no internal or external injuries on his body. Liver and gastric contents were submitted for toxicological analysis.

#### Case 3:

The dead body of a 25 year old male was found in a street. His parents showed suspicion that their son was murdered by their relatives, who wanted him to marry their daughter. An autopsy was conducted and findings showed that a wound was present around his nose, and froth was coming out of his mouth. No internal injuries were seen. Postmortem liver and gastric content specimens were submitted for the detection of any drug or poison, if present.

#### Case 4:

A suspicious suitcase was found near a bus stop. Upon police investigation, the dead body of a young female, aged 20, was recovered from it. Blood was coming out of her mouth. A suspected substance was also recovered from the crime scene during later investigations. The dead body was sent for autopsy. Autopsy findings revealed that there were no resistance marks on her body. No significant morphological changes were observed except congestion in lungs, heart, liver, spleen, kidney and stomach. Postmortem blood, liver and gastric content specimens from the deceased female along with the suspected substance recovered from the crime scene were submitted for chemical analysis.

### Toxicological Analysis Results

The postmortem specimens submitted for analysis in the above mentioned cases were subjected to gas chromatographic analysis. Typical chromatograms obtained by analysis of postmortem gastric contents, blood and liver tissue specimens are shown in figures 1 to 3 respectively.

The toxicological analysis revealed cyanide content in all analyzed postmortem specimens ranged from 24 to 2600 mg/mL in gastric contents, 70 to 282 mg/kg in liver, 11 to 12 mg/kg in mixture of viscera (liver, spleen, kidney) and 15 mg/L in blood as shown in



Table 1. Cyanide was also confirmed in the crime scene evidences (empty jar and bottle in case 1 and suspected substance in case 4) using headspace GC/FID method. Toxicological findings of biological specimens and crime scene evidences corroborated with each other in cases 1 and 4. The toxicological reports revealed that

lethal levels of cyanide were found in all four cases and the cause of death was determined as acute myocardial infarction following acute ingestion of cyanide salts.

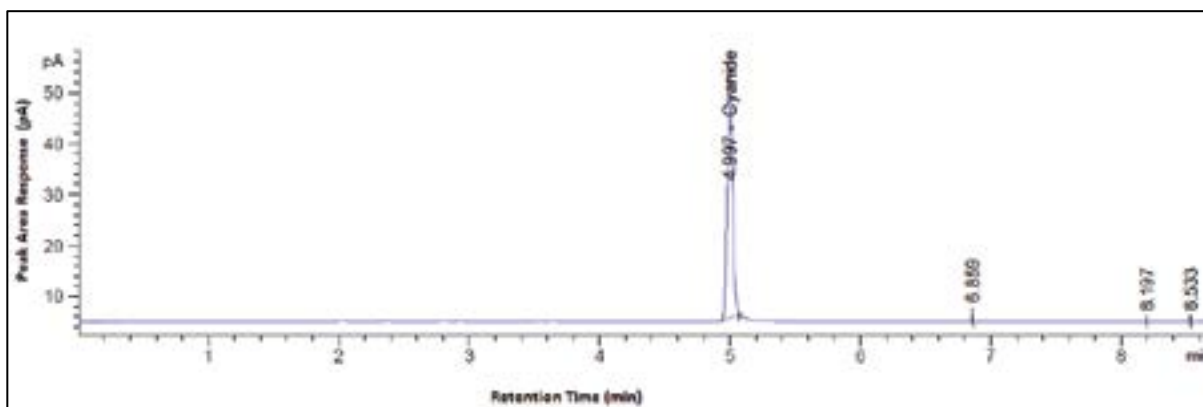


Figure 1- Gas chromatogram obtained for postmortem gastric content specimens.

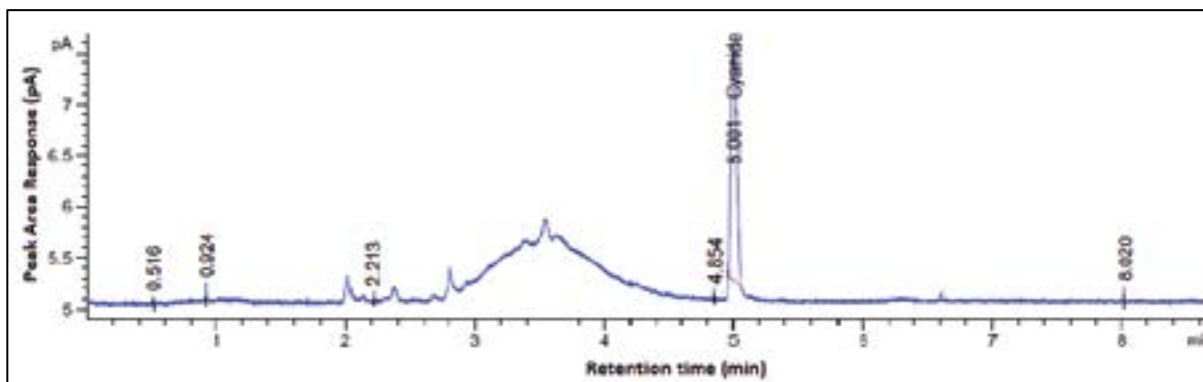


Figure 2- Gas chromatogram obtained for postmortem blood specimens.

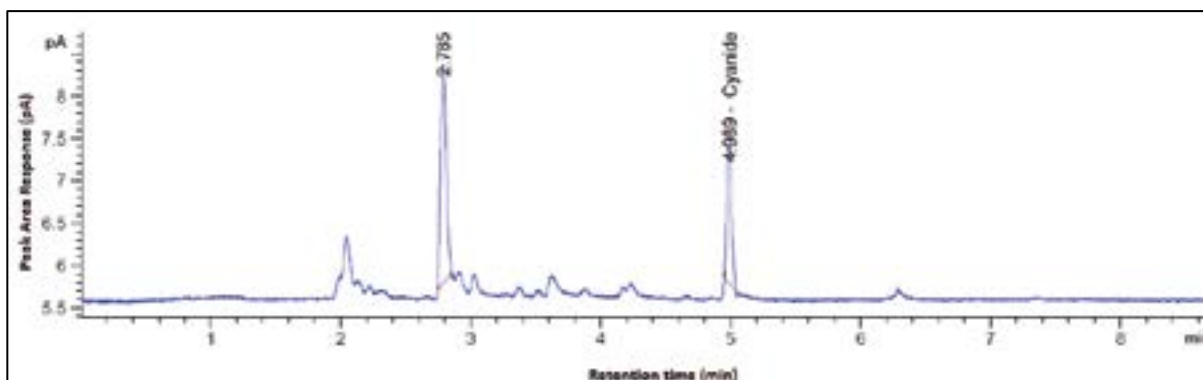


Figure 3- Gas chromatogram obtained for postmortem liver tissue specimens.

## Discussion

Cyanide is among the most potent and deadly poisons, and human exposure to it can occur in numerous ways. The use of cyanide as a suicidal agent has been reported since ancient times. People who use cyanide to commit

suicide often have ready access to the poison through their occupations. These occupations include chemists, jewellers, pest controllers, and people working in mineral refining, photography, electroplating, dyeing, printing, and salmon poaching industries. Jewellers

**Table 1- Hydrogen cyanide concentration in postmortem specimens of deceaseds**

Case No.	Specimen used	Cyanide levels obtained in deceased (mg/L for blood, stomach contents and mg/kg for liver, spleen, kidney)
1	Husband: Mixture of liver, spleen, kidney	12
	Husband: Stomach contents	28
	Wife: Mixture of liver, spleen, kidney	11
	Wife: Stomach contents	500
2	Liver	282
	Stomach contents	2600
3	Liver	93
	Stomach contents	71
4	Blood	15
	Stomach contents	24
	Liver	70

use cyanogenic compounds like potassium or sodium cyanide, mercuric cyanide and silver cyanide to rid gold of tarnish. [1-5,7]

Occupational poisoning can be suicidal or accidental. Most of the cases reported were suicidal in nature and occurred through ingestion [2,5,6-8]. Inhalation exposures to cyanide usually occur through smoke from fires and from fumigation vapours [1-4]. Cyanide poisoning is difficult to diagnose, except in cases of early confession by the person that administered the poison. Regrettably, recognition of cyanide poisoning may be delayed because the majority of clinical and laboratory findings are non-specific [11-13]. Though the manner of exposure may be different, the manifestations are similar through all routes of exposure as cyanide is rapidly absorbed from all mucous surfaces, and even from unabrased skin. Cyanide disappears from the blood of poisoning victims with a half-life of about 0.7 to 2.1 hours and 0.4 L/kg apparent volume of distribution. In fatal cases, the tissue distribution of

cyanide is generally in proportion to the erythrocyte content of each organ. It also demonstrates that liver concentrations following ingestion of the cyanide may be considerably higher than after inhalation. Onset of action depends on the form, concentration and rate of absorption. When the gas is inhaled, consciousness may be lost at once and prompt death may occur due to respiratory arrest. After ingestion, symptoms appear within minutes [10]. However, death may be delayed for several hours if a small dose is taken [3,9]. Exposure to low concentrations may result in a range of non-specific features including headache, dizziness, throat discomfort, chest tightness, skin itching, eye irritation and hyperventilation. As hypoxia progresses, patients may experience progressively lower levels of consciousness, seizures, and coma [3,4]. Cyanide exerts its toxic effects by binding to the ferric ion in the a-a3 complex of cytochrome oxidase, resulting in the inhibition of aerobic metabolism. This may account for cellular damage seen in most of the tissues as metabolism



shifts from aerobic to anaerobic, with consequent production of lactic acid. The sudden collapse and cellular hypoxia results from inhibition of cytochrome oxidase and accounts for sudden deaths [14]. This is because cyanide has a distinct inhibitory mechanism that is exerted at two different levels of the respiratory chain. Carbonmonoxide binding to hemoglobin is potentiated by hydrogen cyanide that binds at the cellular level [15]. This inhibits the mitochondrial cytochrome oxidase causing deprivation of oxygen consumption at the cellular level. These, in turn, result in a shift towards an anaerobic process with energy depletion, intracellular acidosis, and cell death. Lethal levels of cyanide reported in the literature are 1-100mg/L in blood, 0.1-43 mg/kg in liver and 2-4000 mg/L in gastric contents [18].

In our report, the manner of exposure in each case was through ingestion. Clinical data was unavailable because the bodies were recovered from the crime scenes in all four cases and autopsy findings were non-specific. Therefore, according to the toxicology analysis protocol, all presumptive and screening tests, including colorimetric screening of cyanide using vitamin B-12 strips, colorimetric screening of phosphine using silver nitrate strips, screening for drugs of abuse using ELISA, and general screening for drugs and poisons using Gas chromatography-Mass spectrometry technique were performed. The presumptive test for cyanide using the vitamin B-12 strips indicated the presence of cyanide which was confirmed and quantitated using headspace-gas chromatograph coupled to flame ionization detector technique [17]. Toxicological analysis revealed lethal amounts of cyanide in all postmortem specimens ranging from 24 to 2600 mg/L in gastric contents, 70 to 282 mg/kg in liver, 11 to 12 mg/kg in mixture of viscera (liver, spleen, kidney) and 15 mg/L in blood. The probable mechanism of cyanide-related deaths in the five deceased was hypotension and respiratory failure, following which there was loss of consciousness and ultimately cardiac arrest.

Death from cyanide poisoning is rare; it needs to be considered in differential diagnosis in evaluation of cases of sudden death. Also, the forensic pathologist

should give due attention to the background and occupation of the deceased while conducting autopsies in cases of poisoning. This is because cyanide is an easy way to poison someone and is difficult to diagnose without the aid of an autopsy. These cases further highlight the need to carry out an autopsy on all patients experiencing sudden death as this may reveal more cases of cyanide poisoning in our society, making it difficult for the culprits to go unpunished.

## Conclusion

The cause of death in each case study was determined to be acute respiratory failure and cardiac arrest following ingestion of cyanide salts. Its lethality was related to the rapid onset of toxicity and nonspecific nature of the symptoms.

## Conflict Of Interest

None declared.

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