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UNVEILING THE COMPLEXITIES OF COCAINE

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ABSTRACT

This investigation delves into the multifaceted world of cocaine, a potent psychostimulant derived from the Erythroxylon coca plant. We undertake a comprehensive analysis, examining its chemical structure and pharmacological classification, alongside the analytical techniques employed for its detection and quantification in biological matrices. Our journey traverses historical perspectives, tracing the evolution of cocaine use and regulatory frameworks. Subsequent exploration focuses on the pharmacological effects exerted on the central nervous system and peripheral systems, elucidating its abuse potential and the neurobiological mechanisms underlying addiction. The characteristic symptomatology associated with cocaine use and the potentially fatal consequences of overdose are also brought to light. Furthermore, we dissect the dose-dependent relationship with adverse effects, including the concept of lethal dose. Therapeutic interventions and potential antidotes are investigated, alongside both traditional and cutting-edge laboratory techniques for cocaine detection and analysis. Finally, we adopt a global perspective, examining current research trends and the worldwide impact of cocaine-related fatalities. This holistic approach aims to provide a comprehensive understanding of this complex drug and its multifaceted consequences.

Keywords: Cocaine, GCMS, Spectroscopy, Specimens, Techniques.

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INTRODUCTION

Cocaine is a popular but dangerous drug that can be addictive. It has some medical uses, but it's mainly abused for its stimulating effects. Cocaine works by increasing dopamine levels in the brain, which creates pleasurable feelings. People can take cocaine in different ways, and the effects hit them faster or slower depending on how they take it. The body gets rid of cocaine by breaking it down into other chemicals. Cocaine use can mess with your body and mind, and in some cases, it can even be deadly [1]. The history of cocaine is charted with specific reference to its usefulness as a medicine and local anesthetic. It is common knowledge that coca leaves were used as a panacea and local anesthetic throughout the history of the Incan Empire of Peru. In Europe, however, its medical usefulness was not fully recognized until Carl Koller used it to anesthetize the cornea of the eye. Over the next 20 years, cocaine became a popular medicine and tonic in Europe and America, where it was credited with curing a wide variety of diseases and illnesses. However, reports soon started to appear claiming that cocaine was a drug with a high social abuse potential and in America it seemed to underpin growing crime figures. As a result, cocaine was misclassified as a narcotic and its use was restricted to specific surgical procedures and medicinal preparations. Today, cocaine and its derivatives are still popular local anesthetics in operations of the ear, nose and throat and it is also used in a preparation given to alleviate the pain (physical and mental) of terminal diseases. Although cocaine has a high public profile as a drug of addictive potential, this drug has also had a long and distinguished history as a medicine and local anesthetic. The legitimate uses of cocaine exacerbate the problems of controlling this substance of abuse and should provide a stimulus for generating local anesthetics that lack addictive potential [2]. Traditionally, using coca leaves was relatively safe because people could only absorb a limited amount of cocaine through chewing. However, refined cocaine allows for a much quicker and stronger effect, leading to more risks. Cocaine use skyrocketed in the late 1800s due to several reasons. First, famous people like Freud promoted its use. Second, a doctor discovered it could be used as anesthesia. Third, a new method was developed to make cocaine easier to transport and store. Finally, companies like Merck significantly increased production. Unfortunately, this also led to more problems. Medicines containing high amounts of cocaine caused addiction and even death. In addition, the invention of syringes made it easier to inject cocaine, further increasing risks. Crack cocaine, which can be smoked, delivers an even faster and more intense

high compared to snorting it, leading to even worse consequences. The surge in crack use wasn't necessarily due to it being cheaper, but likely because of its quicker and stronger effect. Finally, the plant that produces cocaine can be grown in many places. So, even if production stops in South America, other regions could easily take over [3].

STRUCTURE AND CLASSIFICATION OF COCAINE

Cocaine is classified as a Schedule II controlled substance under the Controlled Substances Act. This classification indicates that while cocaine has a high potential for abuse, it has also accepted medical uses in the United States, albeit with severe restrictions. It is a potent central nervous system (CNS) stimulant and local anesthetic. Cocaine's legal status varies by country, but is generally considered illegal for personal use without a prescription or specific medical indication. The basic formula for cocaine is C17H21N04 [4].

COCAINE IN BIOLOGICAL SPECIMENS

Cocaine remains a prominent illegal drug despite ranking lower than cannabis and certain pharmaceuticals. Notably, Europe witnesses a concerning rise in recreational cocaine use amongst younger demographics. This necessitates reliable methods for cocaine detection in various biological matrices. This review summarizes established bioanalytical techniques for analyzing cocaine in blood (recent exposure), urine (common, non-invasive), hair (long-term history), oral fluid (recent use, gaining popularity), and meconium (newborn/infant exposure). These diverse methods empower researchers and professionals with comprehensive tools for effective cocaine detection and monitoring.

Diverse Matrices for Cocaine Detection: Beyond Biological Samples

Cocaine and its metabolites can be detected in a broad spectrum of biological matrices, including blood, urine, hair, oral fluid (saliva), and meconium. This provides valuable information about various aspects of cocaine use, from recent exposure (blood) to long-term history (hair) Blood, plasma & urine. Additionally, non-biological samples like currency notes can also be analyzed for cocaine presence, offering insights into its circulation and spread within specific environments**.**

Hair

Hair analysis boasts a long detection window for drugs (weeks to months) but faces the risk of false positives from external contamination, especially for smoked drugs. Standardized washing and analyzing parent drug-to-metabolite ratios ensure the detected drug comes from internal incorporation, not just surface contamination

Fluid Drug Testing

Oral fluid analysis is an important alternative to drug screening because it is noninvasive and focuses on pharmacological components. This non-invasive method reduces privacy concerns and reduces the risk of sample tampering compared to techniques such as urine. Additionally, unlike other methods that capture the entire contents of the drug, the fluid in the mouth directly affects the drug's ability to cause damage by indicating protein deficiency. Research shows a relationship between oral fluid and plasma levels of illicit drugs such as narcotic drugs; This suggests that it is effective to try walking in places where blood collection is not usually possible. The concentration of the film in oral fluid is approximately 3 times lower than in blood, but it exhibits a long terminal half-life (up to 17 hours after the end of the dose), thus extending the window of discovery. However, the biggest limitation is that the volume of fluid in the mouth is usually small (usually <1 ml), which requires the use of sensitive techniques such as mass spectrometry, guided spectrometry for accurate analysis.

Sweat, meconium & other specimens

The realm of drug testing expands beyond traditional approaches like urine and hair analysis. Researchers are exploring unconventional biological matrices that offer unique clues to past and present drug use. Sweat, while promising for detecting parent drugs like cocaine, presents complexities such as accurately measuring volume and avoiding contamination from collection tools. Additionally, its metabolic profile dramatically differs from urine, necessitating tailored analytical methods. Meconium the baby's first stool, provides valuable insights into potential prenatal drug exposure, particularly for cocaine. However, the detection window for most cocaine metabolites, except benzoylecgonine, is brief, requiring testing within 48 hours of birth. Furthermore, comprehending the distinct metabolic profile in meconium is crucial to avoid false negatives. The spectrum of unconventional matrices extends far beyond these two examples. The fluid surrounding the heart (pericardial fluid) and the jelly-like substance in the eye (vitreous humor) have both revealed traces of cocaine and its metabolites. Even fingernails can act as historical records of drug use, albeit with challenges in interpretation. Organs and tissues like the brain and bones hold further potential, but extensive research is required to assess their suitability for routine testing.

Time-Sensitivity in Cocaine Detection Across Biological Matrices

Cocaine exhibits a finite detection window in various biological matrices, posing a significant challenge for forensic and clinical investigations. Timely analysis is crucial to ensure accurate and reliable detection, as cocaine undergoes biotransformation and elimination from the body over time. Here's a breakdown of cocaine's detectability in different matrices along with their respective timeframes [5,6]:

Table 1: Biological samples and their life for cocaine analysis.

Specimen	Time
Hair	Months
Meconium	In first 48 h
Oral fluids	12-24 h
Urine	Up to 10 h
Blood	10-48 h

Cocaine in blood

In the past, detecting cocaine in blood relied heavily on a specific gas chromatography detector. While this method is still used, newer techniques like gas chromatography-mass spectrometry and high-pressure liquid chromatography are becoming more prevalent. However, accurate cocaine analysis requires meticulous handling of blood samples. Adding substances like fluoride helps prevent the breakdown of cocaine, which can lead to falsely low readings. Analyzing cocaine's byproducts, known as metabolites, can be valuable because they stay in the body longer and can provide insights into individual differences in how people process the drug. Understanding how cocaine travels through the body and accurately measuring its presence in blood are essential for designing effective research, both in medicine and basic science. Additionally, reliable detection methods and a thorough understanding of cocaine's behavior in the body are crucial for interpreting drug abuse screenings accurately and responsibly [7].

SYNTHESIS OF COCAINE

Cocaine production is a clandestine and hazardous undertaking, escalating in complexity and danger with each step. The initial stage, transforming coca leaves into a crude paste, often occurs near water sources for easy access. This multi-day process utilizes a simple pit lined with plastic or even a modified drum. The leaves are submerged in a solution containing a common household ingredient (similar to baking soda) that facilitates the extraction of the desired alkaloids. Kerosene, a readily available solvent, is then added, and the mixture is agitated – sometimes even by people treading on the leaves. This agitation helps transfer the desired alkaloids from the leaves into the kerosene layer. The kerosene layer is then separated from the remaining water and leaves. Finally, the kerosene is mixed with a diluted acid and another basic substance, causing a solid to precipitate out. This solid, after being filtered and dried, becomes the rough, light-colored coca paste. The second stage, refining coca paste into cocaine base, necessitates more sophisticated equipment and skilled labor. These clandestine "base labs" are often situated near waterways or hidden airstrips, potentially far from the initial coca cultivation areas. This stage involves dissolving the coca paste in a strong acid solution. A specific chemical (potassium permanganate) is then introduced to remove unwanted materials and alkaloids, particularly crucial for certain coca plant varieties. The mixture is then filtered, discarding the impurities. Finally, another chemical (ammonia) is used to create a new solid, the cocaine base, which is subsequently dried using heat lamps. Notably, Colombia frequently bypasses this stage altogether, directly converting coca paste into cocaine hydrochloride. The final and most perilous stage transforms cocaine base into the highly addictive and illegal cocaine hydrochloride (HCl). This complex process demands highly skilled workers, specialized equipment that is not readily available, and strictly controlled chemicals, making it the most challenging and expensive stage. The cocaine base is dissolved in a specific solvent, such as acetone or ether. Then, hydrochloric acid is carefully added, causing the cocaine to crystallize out of the solution as cocaine hydrochloride. The remaining solvent is removed, and the cocaine hydrochloride crystals are dried using heat lamps, fans, or even microwave ovens (though this method is particularly risky) [8].

PHARMACOKINETICS (ADME)

Its pharmacokinetics, which refers to the absorption, distribution, metabolism, and excretion of a drug (ADME), can provide insights into how the body processes and eliminates cocaine [9].

Absorption

As previously mentioned, users differ in the form of cocaine they choose (cocaine salts or free base), routes of administration, and patterns of use. Because of its hydrophilic nature, cocaine hydrochloride is usually taken by "snorting". "Crack" cocaine is the only form of cocaine that is commonly smoked. This is due to the fact that cocaine hydrochloride has a high boiling point and does not volatilize at combustion temperatures. These routes, including the respiratory system, are favorable for both forms of cocaine because the stimulant can reach the cerebral circulation in about 6 to 8 seconds. The inhalation route shows a higher peak plasma concentration and is achieved faster compared to intranasal injection. It should be noted that for the intranasal route, the vasoconstrictor properties of cocaine slow down the absorption of the drug itself and delay the maximum plasma concentration by 60 minutes. In terms of bioavailability, the inhalation route has the highest bioavailability, over 90%, while the intranasal route has approximately 80% bioavailability. According to the time to peak effect and duration of effect, inhalation causes stimulation at most 1-3 minutes after administration and stimulation lasts 5-15 minutes. For the intranasal route, longer effects are determined in the range of 15 to 30 minutes.

Intravenous administration of cocaine hydrochloride by dissolving the powder in an aqueous medium has also been used by users. Compared to the inhalation and intranasal routes, when cocaine is administered intravenously, it takes twice as long to reach the

cerebral circulation, and peak plasma concentrations are higher and are reached earlier. Bioavailability is close to the inhalation route. In 1995, Edward Cohen directly investigated the pharmacokinetics of cocaine via inhalation, intranasal injection, and intravenous injection (42 mg of "crack" cocaine, 32 mg of cocaine HCl, and 25 mg of cocaine HCl, respectively) using the same people compared. Published research. We used a different route (crossover design) and concluded that the maximum plasma concentration is reached within 5 minutes of intravenous administration [10,11].

Distribution

Cocaine is rapidly processed in tissues and its volume of distribution is between 1 and 3 L/kg [12]. Cocaine is approximately 90% bound to albumin and alpha-1 acid glycoprotein, and the highest concentrations are found in the brain, spleen, kidneys, and lungs, followed by blood, heart, and muscle tissue [13,14]. The average half-life of cocaine is 40 to 90 minutes, depending on the route of administration (shorter for the intravenous route and longer for the inhalation route).

Metabolism

Cocaine breaks down in the body mainly into two inactive substances: benzoylecgonine (BE) and ecgonine methyl ester (EME). These can break down further into ecgonine (EC). Cocaine can also turn into a toxic substance called norcocaine (NCOC) in a small amount. This can cause liver damage and reach the brain. When cocaine and alcohol are used together, they form Cocaethylene (CE), which is more dangerous than cocaine alone and can increase heart rate and be more toxic. Smoking crack cocaine creates another substance, anhydroecgonine methyl ester (AEME), which can harm the heart and brain. AEME can break down further into ecgonidine (ED) or ecgonidine ethyl ester (EDEE) if alcohol is present. The presence of AEME or EDEE in the body can indicate crack cocaine use [15-19].

Excretion

Cocaine and its main metabolites are eliminated through urine, but the exact timing can vary depending on the study. Some research suggests that the route of administration (swallowing, smoking, or snorting) doesn't significantly impact how long it takes for cocaine to leave the body. However, other studies have shown conflicting results, indicating that elimination might be fastest after inhaling, slower after injecting, and slowest after snorting. Additionally, the detection window can vary depending on the specific metabolite. For instance, one study found that EME lasted the longest in urine (up to 164 hours after smoking a 40mg dose), while another study showed BE peaked in urine within 10-3.5 hours after drinking coca tea [20,21].

MODE OF ACTION

The mechanism of action of this substance involves disrupting the reabsorption process of specific neurotransmitters, primarily dopamine, norepinephrine, and serotonin. This interference leads to an accumulation of these neurotransmitters in the space between neurons, extending their impact on the receiving neurons. More specifically, cocaine operates by obstructing the reuptake of dopamine, norepinephrine, and serotonin from the synapse back into the neuron that released them. Normally, after transmitting signals between neurons, these neurotransmitters are taken up again by releasing neurons through transporters. Cocaine attaches itself to these transporters, impeding their function and preventing the reabsorption of neurotransmitters. Consequently, dopamine, norepinephrine, and serotonin remain in the synaptic gap for a prolonged period, resulting in increased stimulation of the receiving neuron. This extended presence of neurotransmitters intensifies their effects and contributes to the intense sense of euphoria, heightened energy, enhanced focus, and improved mood associated with cocaine usage. The accumulation of dopamine plays a vital role in the reinforcing effects of cocaine. Dopamine is involved in the brain's reward pathway, which governs feelings of pleasure and motivation. By elevating dopamine levels in key brain regions associated with rewards, cocaine generates a potent signal of reward, reinforcing the desire to use the drug and leading to addiction. It is worth noting that the extended presence of neurotransmitters caused by cocaine can have various short-term and long-term effects on the brain and body, including increased heart rate, elevated blood pressure, narrowing of blood vessels, and potential harm to the cardiovascular system. Persistent cocaine use can also result in adverse effects on mental health, cognitive function, and overall well-being.

EFFECTS OF COCAINE ON HUMAN BODY

Cocaine gives a quick high that fades fast. Small doses cause euphoria, alertness, and increased energy. However, these effects are short-lived, lasting from 5 minutes to 30 minutes depending on how the drug is taken. Cocaine also has negative effects. Large doses can lead to erratic behavior, anxiety, and paranoia. Cocaine use can also cause serious health problems like heart attacks, strokes, and seizures. In rare cases, even the first use of cocaine can be fatal. Mixing cocaine with other drugs is especially dangerous. Cocaine and alcohol together create a toxic substance that can harm the heart. Combining cocaine and heroin can lead to heroin overdose because the cocaine's effects wear off first. There are also long-term effects of cocaine on human bodies these effects are also discussed here. Chronic cocaine use rewires the brain, making it harder to feel pleasure from natural things and increasing cravings for the drug. People need more and more cocaine to get the same effect, but also become more sensitive to its negative effects like anxiety and seizures. This can lead to dangerous

binges with psychosis and severe health problems. Cocaine use damages various organs. Snorting it can irritate the nose, smoking it hurts the lungs, and injecting it increases the risk of infections. Cocaine messes with digestion, causing malnutrition. It also wreaks havoc on the heart and brain, increasing the risk of heart attacks, strokes, and cognitive problems. Quitting cocaine is difficult because even after abstinence, strong cravings can be triggered [22].

Deprivations in Health

The effects of cocaine use snowball into a series of health problems. Initially, the drug suppresses appetite and sleep, enticing users to binge for extended periods while neglecting basic needs. This neglect, compounded by the inevitable crash after the high wears off, leads to visible signs of deterioration like extreme weight loss, fatigue, and a gaunt appearance. Furthermore, cocaine users frequently mix it with other drugs, creating a dangerous synergy. A prime example is the combination with alcohol, which intensifies the euphoria but dramatically increases the strain on the heart, raising the risk of sudden death. Despite the escalating health risks, cocaine abusers are often hesitant to seek medical or addiction treatment, often persisting with their habit until a catastrophic event forces them to confront the issue. Even first-time users aren't exempt from the dangers of cocaine, as it can lead to overdose, toxicity, and long-term health consequences.

Cardiovascular Problems

One of the main reasons people go to the emergency room for cocaine-related problems is chest pains from cardiovascular problems. Cocaine constricts blood vessels while increasing heart rate and blood pressure. Irregular heart rate and blood pressure can lead to heart attack, stroke, cerebral hemorrhages, seizures, comas, damages to other vital organs, and death. Over time, the muscles and valves of the heart along with the arteries and veins of a cocaine abuser begin to weaken and the potential for cardiovascular problems, heart diseases, and the rupturing of blood vessels increases.

Respiratory Problems

Cocaine's overstimulation of the central nervous system (CNS) often leads to breathing difficulties and irregular patterns. For crack cocaine users, the dangers are even greater. Inhaling the toxic mix of cocaine, chemicals from the lighter used to ignite it, and hot metal from the pipe damages the lungs. This damage, known as "crack lung," turns the lungs black and severely restricts their ability to absorb oxygen and deliver healthy blood throughout the body.

Damage of liver

Cocaine abusers face a double threat to their liver health. Firstly, the liver is responsible for detoxifying the body, and cocaine itself puts a strain on this function. Secondly, sharing needles, straws, and pipes with other users increases the risk of contracting hepatitis, a liver disease that can be life-threatening.

Communicable Diseases and Infections

Cocaine abuse creates a dangerous cycle that increases the risk of contracting and spreading a variety of diseases. Sharing needles and straws during intravenous injection exposes users to blood-borne illnesses like HIV, AIDS, hepatitis, and other STDs. Unsafe sexual practices further compound the risk. These diseases, along with the external signs like herpes, skin infections, and bacterial infections, take a toll on the immune system, making it even harder for cocaine abusers to fight off infections.

Over-heating

Cocaine cranks up the body's thermostat, leading to excessive sweating and dehydration. This dehydration can wreak havoc on vital organs like the brain, heart, kidneys, and liver. Even more dangerous, the inability to regulate body temperature can spiral into seizures, coma, and even death [23].

Effects on brain

Cocaine wreaks havoc on the brain in multiple ways. The surge in blood pressure it causes raises the risk of strokes and bleeding within the brain, often leading to headaches as well. Even a single dose can trigger seizures by disrupting brain chemicals. Studies have shown that cocaine can kill brain cells and damage their function. This damage is evident in scans of cocaine users' brains, which reveal shrinkage in regions responsible for pleasure, decision-making, and motivation [24,25].

Respiratory System

Cocaine wreaks havoc on your respiratory system depending on how you use it. Smoking crack exposes your lungs to a toxic cocktail of cocaine itself, byproducts from heating the drug, and fillers used to make crack. This irritates the lungs and can lead to serious problems like chest pain, fever, coughing up blood, and difficulty breathing, sometimes called "crack lung." Snorting cocaine isn't much better. The constant constriction of blood vessels in your nose from snorting can damage them, potentially leading to a hole in the septum, the wall dividing your nostrils. In addition to these specific effects, cocaine can also generally tighten airways and cause other breathing problems [26].

Renal System

Chronic cocaine abuse puts your kidneys at serious risk. The drug creates oxidative stress and damages blood vessels in these vital organs, making it harder for them to filter waste products from your blood. Additionally, cocaine can break down muscle tissue, releasing substances that harm the kidneys. To make matters worse, cocaine can increase blood clot formation and inflammation within the kidneys, further hindering their ability to function. Studies have even shown that high doses of cocaine can directly damage kidney cells, although the exact

mechanisms are still being investigated. All of these factors can lead to acute kidney failure, a sudden and dangerous condition where the kidneys shut down [27,28].

Subjective and physiological effects

Cocaine can be a deceiving drug. While moderate doses may bring a temporary high, increased alertness, and even a boost in sex drive, these effects come with a dark side. Users often experience anxiety, irritability, and bad moods alongside the initial euphoria. These negative effects tend to worsen with continued use. Cocaine also wreaks havoc on the body. It narrows blood vessels, raises heart rate and blood pressure, and can lead to sweating, tremors, and even seizures. Headaches, stomach pain, and muscle problems are also common. In severe cases, cocaine use can cause convulsions, heart failure, or even death [29].

Effects and toxicity of cocaine

Several studies have investigated the lethal dose (LD50) of cocaine in different animals. In mice given cocaine through injection into the abdomen, the LD50 was 95.1 mg/kg. For rats and dogs given cocaine intravenously, the LD50 was much lower at 17.5 mg/kg and 21 mg/kg, respectively. Cocaine primarily affects the central nervous system (CNS), causing a wide range of physical, psychological, and behavioral effects. These effects depend on the user's individual characteristics, how the drug is taken, and the amount consumed. While chronic cocaine use can lead to serious health problems like neurodegeneration, premature brain aging, depression, and blood vessel damage, even a single dose can cause acute effects including rapid heartbeat, high blood pressure, fever, sweating, tremors, seizures, dilated pupils, headaches, stomach pain, muscle hyperactivity, stroke, and organ failure. It's important to remember that some cocaine breakdown products can also cross the blood-brain barrier, contributing to both the pleasurable effects and the unwanted side effects users experience [30].

DOSE OF COCAINE

Normal Dose of cocaine

Numerous studies, including our initial research (Vernotica et al., 1996), have investigated the impact of cocaine on various aspects of maternal behavior in rats. These aspects include pup retrieval, nursing, nest building, maternal pup-grooming involving anogenital and corporal licking, and maternal aggression (Zimmer Berg and Gray, 1992; Johns et al., 1994, 1998; Kinsley et al., 1994). To simulate the drug use patterns and dosages seen in human users who are dependent on cocaine, these studies utilize doses and treatment regimens that resemble those reported in humans. The dosages commonly employed in these studies lead to peak levels of cocaine in the bloodstream ranging from approximately 200 to 900 ng/ml (equivalent to 10-40 mg/kg injected), closely resembling the plasma levels observed in dependent human users and associated with subjective experiences of being "high" (Javaid et al., 1978; Smith et al., 1989).

Over/Fatal Dose

Taken together, these studies conducted on rats strongly indicate that when plasma levels of cocaine surpass 200 ng/ml, it significantly impairs all aspects of maternal caregiving and leads to a complete halt in behaviors directed towards the pups. Once the cocaine is eliminated from the bloodstream, most maternal caregiving behaviors tend to return (Zimmer Berg and Gray, 1992; Johns et al., 1994, 1998; Kinsley et al., 1994). However, in female rats exposed to prolonged cocaine use during pregnancy, certain effects on maternal behavior after giving birth can persist long after the cessation of cocaine treatment. Furthermore, the offspring of these females may exhibit transgenerational effects unrelated to their own exposure to cocaine (Johns et al., 1994, 2005; McMurray et al., 2008) [31].

PLASMA LEVEL DETERMINATION

Cocaine investigation by using different techniques

Hair analysis is increasingly prevalent in forensic toxicology for detecting drug abuse. Unlike traditional body fluids, hair allows retrospective examination of substance use. Sensitive measuring techniques can even identify single instances of drug use. Segmental analysis, based on hair length, enables investigation of abuse history over months. However, precisely estimating quantitative parameters of drug abuse remains challenging. The intricate process of drug incorporation into hair is not fully understood. Additionally, sampling, sample preparation, and measurement methods significantly influence results. Our paper reviews commonly encountered drugs in forensic toxicology, including opiates, cocaine, amphetamine derivatives, cannabinoids, and alcohol consumption markers, as determined by hair samples. Furthermore, a rapid, sensitive, and reliable quantitative GC/MS method was developed for cocaine confirmation using 0.2 mL of urine. After simple organic solvent extraction and derivatization with Pentafluoro propionic anhydride, cocaine, benzoylecgonine, and ecgonine methyl ester were identified by GC/MS. Quantitation involved calibration curves for molecular ion ratios of the analyte/ketamine (IS) across a range of 12.5-250 ng/mL (0.1-2 ng total). Extraction efficiency for these analytes ranged from 70 to 82%, with a sensitivity limit of detection of 12.5 ng/mL (0.1 ng) at $p < 0.01$. Intra- and inter-day precision for these analytes varied between 14.7 and 29.5% CV. This method is in routine use in our laboratory for the GC/MS confirmation of enzyme immunoassay cocaine-positive urine samples [33]. Cocaine is a widely abused stimulant drug that is quickly broken down by the body into metabolites like benzoylecgonine and ecgonine methyl ester.

These metabolites are easier to detect in urine, sweat, saliva, and feces than cocaine itself [34]. There are various methods to detect cocaine and its metabolites, including immunoassay [35], In the fight against illegal drugs, researchers have developed two novel tools for detection and analysis. The first, known as HPLC-DAD, acts like a "cocaine fingerprint scanner." It can not only identify cocaine itself, but also the byproducts it forms when it breaks down and any substances mixed with it. This information proves valuable to forensic scientists, helping them understand the composition of confiscated cocaine samples. The second method utilizes a high-resolution mass spectrometer, which functions like a powerful and versatile "drug detector." This technology boasts the ability to identify a wide range of illegal drugs, including common ones like cocaine, marijuana, and amphetamines, even in extremely small quantities. Its effectiveness has been demonstrated in real-world situations, successfully analyzing a suspected drug user's urine sample. These advancements provide valuable tools for law enforcement and forensic analysis, offering crucial insights into the presence and nature of illegal drugs [36-38], gas chromatography (GC) [39], and GC-mass spectrometry (GC-MS) [40]. While immunoassay is simple, it can be less specific. HPLC is commonly used but may require additional steps to improve sensitivity and has limitations in reproducibility. GC-MS offers the best combination of accuracy, sensitivity, and structural information.

This study focused on developing a GC-MS method using liquid-liquid extraction for detecting cocaine in human urine. This method is advantageous because it's simple, uses inexpensive chemicals, requires only one extraction step, and has a short run time. And thin layer chromatography is also used for the analysis of cocaine and its metabolites [41] completely automated LC-MS/MS method for quantifying cocaine and its key metabolites [42].

GC-MS with SIM

This study presents a novel approach for the simultaneous determination of multiple cocaine metabolites in human urine samples. Traditionally, analyzing these metabolites involved intricate methods employing several extraction steps and costly chemicals. These methods also lacked the capability to analyze cocaine alongside its metabolites in a single analysis. The innovation lies in the utilization of copolymeric bonded phase columns. These columns possess the unique ability to extract both basic and anaphoretic cocaine metabolites. This characteristic facilitates the design of an assay that enables the simultaneous determination of these metabolites within a single, streamlined extraction procedure. This method surpasses existing methods in terms of comprehensiveness, offering a more efficient analysis. A comprehensive literature survey revealed the absence of reported liquid-liquid phase extraction methods for cocaine determination by GC-MS in human urine. To address this gap, the present study employs a liquid-liquid phase extraction system coupled with GC-MS utilizing the Selected Ion Monitoring (SIM) mode for cocaine detection in human urine samples. The developed method adheres to rigorous validation protocols based on International Conference on Harmonization (ICH) [43] guidelines, ensuring its linearity, stability, precision, accuracy, and sensitivity. The significant advantages of this novel method lie in its simplicity. It requires only a single extraction step, significantly reducing complexity and analysis time. Furthermore, the method utilizes readily available and inexpensive chemicals, enhancing its cost-effectiveness. This study paves the way for a more streamlined and efficient approach to analyzing cocaine and its metabolites in urine samples. And the advantage of this is Specificity, Linearity, Precision and accuracy, sensitivity, recovery and stability are the main advantages of this system.

Techniques used for the investigation of cocaine

There are many other techniques which are used for the investigation of cocaine these techniques are GC-MS [44], ELISA [45], EIA [46], RIA [47], HPLC [48], and Roman spectroscopy [49].

SIGNS & SYMPTOMS OF COCAINE

Cocaine can cause various short-term and long-term signs and symptoms. Cocaine, a strong stimulant, has a rapid onset and wears off within an hour. Even in small doses, users feel euphoric, energetic, talkative, and sensitive to their surroundings. Appetite and desire to sleep also decrease. Some users report improved physical and mental performance, while others experience the opposite. The strength and duration of the high depends on how the drug is administered. Snorting cocaine slows the onset of the high, but prolongs its duration. Smoking cocaine, on the other hand, produces an immediate but short-lived high.

Physiological effects of short-term cocaine use include constriction of blood vessels, dilation of pupils and increase in body temperature, heart rate and blood pressure. In large doses, it can cause erratic and violent behavior, restlessness, irritability, anxiety, panic, paranoia, tremors, dizziness, and muscle spasms. Serious health effects can occur, including cardiovascular problems such as heart rhythm disturbances and heart attacks, neurological problems such as headaches, seizures, stroke and coma, and gastrointestinal problems such as abdominal pain and nausea. There is gender. In some cases, cocaine use can cause sudden death.

Cocaine is particularly dangerous and is often used in combination with alcohol and heroin. Cocaine and alcohol can react to form cocaethylene, which can increase cardiotoxicity. Combining cocaine and heroin can lead to heroin overdose because the

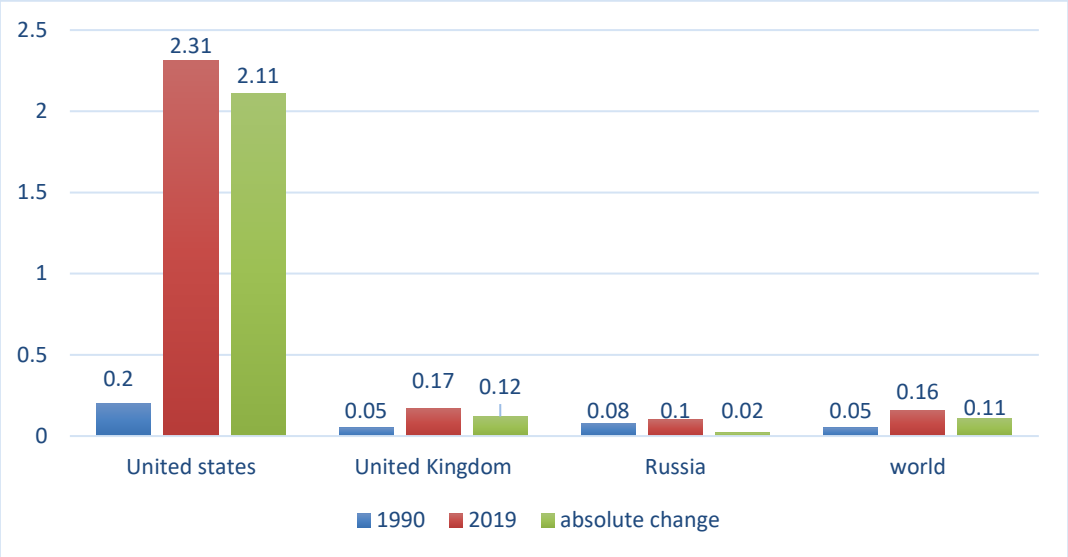

Figure 1: Estimated death rate due to cocaine use disorder during 1990-2019.

stimulant effects of cocaine are offset by the sedative effects of heroin. This can cause a dangerous slowing or cessation of breathing, which can lead to death [50,51]. Chronic cocaine use can cause significant changes in the brain, resulting in reduced sensitivity to natural rewards and increased sensitivity to stress. As a result, the desire for the drug increases and withdrawal symptoms may occur in the absence of the drug. Over time, users may develop a tolerance and require higher or more frequent doses to achieve the same effect. It may also make you more sensitive to the harmful effects of drugs and increase your risk of overdose [52,53].

COCAINE Impact on DEATH RATES

Cocaine use disorder death rate,1990 to 2019. Annual number of estimated deaths due to cocaine use disorders per 100,000 people. Deaths - Cocaine use disorders in both Sex and age-standardized (Rate) deaths per 100,000 people

Table 2: Death rate due to cocaine.

Country	Rate in 2019
Afghanistan	0.06
African Region	0.02
Australia	0.03
Bangladesh	0.01
India	0.03
Pakistan	0.03
Poland	0.02

CONCLUSION

To summarize, an all-encompassing and diverse strategy is necessary to regulate the use of cocaine. It entails raising public awareness, implementing preventive initiatives, enforcing laws and reducing the drug supply, providing treatment and rehabilitation options, employing harm reduction methods, fostering international collaboration, and fostering social support and community involvement. By integrating these approaches and fostering cooperation at local, national, and global levels, we can strive to decrease the prevalence of cocaine use, mitigate its adverse consequences, and offer assistance and avenues for recovery to those struggling with addiction. By working together, we can significantly impact the control of cocaine consumption and foster healthier and safer communities. Cocaine isn't always the direct cause of death. Investigators need to consider other factors before deciding cocaine played a role. This is especially important in high-profile cases or unusual deaths. To understand cocaine's involvement, they should gather as much information as possible, such as the scene, past medical history, autopsy results, and toxicology tests. Finally, investigators should be familiar with the latest research on cocaine and death.

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