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Crack cocaine, a systematic literature review

Abstract

Forensic analyzes that allow the differentiation of crack and cocaine combined with the verification of crack adulterants allow inferences about the implication of this drug in human health, since several studies show that there is a growing number of crack users, which when compared to crack cocaine. Make use of this drug, are exposed to products occurring due to the procurement processes as well as the adulterants placed in the samples. The addition of different substances (adulterants and diluents) in crack (freebase) is a well-known phenomenon in the illicit market. Adulterants may interact with cocaine and determine new toxic syndromes by inferring the clinical state of poisoning, especially in cases where the routes of administration are changed. In Brazil, the analysis of adulterants, contaminants and/or diluents added to crack is not routine in official laboratories. Cocaine is the second most commonly used illicit drug (after marijuana) in the United States.

According to national sense 2003, more than 34 million Americans (14.7%) 12 years of age and older have used cocaine at least once in their lifetime. There are no drugs approved for pharmacotherapeutic substitution (drugs taken chronically as a substitute for drug abuse, such as methadone for heroin addiction). In this context, a bibliographic survey was carried out in original articles, review articles and analysis analyzes obtained from the PubMed database. As inclusion criteria, the association between the terms "cocaine" and "crack" was used. Found 2,642 works related to the theme, being selected 48 scientific papers for the development of the present work, among them, original articles, review articles, journal articles and book chapters, because they have greater relevance to the main objective, i.e. pharmacological approach, mechanism of action, biosynthesis, adverse effects, tolerance, among others, to compose the context of this study.

Keywords: crack, cocaine, systematic review, forensic aspects

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Introduction

Forensic analyzes that allow the differentiation of crack and cocaine combined with the verification of crack adulterants allow inferences about the implication of this drug in human health, since several studies show that there is a growing number of crack users, which when compared to crack cocaine. Make use of this drug, are exposed to products occurring due to the procurement processes as well as the adulterants placed in the samples. Knowledge of these data allows us to predict and even detect possible interactions between the active ingredient, adulterants and solvent residues resulting from the numerous drug procurement processes, guiding improvements in patient emergency and outpatient care and assisting the police intelligence service in traceability. The route of its entry into the national territory, in addition to contributing to the understanding of the problem in the country consequently helps in public policies to control the use of this drug. Cocaine is the second most commonly used illicit drug (after marijuana) in the United States.

According to national sense 2003, more than 34 million Americans (14.7%) 12 years of age and older have used cocaine at least once in their lifetime. There are no drugs approved for pharmacotherapeutic substitution (drugs taken chronically as a substitute for drug abuse, such as methadone for heroin addiction). Treatment for cocaine dependence consists of psychotherapy and the use of antidepressant drugs to alleviate some of the effects of cocaine.[1] The growth of crack use is much more evident in São Paulo than in other Brazilian cities, with significant differences in the prevalence of cocaine in its forms of administration in the various regions of the country,[2] such as the most commonly used form in the District. Federal is the merla, while in Rio de Janeiro hydrochloride cocaine is more widely used by the consumer population. In Brazil, it is observed that cocaine has aroused increasing interest from the media and researchers in recent years. Regarding crack, several researchers have been raising this theme[3–5] Ferri et al.,[2] Sanchez et al.,[6] Cunha et al.[7] Leite et al.,[8,9] and,[10,11] probably due to the increased consumption of this form of drug presentation. Determination of cocaine hydrochloride components illegally traded in the metropolitan region of São Paulo in 1997 showed that cocaine contents ranged from 0.5 to 75%, with the highest percentage ranging from 25 to 60% with an average of 37.5% and prevalence of lidocaine and caffeine as adulterants.

As crack comes from cocaine, these adulterants and eventually some diluents are carried along during the street interconversion process. In addition, there are the remaining products of the extraction process (waste), mainly organic solvents. Ignorance of the composition of street drugs sold as crack is an additional problem in the implications related to its use. This paper aims to contribute to the elucidation of this fact. Cocaine abuse cycles have been occurring worldwide for over one hundred years, thus having a very rich historical origin.[12] The use of the coca plant is known to predate the Inca civilization, but its use is most commonly associated with this empire that encompassed the present-day territory of Peru, Bolivia, Ecuador, and Colombia. The coca plant was carefully cultivated in its own plantations and had a religious significance, determining the political power being one of the prerogatives of the system.[13,14]

The history of crack is directly linked to cocaine, the term crack has been used for over 20 years, this drug is a potent form of cocaine administration that results in fast and remarkable stimulating effect when smoked.[2] In the mid-1980s, more specifically in 1985, there was the advent of crack, a form of cocaine administration that reaches

high blood concentrations in a short period of time, with high abuse potential and higher dependence rates, making complications more severe. Neuropsychiatric and cardiocirculatory disorders, as well as the socio-occupational, economic and legal disorders associated with cocaine use, making the world witness a new phase of its history.[10] The name crack appears to derive from crackling due to the heating of bicarbonate or sodium chloride which are impurities from the extraction process.[15–18]

Material and methods

For the accomplishment of this article, a bibliographic survey was made in original articles, review and kill-analysis obtained in the PubMed database. As inclusion criteria, the association between the terms "cocaine" and "crack" was used. Found 2,642 works related to the theme, being selected 48 scientific papers for the development of this work, among them, original articles, review articles, journal articles and book chapters, because they have greater relevance to the main objective, i.e. pharmacological approach, mechanism of action, biosynthesis, adverse effects, tolerance, among others, to compose the context of this study.

Toxicological aspects

i. Usage patterns and user effects

Crack, as well as cocaine, has the most varied routes of administration, although the most used is the smoked route, due to its high absorption rate. Several authors such as Ferri, et al. report that euphoria occurs ten seconds after inhalation by smoking, with peak plasma concentrations reaching 5 to 10 minutes after use. Similar concentrations are only reached after one hour of intranasal administration of an equivalent dose. There are more recent reports of intravenous use. Users solubilize crack by using a solution of acetic acid (vinegar) or lemon juice and inject it.[17,19–21] Cocaine/crack abuse is associated with numerous physical, psychiatric and social problems. From a toxicological point of view, the determination of the percentage of active ingredient in street drug samples and the qualitative and quantitative identification of the occurrence products formed during the production process, as well as any adulterants and diluents present, are necessary especially in the cases. Intoxication agents seen at the Poison Control Centers (ICC), since sometimes the products that compose it can interfere with the toxicity of the final product.[4,20,21]

The effects of crack on the body occur 10 to 15 seconds after use and include severe tachycardia, increased blood pressure, mydriasis, intense sweating, tremors, severe arousal, feelings of apparent well-being, increased physical and mental capacity, hypophagy and indifference to tiredness, among others (Table 1).

These effects are followed by withdrawal syndrome that can occur in about 15 minutes characterized by symptoms such as physical exhaustion, prostration and deep depression, which leads the user to reuse the drug during this period. The immediate effect of euphoria experienced by the user, along with the stimulation produced, gives the individual a false sensation of increased physical, intellectual and energy capacity. Decreases appetite and the need for sleep, the individual becomes more anxious and sometimes suspects that he is being observed or persecuted.[8,17] Ferri et al.,[2] add that one of the most important aspects of crack use is the size of the associated physical problems. Respiratory tract problems include cough, blackened sputum, chest pain, reduced lung function, impaired expiratory capacity and, in more severe cases, spontaneous pneumothorax and mediastinal emphysema. In the cardiovascular system, increased heart rate and blood pressure and the remarkable vasoconstrictor effect can lead to cardiac arrest. Other effects associated with crack use are muscle necrosis, neurological problems such as seizures and brain hemorrhages, and psychiatric problems such as paranoia, severe depression and panic attacks.

Table 1 Cocaine-related complications and the route of administration chosen

Organs	Intranasal	Inhalation	Intravenous	Another administration ways
Cardiovascular	-	-	Bacterial Endocarditis	Hypertension Arrhythmias Myocardial ischemia Acute myocardial infarction Cardiomyopathies Aortic dissection or rupture
Respiratory	Bronchopneumonia	Bronchopneumonia Pulmonary hemorrhage Pulmonary edema Pneumomediastinum Pneumothorax Asthma Bronchitis Obliterating Bronchiolitis Waste Deposit Strange body Thermal Injuries	Pulmonary Embolism	-
Central nervous system	-	-	Fungal aneurysms	Headache Convulsions Stroke Intracranial hemorrhage Subarachnoid hemorrhage
Digestive tract	Esophagitis	-	-	Mesenteric Ischemia

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Table Continues...

Organs	Intranasal	Inhalation	Intravenous	Another administration ways
Excretory apparatus and metabolic disorders	-	-	-	Acute renal failure secondary to rhabdomyolysis Hyperthermia Hypoglycemia Lactic Acidosis Hypokalemia Hyperkalemia
Eyes ears nose and throat	Nasal septum necrosis Rhinitis Sinusitis Laryngitis	Thermal Injury	-	-
Infectious diseases	-	AIDS * Hepatitis B and C *	AIDS * Hepatitis B and C *	-

(*) Although crack consumption does not present a risk of infection to the user, he/she ends up exposed to STDs/AIDS due to the greater involvement with the exchange of sex to obtain crack. Ellenhorn et al.[22]

Some studies have detected significant neurological changes in children of crack users, such as intrauterine growth retardation, shorter head circumference, tremors, irritability, muscle stiffness, and transient seizures. The compulsive use of crack interferes with the individual dimension of the user, also compromising their social behavior, so that stable and normalized social bonds weaken and break, which eventually marginalize them progressively, both in the microsocial context (e.g. networks for local use) as well as macrosocial (e.g. community and service systems).[10] In Brazil, according to the First Household Survey on Drug Use, conducted by the Brazilian Center for Information on Psychotropic Drugs (CEBRID) in 2004, it was found that 7.2% of males between 25 and 34 years old had already used cocaine, and recent epidemiological data show that cocaine/crack use has been increasing in recent years among middle and high school students, as well as patients seeking care at specialized clinics.[7]

Also, according to CEBRID, its "V National Survey on Psychotropic Drug Use among Elementary and High School Students in the 27 Brazilian Capitals", conducted in 2004, showed that the use of crack in Brazil referred to by use at least once in life, presented higher percentages in the south (1.1%) and southeast (0.8%). The percentage of heavy use, which is defined by daily use, in the 27 Brazilian state capitals was around 0.2% 24. Crack use is a worldwide public health problem, as the user, as reported by Ferri et al.,[2] Sanchez et al.,[6] Cunha et al.,[7,8–21] require individualized care due to dependence, individualized physical treatment due to the numerous related pathologies, both physical and mental of a psychic nature, especially pregnant women who can produce children with serious physical problems, disabling them for normal activities.[10,15,18,20]

ii. Obtainment, properties and presentation forms of the drug

Crack stones are white or yellow or cinnamon and usually weigh between 1 and 5 grams. According to the U.S. Drug Enforcement Agency, crack stones contain 75% to 90% pure cocaine.[1] Crack can be obtained in two ways, the first by dissolving cocaine hydrochloride in water and adding sodium bicarbonate or ammonia solution, heating to boiling for as long as cocaine precipitate occurs-based oil. After this conversion the ice is cooled to solidification and precipitation of the oil, finally collecting the precipitated cocaine base from the bottom of the container, breaking into small stones and drying the light from a strong lamp or in a microwave oven. Thus it is common when analyzing crack to find impurities such as sodium bicarbonate.[22–25] Freebase is a derivative of the Erythroxylon coca plant, like cocaine, but freebase comes in a free base form. It can be obtained by two methods being the first from the cocaine refining residue or from the raw material (unrefined paste) used for the production of cocaine mixed with water and sodium or ammonium bicarbonate, by this process promoting a lowering at the melting point and can thus be smoked.[26,27]

The second proposed method for free base production, also called freebase, starts from the same principle as the previous method, with the addition of water to cocaine hydrochloride until dissolution and subsequent addition of sodium or ammonia bicarbonate and stirring is then added. Ether and further stirring is performed, providing a liquid-liquid extraction, in the next step phase separation occurs between ether and water. Only the etheric portion is used, which upon evaporation results in purified cocaine called freebase.[26,27] Therefore, crack and freebase are distinct forms of base cocaine, crack should be less pure than freebase, due to the conversion of crack from street-based cocaine and freebase from base paste of first leaf alkaloid extraction. Coca Base paste, cocaine base, crack and merla are forms of presentation of free base cocaine, with different physical characteristics and composition.[28–30] Base paste is the first product obtained from the extraction of coca leaves. Contrary to the name, it usually does not appear in seizures in Brazil in a pasty form, but in powder and lumps due to the evaporation of solvents. Transport preparation, which often involves pressing the material, can produce larger stones, allowing (on preliminary analysis) confusion with the crack presentation form.

In base paste it is observed in gas chromatography that the content of the unsaturated alkaloids of cis and trans-cinnamoyl cocaine is very significant (DEA studies consider base paste to be>5% cis / trans cinnamoyl cocaine in relation to cocaine).[10,28–30] The base cocaine is the refined base paste, that is, which underwent additional oxidation and washing processes (with potassium permanganate and ethanol, for example), which significantly removed cis and trans-cinnamoyl cocaine alkaloids from the obtained material. It is often presented as whiter dust and lumps than the base paste.[10,28–30] Since the differentiation between base paste and base cocaine can only be done by GC quantification, the broader definition of free base form cocaine should be chosen in the characterization of samples of this nature.[10,28–30] Crack is also cocaine free base in the form of stones, whitish, ivory or yellowish, intended to be smoked. Its manufacture involves a heating step, where the base cocaine is mixed and fused with sodium bicarbonate and, when cooled, solidifies to form stones. Contrary to the current idea, crack is not a refining by-product, but a form of presentation of cocaine prepared especially for exclusive

consumer markets and which often contains residues of sodium salts (bicarbonate, sulfate and carbonate) in its entirety constitution.

The definition of the crack presentation form depends on the characteristic of the sample's molten stone, which does not easily crumble (such as base paste or base cocaine) and breaks (with difficulty) with well-defined cleavage plans.[10,28–30] Merla comes in the form of a wet white paste containing free base cocaine, high water content (up to 70%) and sodium salts (sulfate, carbonate, bicarbonate). The high moisture content provides high decomposition rate of free base cocaine, forming mostly benzoyl ecgonine in short time (days). Merla is a form of presentation found in Brazil, more specifically in the Federal District and surrounding areas, and is also intended for smoking by mixing the paste with tobacco or marijuana. Therefore, even cocaine-free base being resistant to thermal degradation and having lipid solubility46 can form products as a result during its synthesis.

iii. Adulteration

Regarding the illicit form, to increase profits, traffickers have tampered with or diluted the drug with other compounds, either inert or active substances, making up the "street drug".[10,31,32] Crack has a lower degree of purity than freebase because it carries cocaine hydrochloride adulterants, as well as resulting products and surplus from the extraction process, so that its purity percentage is reduced to 40% 10 The process of obtaining freebase involves a purification process prior to the formation of the final product which in fact makes it purer than crack. Street drugs can generally be marketed almost pure, adulterated, diluted or contaminated.[4,32–41] It is well known that tampering is generally a widespread phenomenon in illicit drug market. The obvious purpose is to increase the amount of the final product, which involves mixing various substances. According to Chasin[11] cocaine in its hydrochloride form is the most frequently and widely adulterated and diluted form today.

Since cocaine hydrochloride is a raw material for crack production, it can be assumed that crack cocaine also presents products occurring during the production process, adulterants and diluents in its composition. Cocaine is generally distributed as a white crystalline powder as a raw material. Powder, usually cocaine hydrochloride, is often diluted with a variety of substances, the most common being sugars such as lactose, inositol, and mannitol and local anesthetics such as lidocaine. Tampering increases, the volume and thus multiplies profits. Cocaine hydrochloride is usually clogged or dissolved in water and injected. Rarely smoked as it is labile term destroyed by high temperatures. Oliveira[10] reports that the cocaine present in the streets is presented as white powder, is usually added with other white inert compounds to increase the volume. These compounds are represented by diluents, such as talc, flour, sugars and salts. as sodium bicarbonate and magnesium sulfate.

Adulterants are active drugs, such as local anesthetics (procaine, benzocaine, lidocaine or tetracaine) or low cost stimulants (adrenaline), which may potentiate the sympathomimetic effects of cocaine, increasing the risk of toxicity associated with use. This becomes relevant. Since white powder cocaine can be used to make crack. Identification of products occurring during the procurement processes, adulterants and diluents present in illicit drug samples, as well as their purity content, may provide information, sometimes useful for investigations into their trafficking. Such conduct may also help to establish a common source of seizures.[4] According to Chiarotti and Jesus the analysis of solvent residues in illicit cocaine (hydrochloride as well as freebase) has been proposed as a strategic aid and tactical intelligence. Periodically provided information on the type of solvents used during the clandestine drug preparation process is important for controlling the availability of these solvents. However, solvent residue identification is considered a tool for police investigation, comparing with different types of samples.

iv. Crack burning process

Cocaine (COC) in the form of crack when smoked forms the methylyroecgonine ester (EMA) as a pyrolysis product. The EMA in the body is converted to anhydroecgonine (AE). These substances when present in the urine allow us to differentiate the use of cocaine-COC, in this case, showing the use of crack.[3,42] Volatilization and pyrolysis of COC from its basic form is thermo-dependent, i.e. as temperature increases, EMA production increases and COC decreases. In crack pyrolysis the amount of COC is approximately 68 to 77% at 230ºC and about 30% at 255ºC.[43] Casale[39] reports that some solvents promote COC degradation, such as diethylether-enriched peroxide promotes COC degradation by converting it to norcocaine, methanol promotes methylation to carboxylic acids and ethanol promotes epimerization or transesterification of ester groups. Ethyl anhydroecgonine ester-EEA may be formed by cocaine pyrolysis due to the transesterification reaction. In addition to EMA formation, COC degradation can result in the formation of methylecgonine ester (EME) and ecgnonin.

v. Legal aspects

At the international level, the control of psychotropic drugs is done through treaties, agreements or conventions carried out by UN member countries.[44–47] The Shanghai Conference (1909) was the first international attempt by 13 countries to address the Opium problem in India. In 1911 there was the International Opium Conference which resulted in the International Opium Conversion in 1912, which was the first to regulate production. morphine, heroin, and cocaine, but World War I undermined the Opium Convention, which only came into force in 1921 with the creation of the Advisory Commission on Opium and Other Harmful Drugs, succeeded by the United Nations Commission on Drugs and Narcotic Drugs (CND) Narcotic Drugs). In 1924 there was the Geneva Convention in which the concept of narcotic substance was expanded and the system of control of international trafficking was established by means of import certificates and export authorization. In 1925 the Geneva agreement took place, being revised in 1931 and 1936 establishing the obligation of participating states to take steps to prohibit the spread of psychotropic drug use at the national level.[47]

In 1938, Decree No. 891 was issued which dealt with narcotics control and criminalized the use, trafficking, possession and production of opium and its derivatives, cocaine and its derivatives, and Cannabis sativa (marijuana). However, repressive control in Brazil should not be neglected under the influence of the international conventions previously presented.[47] The Penal Code of 1940 in its art. 281 provided for a sentence of imprisonment of one to five years and a fine in case of trade, possession or delivery to the consumption of narcotic or substance that determined physical or mental dependence. This article was amended in 1964 by Law 4,451, which updated the amount of the fine, and the main change was the inclusion of the act of planting narcotic substance in the description of the typical fact.[47] Later, after several protocol updates and UN signing, in 1961 New

York's unique conversion to narcotics was signed, consisting of 51 articles where narcotics are listed and classified according to their properties into four lists. Control, inspection and competent measures were also established.

Also, this convention dealt with the measures that should be taken at the national level for effective action against illicit trafficking, providing the state with reciprocal assistance in coordinated struggle, providing that international cooperation commenting that all willful forms of trafficking, production, possession, etc., of narcotics in disagreement with it, were punished accordingly; drug treatment was recommended for drug addicts and conditions were created for their rehabilitation.[47] In 1968, Decree-Law No. 385 makes a new amendment to Article 281 of the Penal Code and describes as typical fact, beyond that described in previous laws, the act of preparing and producing. Adds the text: "brings with it, for its own use, narcotic substance, raw materials, plants for the preparation of narcotics or substances that determine physical or mental dependence" we can observe that this change in law reflects the evolution in technology related to consumption and drug trafficking, when quoting "preparing and producing" and emphasizing the repressive nature of consumption, "brings with it for its own use".[47] In 1971, in Vienna, the issue of drugs was again discussed, resulting in the Convention on Psychotropic Substances that dealt with control, use and trade.

This convention was concluded in 1988 and is now called the Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances. It came into force in 1990 and was added as controlled substances ethyl ether and acetone, which can be used as psychotropic drugs as well as can be used in the preparation of other drugs, is also published the law number 5.726, which brings innovations of include preventive measures involving society in the fight against narcotics trafficking through the prevention and collaboration of legal entities in the fight against the punishment and loss of state aid and subsidies. In 1976, Law No. 6,368 was published, which repealed the previous one and hardened the related penalty.[47] Thus, the crimes related to law 6.368/76, which provides for measures to prevent and repress illicit trafficking and misuse of narcotic substances or that determine "physical or mental" dependence, the materialization of the crime now consists in proving that the material involved is or is not a substance listed in the list of proscribed.[47]

Thus, all compounds suspected to contain cocaine alkaloid are submitted for toxicology or specialized laboratory testing. §3 Offer drug, eventually and without profit purpose, the person of their relationship, to consume together: Penalty - detention, from 6 (six) months to 1 (one) year and payment of 700 (seven hundred) to 1,500 (thousand and five hundred) fine-days, without prejudice to the penalties provided for in art. 28. Article 28, Paragraph 1 of Law 11,343/06 states:

Paragraph 1; The same measures shall apply to those who, for their personal consumption, sow, cultivate or harvest plants for the preparation of a small amount (if skill is required) of a substance or product capable of causing physical or mental dependence. With this, we can note that Law 11.343/06 is a less restrictive norm in some respects in relation to Law 6.368/76, showing that society is adopting a more humane view on the use of drugs of abuse, by virtue of legislation in effect differentiate user from trafficker and cite treatment and rehabilitation of the user. Brazil seems to be heading in the same direction as some countries in relation to the legalization of some types of substances considered to be substances outlawed in the current legislation due to this openness and humanization of the legislation.

Analytical Aspects

Available methods for cocaine identification and quantification

Colorimetric reactions are quite common in the characterization of street drugs. A widely used test is the Scott Test. It consists of three steps involving the addition of certain reagents and the observation of reactions that occur through color change. The reagents used are in the order of addition: cobalt thiocyanate solution dissolved in water; concentrated hydrochloric acid and; chloroform. For a test tube containing cocaine powder, the reactions are as follows: In the first step, cobalt thiocyanate is added to the container and a blue precipitation will be the immediate reaction. In the second step, hydrochloric acid is added over the same container as the first step and the blue precipitation disappears completely. In the third step, chloroform is added to the test tube and precipitation reappears, however, this time at the bottom of the tube, unlike the first step.[44] Several instrumental techniques can be used individually or together for the characterization of drugs of abuse such as GC, high performance liquid chromatography (HPLC), 1H and 11C nuclear magnetic resonance spectroscopy (MRI), inductively coupled plasma mass spectrometry (ICP-MS), atomic absorption spectroscopy (AAS), infrared (IR) absorption spectroscopy, etc.

The choice will depend on the type of information you wish to obtain. For example, for trace element analysis, EAA and ICP-MS, preferably GC and HPLC for organic substances, although none of these instruments, except for IV equipment, can distinguish salt-based cocaine from cocaine in free base form.[45,48] However, it can be said that the technique that provides the largest number of simultaneous information according to studies involving drug characterization is the CG, being the main technique currently employed by professionals from the US Drug Enforcement (STRL-DEA) Administration's) in works of this kind. Depending on the availability of certain accessories (detectors and samplers), it allows to detect with excellent resolution and reproducibility small amounts of substances in the order of picograms (10-12 g), even if they are in the form of complex mixtures, thus allowing to identify and quantify in a single analysis various components (including natural impurities, adulterants and many diluents) and traces of solvents (contaminants) present in a given cocaine sample. In general, data on these types of compounds are already sufficient to make any comparisons.[45,48]

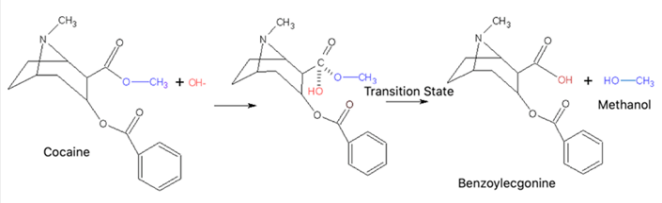

Figure 1 Alkaline hydrolysis reaction of cocaine in crack synthesis.

Final considerations

Given the problem presented in the introduction and generalities that crack represents an important and growing social problem and constitutes a differentiated drug with regard to toxicity and impact on society, this study, which aims to characterize crack, is justified in The premise is that only knowledge of the characteristics of the drug will allow a better understanding of how it acts on the dynamics of use and its consequences aimed at reducing the public health problem and enabling policies related to the prevention of drug damage.

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The classification of cocaine derivatives is a fundamental tool for minimizing health problems related to the abuse of these drugs, as it is not only cocaine that can cause physical or psychosocial problems. Adulterants and contaminants thereof can lead to costly conditions for the state and the user's family. Additionally, this classification may contribute to the control strategies imposed by the competent authorities.

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Conflicts of interest

The author declares that there are no conflicts of interest.

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