

Research Article

Quality analysis of Iranian crack referred to Forensic Department of Khuzestan to determine substances affecting dementia

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ABSTRACT

Pharmaceutical drug abuse refers to conscious consumption of drugs for non-medical purposes such as changing the mood, and fitness, etc. Iranian crack (street crack) is one of the most abused drugs in Iran. This crack has different medicinal compounds, synthetic, adulterants that have pharmacological structure. Determining type and amount of compounds of Iranian crack and its impact on individuals' performance, creation of dementia and abnormal behavior, and crime rate are considered as objectives of this study. In this cross-sectional study, 61 crack samples were analyzed in forensic toxicology laboratory of Khuzestan. Samples were evaluated using thin layer chromatography (TLC). Verification tests and identification of pharmaceutical substances were performed qualitatively by HPLC and GC / MS methods. Statistical examination of data by SPSS (V22) (p value <0.05) indicated that 93.4% of crack samples contained morphine, 83.6% of them contained caffeine, nescapine and dextromethorphan, 27.9% of them contained heroin and codeine, 37.7% of them contained monoacetyl morphine, 34.4% of them contained acetyl codeine, and 13.1% of them contained narceine and acetaminophen. Other compounds included methyl amphetamines, diphenhydramine, lidocaine, thebaine, amoxicillin, amitriptyline, and nortriptyline. In addition, 6.6% of samples were combination of methyl amphetamine, diphenhydramine and acetaminophen, playing an important role in dementia and mental illness similar to schizophrenia due to presence of amphetamine. Iranian crack not only differs from real crack (cocaine), but also they differ in terms of variety and amount of adulterants, opioid, and diluent substances. In fact, crack has different amounts of substances affecting central nervous system, and other drugs and substances play important role with their pharmacological and non-pharmacological properties in this regard.

Key words: Forensic Toxicology, psychotropic, Iranian crack, GC-MS, HPLC, dementia

INTRODUCTION

The term "drug abuse" is defined differently in different societies and cultures. The term drug abuse is different from drug misuse. Drug abuse refers to any deliberate and conscious use of drugs for non-medical purposes, including changing the

mood, and fitness (1). Drug abuse leads to mental and physical disorders and detrimental social, cultural, and economic consequences. It also threatens individual and public health. Dementia is associated with personality changes, disorder in

memory, judgment, and thinking in medical or psychiatric areas and chronic and sometimes acute mental processes due to organic disease of the brain. The most common type of dementia is senile dementia or Alzheimer. Other causes of dementia include stroke and delirium caused by the toxic effects of drugs and psychotropic substances in the body and uncommon but known diseases such as mad cow. By definition, dementia is the progressive destruction of cognitive functions occurring in the full consciousness (without delirium depending on the type of its cause). Dementia appears by symptoms and a set of bad clinical functions, including memory disorder, language and psychiatric disorder, and impaired daily activities (2). In this study, we tried to identify the crack and to examine the effects of this substance in dementia

Cocaine

The history of cocaine use backs to thousands years ago, when the inhabitants of South America were using coca leaves due to its joyous and breezy effect. This substance was giving them more energy, and they were rarely feeling tiredness and hunger (3). They believed that coca is "gift of God". Coca is native plant for some South American countries such as Colombia, Bolivia and Peru. Some group of people living in South America chew coca leaves by putting the between cheek and gum, as tobacco. In another method, coca leaves are shaped as paste and they are used as cigarette after drying. When dry leaves of coca are combined with a strong hydrochloric acid, they become concentrated, pure and more effective hydrochloride. Since that time, this form of cocaine that is more concentrated and more compact than coca leaves is smuggled in various countries. Cocaine hydrochloride is primary substance of cocaine dust that is white and is very similar to sugar or baking soda. Cocaine hydrochloride is usually sniffed by short tube or narrow straw through the nose. In the 1980s, chemists and producers extracted the cocaine hydrochloride by condensing method and obtained 100% pure cocaine. When risks of condensed

cocaine was identified, crack of cocaine was replaced immediately. Crack is crystal form of cocaine produced by adding baking soda and water to hydrochloride and drying it. There is misconception among people that crack is condensed cocaine, while chemical form of crack is completely different from condensed cocaine. Crack seems to be milky small stones or pebbles. It is known rock that is usually distributed in small plastic bags or small jars. The difference between this type of cocaine and primary cocaine relates to presence of added and smokable chemicals. The main psychoactive substance isolated from coca leaf was named "Erythroxyton ". In 1860, chemist, Albert Niemann, isolated it with 100% purity and called it "cocaine". Only 1.0 to 0.9 % of coca leaves weight includes cocaine. By identifying and extracting the major driving substance from coca leaves and combining it with cocaine-containing beverages and soft drinks such as Coca-Cola, this substance was introduced to world markets. Medicinal use of cocaine was discovered in the nineteenth century. At the time, some group of people found that cocaine acts as a strong anesthetic (or anesthesia) agent that can be used in local anesthetics in different surgeries such as surgery of ear, nose, eye, and throat. Cocaine was used to relieve toothache. As cocaine narrows lumen of blood vessels, it is used sometimes to control bleeding and healing heart diseases, including irregular heartbeats. German soldiers were given cocaine in World War II so that their strength in physical activities and military maneuvers to be increased. In 1912, America's government announced 5,000 deaths resulting from cocaine use. Finally, "Harrison Narcotics Act" was passed in 1914. Following Harrison Act enforcement, recreational use of cocaine and drugs such as heroin was diverted to the underground black markets.

Crack

Crack was introduced to New York market for the first time in the late summer and early fall of 1985. By chemical reactions, cocaine is freebased (1). This means that cocaine converts

hydrochloride to pure cocaine. This pure cocaine is resistant to heat and it can also be used through smoking. This substance is called crack. The substance introduced as crack in Iran since 2005 is a new substance that has no similarity to crack obtained from cocaine. Symptoms of its users are similar to heroin not cocaine. The appearance of this substance is usually similar to clod. It also cream color with villus similar to cotton candy. It is also very similar to the pieces of curd. It is also small and light. In recent years, this new substance introduced into the Iranian market has caused that new substance to be introduced for many users when they refer to drug dealers to take heroin or opium. This new substance operates quickly, it is easier to use, it could be hidden easily, and more importantly, it is cheap. This new substance is called crack.

Street Crack

According to studies conducted on street crack referred to forensic toxicology laboratories of Iran, Iranian crack contains high percentage of heroin and narcotic pills and other adulterants. These adulterants are among the substances affecting central nervous system (benzodiazepines, barbiturates, etc.) or substances increasing the size (starch, talc). Large number of toxicology laboratory investigations have focused on identifying the compounds of crack obtained from defendants by the judicial and law enforcement authorities. Specifying the existing components in crack samples and obtaining relative frequency of them can be helpful in adopting appropriate therapeutic protocols in dealing with patient poisoned with these substances and relevant judicial and security issues. In reference books on street cocaine names, the name of crack is not seen. Based on books and articles on crack, street name of cocaine is seen. (4) Appellation of crack is due to breaking as result of heating this kind of cocaine. Crack or rock is in fact solid form of cocaine that can be used by smoking and sniffing (5). Crack can be used easily and quickly so that it can be used even by one lighter at any place. Therefore,

the crack has been called as 1, 2, and 3 since it can be used by counting three numbers. It also leaves no certain smell. These cases are considered advantages of this substance compared to other drugs. However, the clinical effects and complications after crack use are very severe and terrifying.

It seems that compounds used in producing crack available in the Iran market have no fixed formula and its producers use various substances. Heroin is usually considered as the base and primary substance in all of them. Iranian crack is more dangerous than American crack due to the abundance of impurities. Generally, adulterants are mainly substances with medicinal or pharmacological properties added to heroin in order to change its pharmacologic effects. Some of these compounds are acetaminophen, dextromethorphan, antihistamines, anti-depressants, three-ring benzodiazepines, barbiturates, central nervous system stimulants such as caffeine. Alkaloids of opium as source of morphine are used to produce heroin. Other byproducts such as acetyl codeine (resulted from acetylation of codeine available in opium, papaverine, noscapine and other opium alkaloids) are found in heroin. The diluents are substances such as starch or sugar added merely for increasing the size or weight of this illegal substance. Adulterants can be added to heroin during the production, before or after the smuggling.

Due to major differences in structure of the Iranian crack and cracks known in other points of world, it seems to be necessary to conduct a study examining the compounds of cracks referred to forensic toxicology laboratory. The results of this study are also valuable in guiding physicians working in addiction treatment centers to adopt appropriate treatment protocol considering nonspecific clinical signs and symptoms. In space where crack is used, special bitter smell can be felt, indicating the presence of heroin. Some crack users say that special pickle smell can be felt for a long time that can be due to presence of

ammonia. Some others say that strong acidic compounds recently used in producing drainage channels cleaners such as (pouch) are also used in the production of crack. Others believe that hallucinogenic substances like methamphetamine are also used in production of crocks.

Crack clinical consequences and symptoms:

Apart from the effects on the brain, cocaine and crack cause the most cardiovascular problems such as heart and blood vessels problems. In fact, they cause tachycardia by releasing adrenalin (30). Another neurological problem caused by cocaine is seizure or convulsion in which muscles of some parts of the body contract involuntarily, leading that person to lose his motor control and to fall into ground as stroke disease patient. Another cocaine harmful effect on the nervous system is motor disorders (in medical science, it is known as aphasia) (6). In addition, abnormal movements caused by continuous use of cocaine are known as "crack dancing". People who sniff cocaine regularly experience inflammation in the nasal passages (rhinitis) and corrosion of cartilage separating the nostrils (6). On the other hand, crack leaves other symptoms. For example, crack eye refers to ulcer or inflammation of retina caused by repeated exposure of the eyes to smoke produced from the crack. These vulnerable areas are prone to bacteria or virus infection (6). In scientific and research meeting held under title of "investigating the crack substance" in cultural complex of Shagayegh, Doctor Ali Farhoudian said: all over the world, crack is the name of free form of alkaloid cocaine. In Iran, clinical symptoms of using crack and symptoms of deprivation in the course of treatment in patients indicate that the crack in the Iran's market is different from crack of other countries, where it is a form of cocaine (6).

Generally, the complications of crack and cocaine are stranger due to high concentrations of substances and various chemicals. Mortality rate is high among their users. As result of excessive use, especially crack and cocaine, clinical symptoms increase and person experiences

consciousness disturbance, pain in the chest, nausea, muscle spasms, and seizures and eventually death (6). However, complications and clinical symptoms of Iranian crack and cocaine crack are different. The effects of using crack remain up to 8 hours after using it. If it is not used, side effects such as lethargy and depression prevent the treatment process. It is associated with nausea and vomiting, reduced pain, feeling hot, hot flashes, nasal itching, heaviness in arms and legs and lethargy, dry mouth, oral cancer, lower blood pressure, contraction of the pupil, contraction in smooth muscles and biliary tract, effect on blood platelets, and weakened white blood cells. Long-term complications of using crack include darkened skin, decreased sexual desire, infertility, weight loss and malnutrition, multiple wounds in the body and delay in healing, aging, dementia, mental illness similar to schizophrenia including hearing and visual hallucinations, cynicism, and aggression, behavioral or psychological changes (initially euphoric and then apathy, irritability and aggressiveness, restlessness and impaired judgment) and, ultimately, dementia that manifests as a set of bad clinical symptoms including disorders in memory, language disorders, psychiatric and psychological changes, and impaired daily activities. Intravenous injection side effects, abscesses, skin infections, endocarditis, tetanus, AIDS, hepatitis B and transferring them to other people are different clinical symptoms and side effects, making it necessary to adopt an appropriate treatment protocol in dealing with drug abusers and poisoning with this malicious substance.

Method of examination

This cross sectional study was conducted for six months on all crack samples referred to forensic toxicology laboratories of Khuzestan during 2012-2013. All samples were evaluated at explosive laboratory of toxicology sector, in terms of physical properties such as color, shape and weight. To carry out the test, samples were initially examined and evaluated using thin layer

chromatography (TLC). Approximately 0.1 to 0.01 g (depending on the amount of sample available) of sample was solved in 10 cc of methanol 99%. Then, samples were centrifuged for 10 minutes in a centrifuge at 13000 rpm per minute to remove impurities of centrifuge. After centrifuge, the supernatant of test tube was used to perform TLC. Each of plates contained unknown crack samples with pharmaceutical standards in the laboratory (opium, heroin, etc.). In order to do screening test, two solvent systems were used. Tank solvents are placed at solvent tank with mentioned ratios. After rising the stains in the tank and isolating stain compounds, plates were removed from solvent tank and they were prepared by iodine and acidic platinum for painting. It is noted that the plates should be completely dried with iodine and acidic platinum before painting. After preparing the spray solution, plates were sprayed lightly with iodine and acidic platinum in the space under the hood so that stains appear. After acidification for approximately 2 to 3 hours (depending on volatility and percentage of solvents used in the mobile phase), in the case of observing the stain on plate, the result of screening test was considered positive on the plate, and was approved as more sensitive test, such as HPLC and GC / MS.

HPLC Method:

Column: Eruospher 100-5 C18 -250× 4/6mm with precolumn

Injeatiou volume: 20ml

Flow rate: 1ml/min

Staitionary phase: Methanol merk (Germany) / Dilution water (0.20×0.80)

Mobile phase:

AcetouitrileMerk (Germany) / phosphat buffer ph= 2/3 mixtures (0.63×0.37)

Agilent

GC Method: GC: 7890A

Column: HP5-MS30mx0.25 mmx0.25□□

Injection type: Splitless

Injection volume:0.2□□

Oven Temperature: 60°C

Ramp 1:20°C/min up to 300°C

Inlet Temperature:250°C

Carrier Gas Flow: Helium 1.5 ml/min

MS Method: MS: 5975 C

Source Temperature: 230°C

Quardrapole Temperature: 150°C

Mode of Scan: Full Scan

All data related to files will be kept secretly in laboratory sectors. The information was evaluated and analyzed statistically during the 6 months. The method of calculating sample size and their number:

A cross-sectional study was conducted during two years and all crack samples were analyzed at this time. After completion of the project, total 61 samples were analyzed. Information of 61 files was extracted from databases belonged to years 2012-2013. In the present study, street cracks referred to forensic toxicology laboratory of Khuzestan were analyzed qualitatively. In the laboratory, 61 cracks were analyzed. In terms of appearance, 52 (85.2%) of samples were clod-shaped and their color was cream, and 9 (14.8%) of samples were brown powder. In examining the weight of samples, we realized that the minimum weight of samples was 0.2 g, the maximum weight of samples was 5.55 g, and mean weight of samples was 0.99 g. Out of the total samples, weight of 36 (59%) samples was less than 1g, weight of 14 (23%) samples was between 1 and 3 g, and weight of 11 (18%) samples was higher than 3 g.

After qualitative analyzing of data by HPLC method, the following results were obtained:

Out of total referred cracks, 55 (93.4%) of samples had caffeine, 50 (83.6%) of them had noscapine or dextromethorphan, 10 (16.4%) of them had diazepam, 8 (13.1%) of them had acetaminophen and narceine, and 4 (6.6%) of them had diphenhydramine and methyl amphetamines. Other compounds of referred cracks included phenobarbital, thebaine, lidocaine, amoxicillin, amitriptyline, and nortriptyline.

After qualitative analyzing of data by GC_MASS method, the following results were obtained. Out

of total referred cracks, 57 of (93.4%) them had morphine, noscapine and dextromethorphan, 23 (73.7%) of them had 6-mono acetyl morphine, 21 (34.4%) of them had acetyl codeine, 17 (27.9%) of them had heroin and codeine, 10 (16.4%) of them had diazepam, and 4 (6.6%) of the had diphenhydramine and methyl amphetamines. In examining the relationship between weight and compounds of cracks referred to Khuzestan Forensic, the following results were obtained.

Out of 36 cracks weighted less than 1 g, almost all of them (100%) had acetyl codeine, heroin, dextromethorphan, and chloramphenicol. Considering $p(v) < 0.05$, this relationship became significant.

Out of 14 (22.9%) samples weighted between 1 to 3 g, all of them (100%) had noscapine, but none of them (0%) had morphine. $P(v) = 0$

Out of 11 (18%) samples referred to Khuzestan Forensic weighted higher than 3g, 7 (6.36%) samples had mono-acetyl morphine, codeine steel, heroin, dextromethorphan, and diazepam. $P(v) < 0.05$.

In fact, samples that were too heavy and too light contained heroin. In examining the relationship between appearance and compounds of cracks referred to Khuzestan Forensic, the following results were obtained.

Out of 9 (14.9%) street cracks that were in the form of brown powder, none of them had codeine that this relationship became significant with $p v = 0.04$. In addition, half of samples had acetaminophen that this relationship became significant with $p v = 0.03$.

Table 1: Frequency of effective substances and pharmaceutical categories in cracks referred to the Khuzestan Forensic using HPLC

Effective substance	pharmaceutical category	Number of referred cracks	Frequency of referred cracks
Caffeine	Opium alkaloids	57	93/40%
Noscapine	Opium alkaloids	50	82%
Narceine	Opium alkaloids	8	13/10%
Dextromethorphan	non-opioid anti-cough	50	82%
Chloramphenicol	antihistamine	6	9/80%
Diphenhydramine	antihistamine	4	6/60%
diazepam	antihistamine	10	16/40%
Methyl amphetamine	Amphetamines	4	6/60%
Acetaminophen	Lenitive	10	16/40%
Amoxicillin	Antibiotics	1	1/60%
Amitriptyline	Tricyclic antidepressants	2	3/25%
Nortriptyline	Tricyclic antidepressants	2	3/25%
Lidocaine	Local mucosal anesthesia	2	3/25%
Phenobarbital	Barbiturates	1	1/60%
Thebaine	Opium alkaloids	2	3/25%

Total		206	
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Table 2: frequency of effective substances and pharmaceutical categories in cracks referred to the Khuzestan Forensic using GC-MASS method

Active substance	pharmaceutical category	Number of referred cracks	Frequency of referred cracks
Morphine	Opium alkaloids	57	93/40%
Codeine	Opium alkaloids	17	27/90%
Caffeine	Opium alkaloids	57	93/40%
Noscapine	Opium alkaloids	50	82%
Dextromethorphan	non -opium anti-cough	50	82%
6 monoacetylphloroglucinol morphine	Acetylated derivative of opium alkaloids	23	37/70%
Acetyl codeine	Acetylated derivative of opium alkaloids	21	34/40%
heroin	Acetylated derivative of opium alkaloids	17	27/90%
Chloramphenicol	antihistamine	6	9/80%
Diphenhydramine	antihistamine	4	6/60%
Diazepam	Benzodiazepines	10	16/40%
Methyl amphetamine	Amphetamines	4	6/60%
Lidocaine	Local mucosal anesthesia	2	3/25%
Phenobarbital	Barbiturates	1	1/60%
Thebaine	Opium Alkaloid	2	3/25%
Total		264	

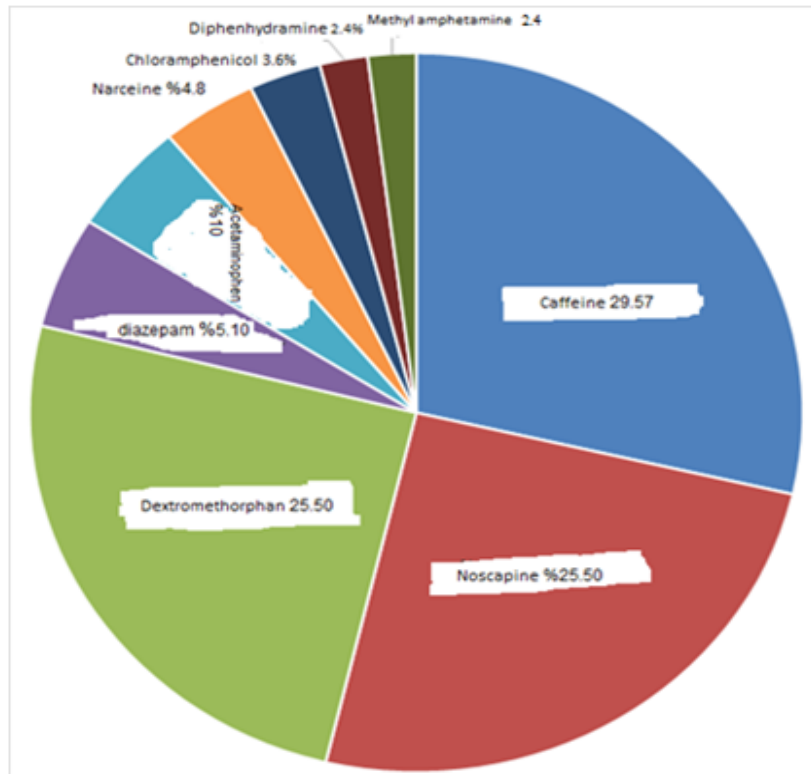


Chart 1: Frequency of effective substances and pharmaceutical categories in cracks referred to the Khuzestan Forensic using HPLC

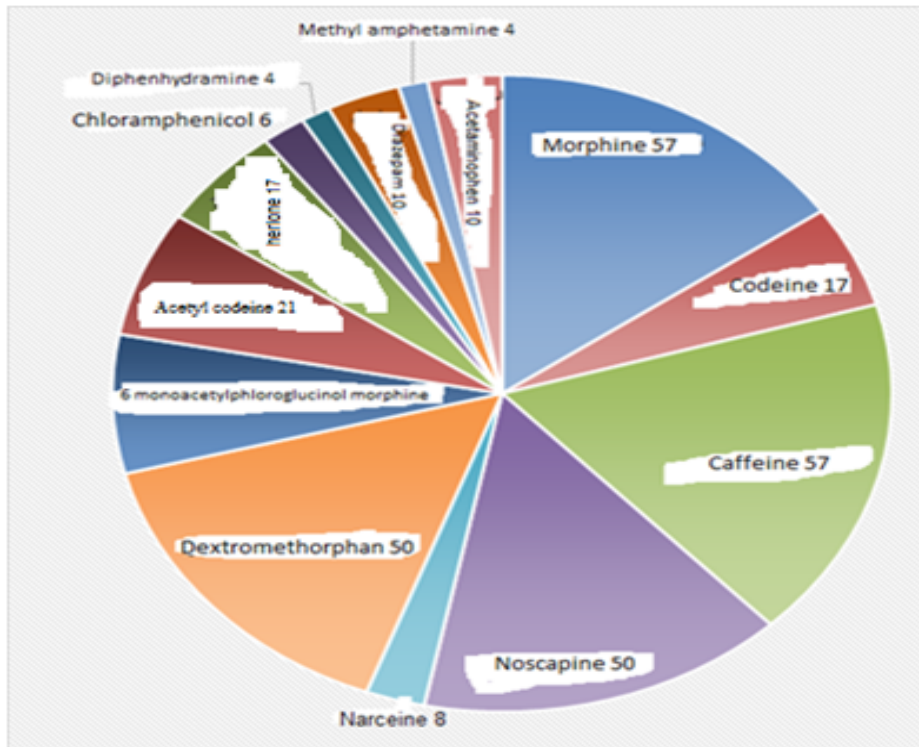


Chart 2: frequency of effective substances and pharmaceutical categories in cracks referred to the Khuzestan Forensic using GC-MASS method

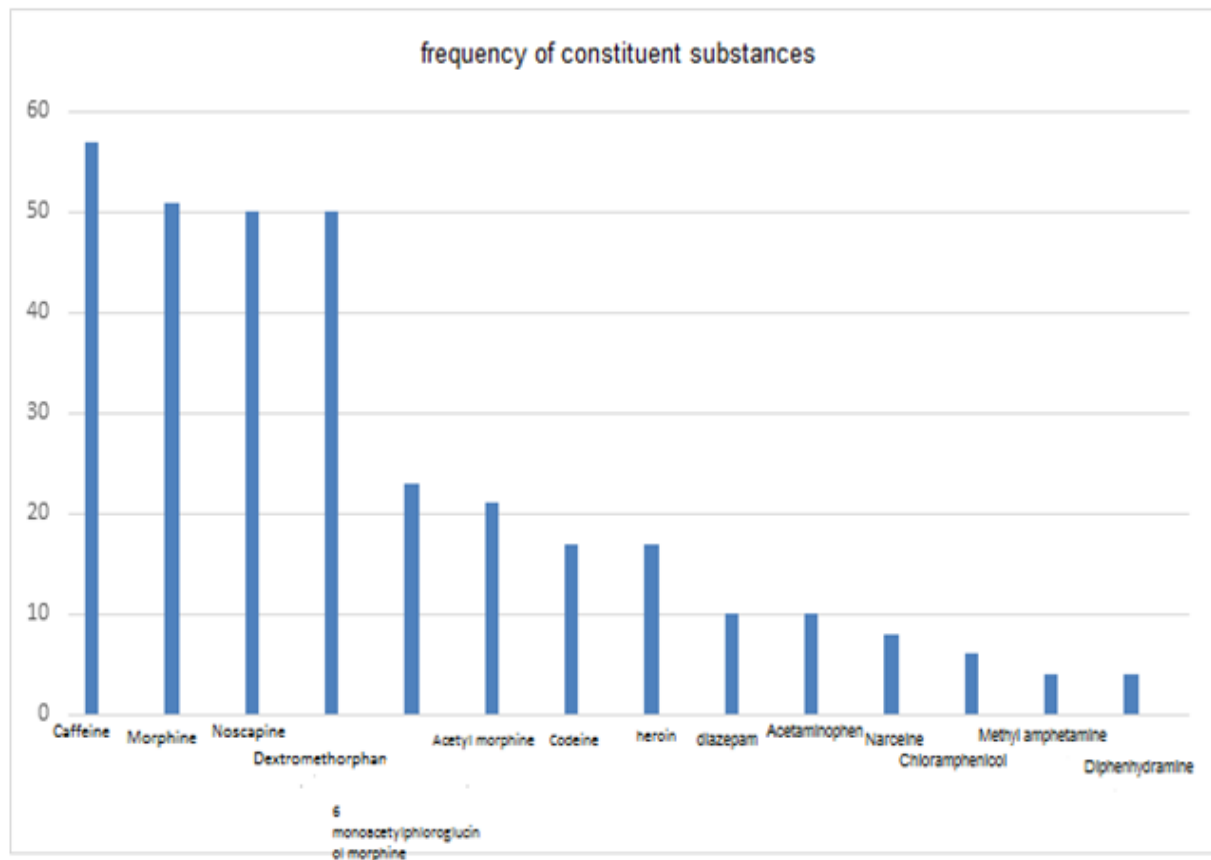


Figure 3: The frequency of compounds of referred cracks

In this study conducted on 61 samples referred to the Forensic Department of Khuzestan, we found that compounds of street cracks included caffeine, morphine, noscapine, dextromethorphan, 6-mono acetyl morphine, acetyl codeine, heroin, codeine, narceine, diazepam, acetaminophen, diphenhydramine, methamphetamine, papaverine, thebaine, lidocaine, chloramphenicol, phenobarbital, amitriptyline, nortriptyline, and amoxicillin. In our country, some studies have been conducted in this regard, including a study conducted by Dr. Jokar and Akhgari et al on 80 street crack samples referred to Forensic Department of Tehran and a study conducted by Dr. Ali Farhoudian et al on 18 street crack samples. After comparing the research data and results of the current study, we observed differences and similarities in this regard. In three

studies conducted in this regard, cocaine was found in none of the street crack samples, indicating significant difference between street crack and real crack found in the world where cocaine is its main substance. Amphetamine and diphenhydramine found at amount of 6.6 in referred crack samples were not found in none of the samples of two previous studies. In addition, in four samples, triple combination of amphetamine, diphenhydramine, and acetaminophen was found that this combination was not observed in previous studies. Acetaminophen was found at amount of 16.4 in crack samples, that the amount of acetaminophen in cracks referred to Forensic Department of Tehran was 2.2 in one sample among 80 samples. In investigation of Tehran cracks, 2.22 of samples had acetaminophen, among the 18 samples. In the

samples referred to Forensic Department of Khuzestan, caffeine (93.4) had the largest percentage of compounds, while caffeine was found in 80% of the samples examined. It may be said that caffeine is the effective and active substance of crack referred to Forensic Department of Khuzestan, while the heroin was the effective and active substance in the examined samples of Tehran (more than 90%).

Heroin was 27.9 in the cracks referred to Forensic Department of Tehran. It means that heroin amount has been reduced and crack structure has been changed. In large scale, heroin is traditionally synthesized by crude morphine in a one-step reaction of acetylation. Generally, three substances are used for acetylation of morphine, including acetic anhydride, ethyl chloride and ethylidene diacetate. In cracks referred to Forensic Department of Khuzestan, 6 Mono-acetyl morphine (73.7) acetyl codeine (34.4) and codeine (27) were found that the amount of these compounds in the studies conducted by doctor Farhoudian on 18 samples and by Akhghar and Jokar on 80 samples was as follows:

mono-acetyl morphine and acetyl codeine amount was approximately 80 and codeine amount was approximately 35. In fact, the amount of heroin and its acetylated derivatives in the samples referred to Forensic Department of Tehran was higher than that in Khuzestan, indicating that street crack structure has been changed. Dextromethorphan was found in cracks referred to Forensic Department of Khuzestan and Tehran (over 80). Other compounds found in the present study are phenobarbital, amoxicillin, amitriptyline, nortriptyline, lidocaine, and thebaine.

In examining the cracks referred to Forensic Department of Tehran, the following compounds were found: phenobarbital, thebaine, pheniramine, chloroquine biperiden, and tramadol. The diversity of these compounds is an evidence on presence of various impurities in the cracks investigated and lack of fixed structural formula. In fact, these compounds are among the

adulterants used by producers to make cracks heavier.

DISCUSSION AND CONCLUSION

Finally, we found that street crack in Iran not only differs from real crack in the world where cocaine is its main substance, but also they differ in terms of variety and amount of pharmaceutical, opioid and diluent adulterants. Due to differences in the compounds of Iranian crack in various studies at different times, we realized that Iranian cracks have no fixed structure and they are changing daily.

They also have different amounts of substances affecting central nervous system and other drugs with pharmacological and non-pharmacological property. Additionally, the presence of amphetamines in cracks is very important issues since its using leads to dementia causing many threats to person, his family and society. Any change in purity of street crack compounds can cause risks for users of these compounds and clinical symptoms and complications for them it necessary to adopt appropriate treatment protocol in dealing with these users. We note that dementia in users followed by crime is very important issue that requires further studies.

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