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The Texture of Psychoactive Illicit Drugs in Iran: Adulteration with Lead and other Active Pharmaceutical Ingredients

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ABSTRACT

Psychoactive illicit drugs are widely used all over the world. Due to the high demand for illicit drugs, adulteration of substances with poisonous and active pharmaceutical ingredients is a common phenomenon in some countries. Lead and other active pharmaceutical ingredients are among adulterants added to illicit drugs intentionally. In the present study, we analyzed four major abused street drugs in Iran's drug black market (opium, Iranian crack, ecstasy tablets, and crystal methamphetamine) to assess active pharmaceutical ingredients and determine a quantitative assay of lead. A total of 40 psychoactive drugs were analyzed using high-performance liquid chromatography, gas chromatography/mass spectrometry, and flame atomic absorption spectroscopy. The results demonstrated that psychoactive drugs were adulterated with different drug categories, such as tramadol, ketamine, methadone, acetaminophen, and caffeine. Lead was found in all analyzed samples, ranging from 9–90 ppm. The smallest lead level was detected in methamphetamine samples. Iranian crack samples contained the highest amount of lead. Psychoactive illicit drugs were adulterated with different drug classes and also lead. Lead-adulterated psychoactive drugs are among the new sources of exposure to lead, while illicit drugs' contamination with different drugs may present a health hazard for drug-abusing patients.

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Active pharmaceutical ingredients; adulteration; analytical toxicology; psychotropic illicit drugs; substance-related disorders

Drug dependence is one of the most challenging health issues all over the world, including in Iran. Drug abuse and addiction place major burdens on society and health care systems. In addition, formal and informal reports have revealed a significant rise in the illegal synthesis, production, and distribution of drugs of abuse and their adulteration with different drug classes and diluents (Alinejad et al. 2018).

Adulterants and diluents can be added to psychoactive substances at different steps in the production, distribution, or storage of the drugs (Akhgari, Etemadi-Aleagha, and Jokar 2016; Alinejad et al. 2018). The motives for drug adulteration are often varied. Diluents and adulterants may be added to illicit drugs to bulk, dilute, increase weight, complement, enhance, modify, or oppose the pharmacologic properties of psychoactive drugs with no possibilities for consumers or buyers to notice (Akhgari, Etemadi-Aleagha, and Jokar 2016; Broséus, Gentile, and Esseiva 2016; Cole et al. 2010; Solimini et al. 2017). Several hypotheses have been offered as to the reason for choosing substances as adulterants, including chemical properties, low cost, and availability (Eiden et al. 2014). Adulterated psychoactive drugs predispose consumers to many health problems. In addition to the side-effects of active ingredients, adulterants may cause chronic diseases and vital organ failure in consumers (Akhgari and Etemadi-Aleagha 2016; Martello et al. 2017).

Aghaee-Afshar et al. (2008), in their study on opium samples in Iran, confirmed the presence of lead as an adulterant. Caffeine, quinine, lactose, and manitol were the most common diluents of heroin during the 1960s–1970s in Europe (Cole et al. 2010). At the beginning of the 1990s, more than 90% of heroin specimens contained caffeine and acetaminophen (Coomber 1997; De La Fuente et al. 1996; Risser et al. 2007; Simonsen et al. 2003). Although psychoactive drug adulteration is an important issue in Iran, few studies have been carried out to detect active pharmaceutical ingredients, non-pharmaceuticals, and lead as adulterants of psychoactive drugs (Akhgari et al. 2012; Aghaee-Afshar et al. 2008; Amini, Etemadi-Aleagha, and Akhgari 2015; Shekari et al. 2016). Khajeamiri et al. (2011), in their study on methamphetamine samples, confirmed the presence of amphetamine, dextromethorphan, chlorpheniramine,

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pseudoephedrine, caffeine, and phenmetrazine in illicit methamphetamine samples in Iran. Previous studies on methamphetamine samples determined that many impurities originate from the synthesis process and others are deliberately added to the final product (Amini, Etemadi-Aleagha, and Akhgari 2015; Shekari et al. 2016).

Previous analytical surveys on seized heroin samples showed that street heroin contained many adulterants and by-products produced during the synthesis process or deliberately added to the final product (Akhgari et al. 2012). Amini, Etemadi-Aleagha, and Akhgari (2015) detected active pharmaceutical ingredients in methamphetamine samples seized in Kermanshah Province, Iran. Additionally, Shekari et al. (2016) confirmed the presence of pharmaceutical adulterants in methamphetamine samples in Tehran, Iran.

Few studies have been done on psychoactive drugs for the detection of lead and other active pharmaceutical ingredients in Iran. The novelty of this study is to detect active pharmaceutical ingredients and lead content of different classes of psychoactive drugs simultaneously. The aim of the present study was to analyze psychoactive illicit drugs for the detection of hidden active pharmaceutical ingredients and lead content as adulterants.

Materials and methods

A total of 40 samples of psychoactive drugs, including Iranian crack (heroin), ecstasy tablets, methamphetamine crystal (known as "*Shishe*" in Iran), and raw opium (10 of each sample), were acquired from drug seizures referred to a forensic toxicology laboratory for analysis. These substances are categorized as controlled drugs in Iran. According to the Ministry of Health and Medical Education of Iran, Food and Drug Organization Division of Pharmaceutical and Narcotic Affairs, possession, distribution, and sale of these substances fall into different categories, and sentences vary, depending on the amount of drug dealt and trafficked (FDA n.d.). The forensic toxicology laboratory is responsible for analyzing psychoactive drugs and reporting the results to jurisdictional authorities. All of the samples in the present study were chosen from drugs referred to the lab from March 1, 2016, to February 30, 2017. Approximately one sample in each month was selected using a random sampling method. Ten ecstasy samples were chosen from different shapes. All samples were kept in crimped-cap, air-tight containers prior to analysis. All analytical methods used in the present study were prevalidated and accredited in the forensic toxicology laboratory (Amini, Etemadi-Aleagha, and Akhgari 2015; Foroughi et al. 2017; Shekari et al. 2016).

Reagents

Analytical-grade methanol, chloroform, phosphoric acid, potassium dihydrogen phosphate, and hydrochloric acid (37%) were purchased from the Merck Chemical Co. (Darmstadt, Germany). Water for chromatography (Merck Millipore) was used to prepare the buffer for the mobile phase in the HPLC system, as well as all aqueous solutions and eluents for qualitative analysis of psychoactive drugs. Acetonitrile (HPLC grade) was prepared by Merck Chemical Co. Helium (99.99% purity) was supplied by Roham Co. (Tehran, Iran).

Doubly distilled deionized water 18 mega-ohm (MΩ) (Millipore Corp.) was used throughout the analysis procedure for standard, stock, and sample preparation. Nitric acid (65%) and hydrochloric acid 70% were supplied by Sigma-Aldrich (TraceSELECT). All glass and plastic containers were acid washed by soaking in diluted nitric acid (10%) at least one night prior to each experiment to remove contamination. All containers were then rinsed three times with deionized water. Standard solutions in different concentrations were prepared by diluting 1000 mg/L pb in nitric acid (Lead Standard for Atomic Absorption (AAS), Trace CERT®) stock solution supplied by Sigma-Aldrich.

Qualitative analysis of psychoactive substances for the detection of active pharmaceutical ingredients

All psychoactive drugs (Iranian crack, ecstasy tablets, opium, and methamphetamine samples) were analyzed to detect active pharmaceutical ingredients. Inert adulterants, bulking agents, colors, and other additives were not analyzed during the analysis procedures. All drugs were crushed using porcelain mortar and pestles. Dispersive liquid liquid microextraction (DLLME) was used as a sample preparation method for the extraction of active pharmaceutical ingredients from psychoactive drugs. All prepared fine powders were mixed with 2 mL of 0.1 M borate buffer (pH = 9.2) to make three parts of 1 mg/mL concentrations. Drugs and chemicals with basic chemical properties (benzodiazepines, amphetamine-type stimulants, antidepressants, and narcotic analgesics) were extracted by the pH adjustment to pH = 12. The pH of the experiment medium was adjusted to pH = 2 for the efficient extraction of acidic drugs, such as phenytoin, barbiturates, and primidone. For drugs with amphoteric chemical structure (morphine), the pH was adjusted to isoelectric point (pH = 9). All validation method parameters were assessed in the laboratory prior to sample analysis. Limit of detection (LOD), limit of quantitation

(LOQ), coefficient of variation %, accuracy, and precision were evaluated for drugs with forensic interest in non-biological samples to be extracted and detected (Akhgari, Jokar, and Etemadi Aleagha 2011; Foroughi et al. 2017; Ghasemi Dastjerdi et al. 2018; Hafizi Fard and Akhgari 2018; Iravani et al. 2010; Shekari et al. 2016). Methanol and chloroform were chosen as the best disperser and extractant solvents, respectively, for the DLLME procedure. A mixture of 2.5 mL methanol and +30 µL of chloroform was pushed rapidly to one mL of samples prepared in borate buffer at the previously mentioned pH. The mixture was ultrasonicated for 5 min and centrifuged for efficient separation of watery and organic solvent layers. The organic solvent layer (chloroform) was collected from the bottom of a conical tube and dried under a light stream of nitrogen gas. Dissolved residue in 30 µL methanol was anlyzed using HPLC and GC/MS confirmatory instrumentations, with prevalidated methods routinely used for the qualitative determination of unknown drugs in different matrices in a systematic toxicological analysis procedure (Akhgari, Jokar, and Etemadi Aleagha 2011; Foroughi et al. 2017; Ghasemi Dastjerdi et al. 2018; Hafizi Fard and Akhgari 2018; Iravani et al. 2010; Shekari et al. 2016).

Apparatus

GC/MS instrumentation operating conditions

A gas chromatograph (7890 A, Agilent Technologies, Sdn Bhd, Selanger, Malaysia) equipped with a split/splitless injector was used. A capillary column (HP5-MS model, crosslinked 5% methylphenyl silicone, 30 m length x 0.25 mm ID x 0.25 µm film thickness) was used in GC. An agilent mass detector (MS 5975 C) was connected to GC. The injection ports and transfer line temperatures were 250°C and 280°C, respectively. The column oven was set to 60°C for one min. The temperature program rate was 2°C/min up to 280°C and final hold for 15 min. Electron impact (70 ev) in positive full-scan mode (50–550 m/z) was used for the mass system operation. Qualitative analyses of psychoactive drugs were performed using Wiley, NIST, and MPV 2011 libraries.

HPLC instrumentation operating conditions

An HPLC system (Knauer, Berlin, Germany) with a diode array detector (DAD 2800–4 channels) was used. The column was Eurospher-100–5 C18 (250 mm x 4.6 mm x 5 µm particle size, 100 Å pore size). Elution solvent was a mixture of acetonitrile and phosphate buffer (38:62). Toxicology analysis was performed in isocratic mode at a flow rate of 1 mL/min and 400 bar pressure.

Instrumentation

The lead flame atomic absorption spectroscopy (FAAS) measurements were carried out using a Varian Spectra AA 220 atomic absorption spectrophotometer equipped with an autosampler. A Hallow cathode lamp operated at a current of 5 mA was used. The measurements were performed at 283.3 nm (offering a better signal-to-noise ratio and lower background interference) with the slit fixed at 1.0 nm using air/acetylene. Air and acetylene flow rates were kept at 12.5 and 2 L/min, respectively.

Quantitative analysis of lead in psychoactive drugs

All validation method parameters were assessed in the laboratory for quantitative measurements of lead in all analyzed samples.

Linearity assessment

The linearity of FAAS for the quantitative determination of lead was evaluated using seven concentrations of 0, 10, 20, 40, 60, 80, and 100 ppm of lead with triplicate measurements for each concentration. Least square method was used for the preparation of the regression line and expressed as correlation coefficient ($R^2 > 0.99$) (Figure 1).

Detection and quantitation limits

Limit of detection (LOD) and limit of quantitation (LOQ) were evaluated as the concentration with a signal/noise equal to 3 and 10, respectively. Low and decreasing concentrations of lead were analyzed until signal/noise of about 3 was achieved. The same manner was used for LOQ definition. It should be noted that the background was < limit of detection (LOD).

Intra- and inter-day accuracy and precision

Inter-day precision was achieved in a single run, analyzing triplicates of standard samples ($n = 9$). Intra-day assay was carried out by analyzing standard lead concentrations over three consecutive days ($n = 27$).

Determination of lead concentration in drug samples

All powder and tablet dosage forms were crushed to a fine powder using a mortar and pestle. A mixture of 3:1 of nitric acid (65%) and hydrochloric acid (70%) was prepared. One half gram of each fine powder was weighed and mixed with 2 mL of nitric acid/hydrochloric acid mixture. The mixture was sonicated for 20 min prior to being placed in an oven for 24 h at 90°C. Samples were centrifuged at 1000 RPM for 5 min and decanted to be prepared for analysis using FAAS. Lead

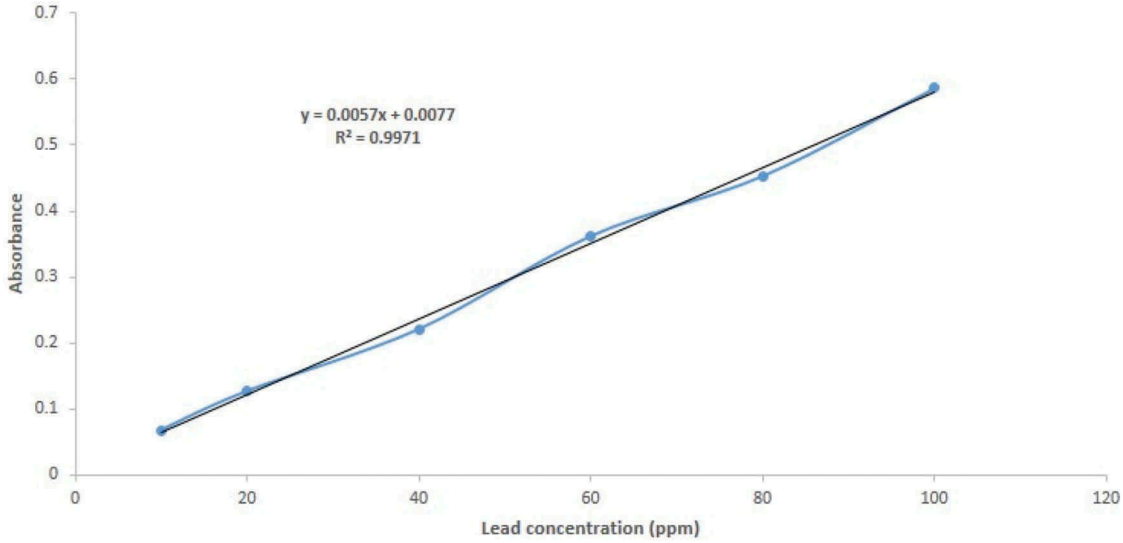

Figure 1. Linearity plot for seven different concentrations of lead using described flame atomic absorption spectroscopy instrumentation.

concentration was determined via three replicates on three separate occasions of each sample, resulting in a total of nine measurements for each sample.

Statistical analysis

To analyze the data statistically, we performed a one-way analysis of variance (ANOVA) for repeated measurements of the same concentration of lead in samples.

Results

In the present study, 40 samples of psychoactive drugs that were sold in Iran on the drug black market were analyzed to detect active pharmaceutical ingredients and lead content using HPLC, GC/MS, and FAAS.

Characteristic features of psychoactive drugs

All of the drugs were in powder form except for ecstasy, which was sold as multicolored tablets with a groove on one side. Shaped tablets had different logos, such as a heart. Opium samples were in brilliant brown sticky gum form (Figure 2). Iranian crack samples were prepared as creamy to beige lumps. Methamphetamine samples were in colorless or white crystalline form with different sizes of crystals. The results of the sample analysis for the detection of active pharmaceutical ingredients are shown in Table 1.

Quantitative analysis of all samples for the detection of lead adulteration showed that all psychoactive drugs tested in the present study were contaminated with lead. Table 2 illustrates the results of the analysis of samples using FAAS.

Figure 2. Lead adulterated opium containing tramadol and chloroquine as hidden pharmaceutical ingredients.

Discussion

The results of the present study demonstrated that illicit drugs in Iran's drug black market are adulterated with active pharmaceutical ingredients and lead. Some important insights have been gained from illicit drug profiling. Specific active pharmaceutical ingredients were detected in illicit drugs in Iran (Amini, Etemadi-Aleagha, and Akhgari 2015; Khajeamiri et al. 2011; Shekari et al. 2016) referred to forensic toxicology laboratories. Routine drug tests to detect active pharmaceutical

Table 1. The most prevalent active pharmaceutical ingredients in illicit psychoactive drugs detected using HPLC and GC/MS instrumentation in Tehran, Iran.

Seized psychoactive drug	Combined hidden active pharmaceutical ingredients (number)
Methamphetamine	Methamphetamine+ Phenmetrazine+ Pseudoephedrine+ Dextromethorphan (3)
	Methamphetamine+ Caffeine+ Phenmethrazine+ Pseudoephedrine (2)
	Methamphetamine+ Caffeine+ Ecstasy (1)
	Methamphetamine+ Phenmethrazine (1)
	Methamphetamine+ Ketamine (1)
	Methamphetamine (2)
Iranian crack (Heroin)	Heroin+ Morphine+ Codeine+ Papaverine+ Noscapine+ Phenobarbital+ Acetaminophen+ Tramadol+ Caffeine(2)
	Heroin+ Morphine+ Codeine+ Papaverine+ Noscapine+ Methamphetamine+ Chloroquine+ Methadone (2)
	Heroin+ Morphine+ Codeine+ Papaverine+ Noscapine+ Chloroquine+ Methadone+ Caffeine (1)
	Heroin+ Morphine+ Codeine+ Caffeine (3)
	Heroin+ 6-Monoacetylmorphine+ Caffeine (2)
Ecstasy	3,4- Methylenedioxymethamphetamine+ Methamphetamine (4)
	3,4- Methylenedioxymethamphetamine (4)
	3,4- Methylenedioxymethamphetamine+ Heroin (2)
Opium	Morphine+ Codeine+ Papaverine+ Noscapine+ Acetaminophen (6)
	Morphine+ Codeine+ Papaverine+ Noscapine+ Acetaminophen+ Chloroquine (2)
	Morphine+ Codeine+ Papaverine+ Noscapine+ Chloroquine+ Tramadol (2)

Table 2. Lead concentration in different psychoactive substances determined by flame atomic absorption spectroscopy instrumentation in Tehran, Iran.

Psychoactive drug	Lead concentration (ppm*)
Methamphetamine	8.78–15.45
Iranian crack (heroin)	60.37–90.18
Ecstasy	16.72–30.46
Opium	10.25–13.93

*ppm: part per million.

ingredients in illegal drugs are most common in Iran and have resulted in jail sentences or other kinds of punishment. Drug use touches on many health, legal, political, and economic consequences in the society. Therefore, drug testing and component analysis of drugs have been adopted by many countries as part of a harm-reduction strategy (Brunt et al. 2017).

Adulteration of psychoactive drugs coincided with an increased popularity of many abused substances among drug abusers, used to enhance drug pharmacologic effects, such as additional energy, self-confidence, and sedation (Brunt et al. 2017). In agreement with the obtained results, other scholars have confirmed that street heroin samples are not pure heroin; they are heavily adulterated cocktails often varying in purity and adulterants (Akhgari et al. 2012; Akhgari, Etemadi-Aleagha, and Jokar 2016; Mars et al. 2016). Previous analytical surveys on seized heroin samples showed that street heroin contained diacetylmorphine, 6-monoacetylmorphine, codeine, acetyl codeine, morphine, codeine, papaverine, and noscapine, known as opium alkaloids as a source for illicit heroin production in clandestine laboratories. Diazepam, caffeine, and phenobarbital were other components that were added to the final product (Akhgari et al. 2012). Heroin is cut with diluents to add weight or enhance its pharmacologic effect (such as benzodiazepines), or diminish side-effects (diphenhydramine to cure itching), both of which are appealing to drug users (Mars, Ondocsin, and Ciccarone 2017). Powdery forms of psychoactive drugs such as cocaine and heroin are predominantly adulterated to obtain more doses and get more revenue (Solimini et al. 2017). In this way, heroin samples (Iranian crack) analyzed in the present study were adulterated with lead to obtain more profit. The other findings from our toxicological analysis of heroin samples showed that active pharmaceutical ingredients such as phenobarbital, methadone, tramadol, and methamphetamine were present in illicit Iranian crack. These results are in agreement with those of Akhgari et al. (2012), who found all of the active pharmaceutical ingredients, except for methadone and methamphetamine.

A comparison of the results obtained from the present study with those from a similar study conducted five years earlier (Akhgari et al. 2012) shows that some active pharmaceutical ingredients, such as methadone and methamphetamine, were newly added to illicit heroin samples. Evidence from Denmark supports the results of the present study. More than 95% of heroin samples in Demark contained acetaminophen and caffeine (Andreasen, Lindholst, and Kaa 2009). Overall, 80% of Iranian crack samples were contaminated with caffeine. Caffeine vaporizes heroin at lower temperature and promotes the uptake of diacetylmorphine during heroin base smoking. Also, it may be added to heroin as a stimulant drug (Andreasen, Lindholst, and Kaa 2009). Opium alkaloids were detected in the majority of samples. This finding was supported by Andreasen, Lindholst, and Kaa (2009). Tramadol and phenobarbital were detected in two samples, endangering the lives of consumers, who might be unaware of their presence or quantity. However, the results are in

disagreement with those of Farhoudian et al. (2014), who did not detect tramadol and phenobarbital in Iranian crack samples in 2014. This difference may be due to the fact that drug availability is different at different time points in one geographic area.

Scramble heroin, a kind of heavily adulterated or even replaced heroin, which has been reported in Baltimore, Maryland, is a combination of fentanyl, benzodiazepines, and crushed opioid pills (Mars, Ondocsin, and Ciccarone 2017); heroin samples in the present study did not contain fentanyl. Some chemical adulterants, such as 6-monoacetylmorphine, are not deliberately added to heroin samples. Whether the presence of some hydrolysis products in the samples originated from degradation, adulteration, or as an analytical procedures' artifact should be considered (Palma-Conesa et al. 2017).

Currently, the most prevalent substance of abuse in Iran is raw opium. Opium is colloquially called "*Taryak*" and is a widely used traditional drug in Iran (Alinejad et al. 2018). The sticky and brown gummy texture of opium motivates drug dealers to adulterate opium with different kinds of substances. Brown illicit acetaminophen that is not obtained from pharmaceutical suppliers is added to psychoactive drugs to get analgesic effects (Broséus, Gentile, and Esseiva 2016).

Over the past few years, an epidemic of methamphetamine use has emerged in Iran's young population (Noroozi, Malekinejad, and Rahimi-Movaghar 2018). Methamphetamine samples' analysis confirmed the presence of drugs and other adulterants in samples. The obtained results were in accordance with the results obtained in Tehran and Kermanshah provinces in Iran (Amini, Etemadi-Aleagha, and Akhgari 2015; Shekari et al. 2016). Component analysis of amphetamine samples in Denmark showed that these samples contained caffeine, creatine, salicylamide, acetaminophen, and phenazone (Andreasen, Lindholst, and Kaa 2009). The difference between the composition of amphetamine samples in Iran and other countries may be due to the production of methamphetamine from different laboratory procedures and precursors. Adulteration of final products with unwanted substances could occur in several ways. Inadequate purification of the products, primary reagents residues, or their incomplete reaction during preparation can contaminate the final material (Iqbal 2002).

Ecstasy is manufactured as pills by mixing the active ingredients with adulterants (Palamar 2017; Rigg 2017). The results of the present study showed that ecstasy tablets not only contained 3,4-methylenedioxymethamphetamine, but also other adulterants, such as methamphetamine and heroin. In a similar vein, Khajeamiri et al. (2011) found ketamine, phenmetrazine, pseudoephedrine, caffeine, and tramadol in ecstasy tablets. Ghafari et al. (2014), in their study on ecstasy tablets in Iran, found that ecstasy tablets contained 0.5–70.7 mg of pure methylenedioxymethamphetamine.

Another adulterant detected during toxicological analyses was lead. Non-occupational lead exposure due to the use of contaminated drugs has recently been noted (Ghaemi et al. 2017). Human exposure to lead occurs via inhalation or ingestion (World Health Organization 2004). Most of the drug seizure samples were laced with lead in different concentrations. Abused psychoactive substances has been analyzed to detect lead content in a few studies (Khajeamiri et al. 2011; Mostafazadeh et al. 2017). Chia et al. (1973) reported lead poisoning from the ingestion of contaminated handmade opium in 1973 for the first time. Domeneh, Tavakoli, and Jafari (2014), in their study on blood lead level in opium-dependent cases in Tehran, Iran, concluded that blood lead level is significantly higher in opium-dependent persons, especially in cases involving the oral route of consumption (Domeneh, Tavakoli, and Jafari 2014). Blood lead level was high in a chronic opium abuser in a study by Jalili and Azizkhani (2009). Lead has a low melting point; therefore, a large quantity of lead may be absorbed through inhalation and miasma from the smoking of opium. The amount of lead absorbed through the gastrointestinal tract is generally 10–15%. This amount produces high blood lead level in oral opium abusers (Alinejad et al. 2018). Previous published papers estimated consumption of 0.6–100 g/day of opium by drug users (Zamani and Hassanian-Moghaddam 2018). The results of the present study showed that analyzed opium samples contained at least 10 ppm of lead. The Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable weekly intake of 25 μg/kg body weight, which is equal to 1750 μg/week for a 70 kg person (World Health Organization 2011). A user consuming 30 g of opium/day would get at least 300 μg/day of lead, a quanity equal to 2100 μg/week. In this case, the person will receive more than the tolerable daily intake of lead via drug use only. If opium is used in the long term, such concentrations of lead may be harmful.

There are some explanations for the presence of lead in opium. One is the contamination of opium during processing and refinement steps. Another is opium adulteration by lead-contaminated soil. Cultivation of the opium poppy near lead mines may explain the presence of lead in raw opium. Dealers and sellers add lead to opium in order to increase weight and

maximize profit (Alinejad et al. 2018). Analysis of opium samples in Kerman Province, Iran, in 2006 indicated that opium samples contained 1.88 ± 0.35 ppm of lead (Aghaee-Afshar et al. 2008), which is about one-fifth of the concentration of lead in opium samples in the present study. This difference may be due to the fact that adulteration practices vary in different time intervals, depending on the availability of adulterants, demand for the drug, and its price.

Methamphetamine samples analyzed in the present study contained about 9–15 ppm of lead. Allcott et al., in their study on methamphetamine abusers in 1987, reported two cases of lead poisoning when the abusers injected illegal methamphetamine (Allcott, Barnhart, and Mooney 1987). However, Mostafazadeh et al. (2017) indicated that lead poisoning was not observed in 20 methamphetamine abusers. Our results provide more evidence for the other studies. Norton et al. declared that lead poisoning among methamphetamine users was related to lead-contaminated methamphetamine. Lead acetate is one of the common reagents in methamphetamine production. Production errors and poor purification of the final product may result in methamphetamine grossly contaminated with lead (Norton, Burton, and McGirr 1996).

Iranian crack (heroin) samples contained about 60–90 ppm of lead. This amount of lead would endanger drug users and result in lead poisoning in chronic heroin abusers. Antonini et al. reported lead poisoning in drug abusers addicted to heroin (Antonini et al. 1989). Production of heroin in lead pots can also be a source of lead in heroin samples (Akhgari, Etemadi-Aleagha, and Jokar 2016).

The content of lead in ecstasy tablets was about 16–30 ppm. Some users believe that only handmade powders and capsules are easy to adulterate with other substances. Therefore, consumers prefer to buy known shaped tablets or pills with some logos (Duterte et al. 2009). French et al.'s study of ecstasy tablets confirmed the presence of lead in different concentrations between disparate batches of tablets (French, Went, and Gibson 2013). Tablets that are produced in clandestine laboratories differ in the concentration of adulterants due to poor premixing of powders prior to tableting processes (French, Went, and Gibson 2013). Sources of lead in ecstasy tablets are different. Lead can originate from reaction vessels, components of dyes, residues of catalysts, or as an added adulterant in ecstasy tablets (French, Went, and Gibson 2013).

One of the limitations that we encountered during this study was that we were unable to analyze active pharmaceutical ingredients quantitatively. However, the main aim of the study was to detect adulteration practices. We recommend future studies using larger sample sizes and analyzing psychoactive drugs to detect active pharmaceutical ingredients quantitatively.

Conclusion

We found that all kinds of tested psychoactive substances were adulterated with active pharmaceutical ingredients and lead. Indeed, health professionals should be aware of and evaluate damage caused by base psychoactive substances and also by eventual contaminants added to increase weight, or mimic or antagonize drug effects with harmful synergistic actions. These results would be beneficial in the prevention and control of drug addiction and also potentially useful in developing intervention programs to persuade patients battling drug abuse to seek help in overcoming their addiction.

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