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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To compare the main and additive components of heroin trafficked in the State of Kuwait during 2012 with those components of heroin traded recently in the country during 2016 and 2017, and to provide a satisfactory explanation for the increase in deaths among heroin addicts during the period 2011 -2018.

Study Design: Selected samples of non-pure powder heroin seized in Kuwait during 2016 and 2017, with pure heroin and a set of 10 pure different heroin component standards, all have been quantitatively analyzed in the Forensic Laboratories.
**Place and Duration of Study:** All qualitative and quantitative analyses for 2016 and 2017 samples were conducted in the Forensic Laboratories of the General Department of Criminal Evidences – Ministry of Interior – State of Kuwait.

**Methodology:** By using Gas Chromatography/Mass Spectrometry (GC/MS) to qualitative and quantitative analysis have been made on a total of hundred samples of non-pure powder heroin seized in Kuwait during the years 2016 and 2017, in addition to ten pure standards.

**Results:** The concentration of the diacetylmorphine (active substance of heroin) in Kuwait during the year 2017 are much higher than the concentration during the year 2016. The additive substances (adulterants) for the years 2016 and 2017, are shared with the year 2012 by the component's paracetamol, caffeine and diazepam with different concentrations. But new adulterants in recent years are recorded in samples 2016 and 2017, including methamphetamine, dextromethorphan, and methylphenidate which is absent in 2016 samples.

**Conclusion:** The concentration % of illicit heroin traded in Kuwait as diacetylmorphine has increase from 10% to 50% for year 2016, and further from 30% - 70% for year 2017, which marks identified a substantial rising in the purity of heroin. In addition, additive substances in the two years include paracetamol (acetaminophen), caffeine and diazepam, previously recorded in 2012. However, totally different new adulterates are recorded in 2016 and 2017 samples, including methamphetamine, dextromethorphan, and methylphenidate. All new three adulterates are detected in quite a few numbers of samples with methylphenidate recorded in a very low concentration of 0.01 mg. Both new adulterates and higher purity of heroin constitute the main reasons for rising the rate of deaths between heroin addicts in recent years. Also, recent UN reports (12,18) provide evidence that the GC countries Afghanistan, Iran and Pakistan are still manufacturing and trading the above mentioned new adulterates.

**Keywords:** Diacetylmorphine; adulterants; derivatives; depressant; diluent; stimulants.

1. INTRODUCTION

Heroin drug is still considered as a huge problem in the world, particularly in the State of Kuwait, due to its geographical location between the "Golden Crescent"(GC) countries(Afghanistan, Pakistan and Iran) which are culturing and manufacturing the drug on a wide scale [1,2].

Heroin is one of the most widely abused drugs in Kuwait, and hence is included in Schedule 1 of narcotic drugs Table [3]; most street heroin samples seized in different countries around the world are not available as pure heroin, but generally contain impurities [1,4,5].

The technique for using street heroin is by injection (intravenous), snorting or smoking [6].

‘Street’ heroin is subject to unpredictable variations in drug purity and may contain a variety of adulterants or contaminants mixed in, making it difficult for the user to determine the amount of active substance to use. However, the picture is far from clear, as large numbers of fatal overdose sufferers have low concentrations of morphine in the blood, often below, or similar to, those of living intoxicated heroin users or of heroin users who died from other causes [7,5,8].

According to the official statistics of the State of Kuwait on heroin the drug amount has increased in the year 2012 (ca. 216.5%); the reference year for first detailed study carried out in Kuwait on the components of heroin seized in the country [1,9]. While in recent years of 2016 and 2017 the amount of heroin has decreased byca. 57% (ca. 124.4%). Despite this decrease in the amount of heroin traded in Kuwait, the deaths rate during the whole period of 2011 to 2018 increased by 283% among heroin addicts [10,11].

Therefore, the main objective of this study to understand the main reason led to rise the rate of deaths between heroin addicts.

2. MATERIALS AND METHODS

Selected samples of non-pure heroin seized in Kuwait and pure standard samples have been analyzed in the Narcotics and Psychotropic Substance Section (NPSS) (the Forensic Laboratories, Ministry of Interior, Kuwait) by using Gas Chromatography/ Mass Spectrometry (GC/MS) in accordance with analytical methods described by the Manual for Use by National Narcotics Laboratories and Clarke's Analysis of Drugs and Poison, for qualitative and quantitative analyses.
2.1 Sample Preparation

2.1.1 Pure standard samples

Ten external pure standard samples, which have been used for quantitative analysis, were supplied from Lipomed AG.; namely, "Diacetylmorphine (Her), Papaverine (Papa), Noscapine (Nos), Acetylcodaine (A.cod), 6-monoacetylmorphine (6-MAM), Caffeine (Caf), Paracetamol (Para) Diazepam (Dia), Methamphetamine (Metha), Dextromethorphan (Dextro) and Methylphenidate (M.phe)[13].

2.1.2 Non-pure samples

A total of one hundred non-pure powder samples of heroin collected from the cases of seized heroin investigated by the Forensic Laboratories, and pure standards have been subjected to the same conditions; each sample is 1 mg in weight, dissolved in 2 ml of a solvent containing (Chloroform: Ethanol: Acetone) in ratio 70:20:10, and filtrated to injection with 1 µL in GC/MS.

2.1.3 Apparatus used for measurements

The following operating conditions have been applied in accordance with Agilent 7890B series Gas Chromatography "Operating Manual:

2.1.3.1 Operating conditions

The following operating conditions are in accordance with Agilent 7890B Series. Gas Chromatography Agilent technologies, with 5977B MSD (High Efficiency Sources), and 7693 autosampler. "Operating Manual" [14]:

GC-MS Agilent Technologies 7890B GC system (integrated LAN) liquid samples and 5977B inert MS (mass selective) single quadrupole detector, with MSD in EI mode (electron ion source) and column (ULTRA 2) with 30 m x 250 µm x 0.25 µm with temperature limits from -60°C to 350°C with 7693 automatic sampler components - Injection Volume: 1.0 µl by syringe size 10.0 µl -. Inlet splitless with 280°C.

Ramp: (temperature Column)
Initial: 100°C hold 4.00 min
Ramp: 8°C - 280°C hold 4 minutes (for 30.5 minutes)
Post: 300°C hold 5 minutes Run time (38.83 minutes).
Pressure: 8.97 psi.
Carrier gas (He) Helium with flow rate:1.4

3. RESULTS AND DISCUSSION

GC/MS is a well-known technique commonly used in the Forensic Laboratories in Kuwait for the analysis of seized heroin samples to detect the diacetylmorphine and the additive components mixed with it. These components can divide into three types; namely, derivative substances, main additive substances (diluent) and the adulterants. Results of analyzing the recent samples are as follows:

3.1 Detecting Active Substances (Diacetylmorphine)

All samples include the main substance diacetylmorphine with concentrations in the range from 1 mg to 3.4 mg in 2016 samples. While in 2017 samples higher values are recorded and range between 1.5 mg to 3.5 mg, and both sample collections have higher concentration than those recorded in 2012 as shown in Fig. 1. A remarkable increase is recorded in their purity from 20% to 40% in 2012, to reach 10% to 50% in 2016, and to 30% to & 70% in 2017. This would strongly suggest that the purity of heroin traded in Kuwait has increased during six years (2012 - 2017) as shown in Fig. 2 and is very close to the purity of the drug in the manufacturing countries (heroin manufactured in Afghanistan has concentration % of 80% (Her)) [9,5].

3.2 Detecting Main Derivative Substances

The substances detected are papaverine and noscapine as derivatives of opium, with acetylicodine, and 6-monoacetylmorphine (6-MAM) as derivatives of heroin during acetylation process. Fig. 3 clearly shows that 2016 samples include papaverine, noscapine, acetylicodine, and 6-MAM with frequency % as; 46%, 82%, 88% and 88% respectively and samples 2017 they are present with frequency % as; 46%, 84%, 98% and 98% respectively. The same substances are detected with close result frequency % in 2012 samples.

3.3 Detecting Main Components in 2012, 2016 and 2017 Samples

Fig. 4 demonstrates that the main components detected in all samples of heroin collected during 2012 – 2017; namely, paracetamol, caffeine as diluent substances and diazepam as adulterate are present with proportions of 32%, 94% and 82% in 2012 samples, and 38%, 74% and 26% in 2016 samples, respectively. While in samples...
2017 they are detected with proportions of 22%, 80% and 24%, respectively. But their concentrations in 2016 collection (see Fig. 5) are in the range of 1.3 mg – 7.5 mg, 0.5 mg – 5.2 mg, 1.4 mg – 6.1 mg, respectively, and in 2017 sample collection (see Fig. 6) are in the range of 0.01 mg – 0.8 mg, 0.1 mg -1.2 mg, respectively. While diazepam has been detected only in two samples with concentrations 0.02 mg and 0.4 mg, compared with their concentrations in 2012 which are lower than these in both years 2016 and 2017 with concentration 0.01 mg -3.1 mg for paracetamol, 0.02 mg -0.8 mg for caffeine, and 0.002 mg-0.4 mg for diazepam which is considered as sharing adulterants with 2016 and 2017 samples.

3.4 Detecting Adulterate Substances in 2012, 2016 and 2017 Samples

Adulterate substances (adulterants) recorded in 2016 and 2017 heroin samples are completely different from those detected in 2012 samples; namely, phenobarbital and alprazolam. Fig. 8 shows that other new adulterate substances have been detected in 2016 and 2017 samples; namely, methamphetamine and dextromethorphan with frequency % as2% and 10%, and 6%, 8% respectively, and with another new adulterant; namely, methylphenidate recorded in 2017 with frequency 2%.

In addition, new additive substances, including methamphetamine and dextromethorphanon, have been identified in 2016 samples (see Fig. 9), including one sample for methamphetamine (conc. 7.3 mg) and five samples with concentrations ranging from 1.1 mg to 6.8 mg fordextromethorphanon. In 2017 sample methamphetamine and dextromethorphanon have been detected into samples ranging from 0.01 mg – 0.04 mg, and from 0.2 mg – 3.9 mg, respectively, while methylphenidate, which is absent in 2016 samples, has been recorded with concentration 0.03 mg in one sample in 2017 (see Fig. 10).
Fig. 3. Derivative substances in heroin traded in Kuwait during 2012, 2016 & 2017

Fig. 4. Frequency % for main components during 2012 – 2017

Fig. 5. Concentration of main adulterate substances in 2016 samples
Fig. 6. Concentration of main adulterate substances in 2017 samples

Fig. 7. Concentration of main adulterate substances in 2012 samples

Fig. 8. Frequency % for adulterants in 2016 – 2017 heroin samples
3.5 General Characteristics of Seized Heroin in Kuwait during the Period 2012 – 2017

From the results of the analytical work carried out on samples of heroin traded in Kuwait in the Forensic Laboratories, which were received at NPSS Laboratory during the period 2016 to 2017 and compared with the results of the analysis of heroin traded in Kuwait in 2012, the following findings have been reached:

3.5.1 Purification of diluent and adulterate substances of heroin traded in Kuwait during 2016 and 2017 compared with heroin traded in 2012

The adulterate substances in heroin traded in Kuwait in years 2016 and 2017 are different from those traded in Kuwait in the year 2012, but all are shared with the main substances as paracetamol, caffeine and diazepam with different concentrations, while other new substances have been detected in both 2016 and 2017, including methamphetamine and dextromethorphan, as well as methylphenidate which was detected only in 2017.

3.5.1.1 Adulterant substances in 2016 collection

Regarding the % concentration of the main adulterate substances in 2016 samples, paracetamol, caffeine and diazepam shown in Fig. 11 are in the range between (10% - 60%), (30% - 40%) and (20% - 40%) respectively, while for new adulterates methamphetamine has a low concentration of 1.5% and dextromethorphan has concentrations in the range between 20% - 50% respectively with methylphenidate completely absent.

3.5.1.2 Adulterant substances in 2017 collection

The % concentration of the main adulterate substances in 2016 samples; namely,
paracetamol, caffeine and diazepam (see Fig. 12) are in the range between (20% - 70%), (10% -90%) and (10% - 90%) respectively, while the new adulterates methamphetamine and dextromethorphan have higher concentrations in the range between 30% - 70%, 10% - 90% respectively, but methylphenidate which is only recorded in this collection, has a very low concentration of 0.01%. Despite their presence in few numbers of samples in 2017, their concentration has higher results than those in 2016 samples.

### 3.6 Legal Legitimacy of the New Heroin Adulterants Traded in the State of Kuwait Recorded in 2016 and 2017 Samples

Heroin traded in the State of Kuwait during the year 2012 is mixed with alprazolam and phenobarbital as adulterate substances. After five years (2016/2017) heroin traded in the State of Kuwait still share with heroin 2012 the adulterants paracetamol, caffeine and diazepam, but a completely new set of other adulterate substances have been recorded; namely, methamphetamine which is included in Schedule 2 of Psychotropic Substances of Kuwait, dextromethorphan which is an illegal drug in the State of Kuwait, as it was classified in the Schedule of Narcotics Tables for a long time, but now it is a legal medicine used to treat cough [15,5] and methylphenidate which is considered also in the State of Kuwait as an illegal substance; it is included in the Psychotropic Substance’s Tables Schedule as the same of methamphetamine [16,5].

They are pharmacologically active adulterants used to improve the bioavailability of heroin when
smoked or injected [17]. UN (United Nations) recent reports for the years 2017 and 2018 have confirmed that the Golden Crescent countries (Afghanistan, Iran and Pakistan) are still manufacturing and trading methamphetamine, diazepam and dextromethorphan, which are used in other way as adulterant for methamphetamine [2,18].

### 3.7 Hazard Effect of Illicit Heroin and the Adulterant Substances

Illicit drugs contain widespread substances which have serious risk impacts on human health. Adulterants are deliberately added to increase bulk, enhance or mimic a pharmacological effect, or to facilitate drug delivery. Those present unintentionally are as a result of poor manufacturing techniques. The adulterants are predominantly substances which are readily available, commonly being caffeine, paracetamol. These are likely to have minimal impact on users’ health at low dosages. Other adulterants, particularly in injectable drugs, have the potential to cause serious health issues. [19,20,21].

Heroin intoxication causes a classical syndrome of respiratory and central nervous system depression with pupillary constriction. However, modification of the street drug with other substances can result in unusual or atypical presentations. Adulteration is the intentional addition of a pharmacologically active substance in an attempt to use less of the active drug without the user being aware. This led to evaluating damages caused not only by the base substance, but also by other eventual compounds added to mimic or antagonize drug effects or simply dilute the drug amount, with a possible harmful synergic toxic action, which appears after repeated use of the drug. Chronic users often develop collapsed veins, abscesses, cellulitis, liver disease, and infections of the heart lining and valves. Because heroin is a CNS (Central Nervous System) depressant, it may affect respiration [22].

The wide availability of illicit psychotropic drugs is the most serious hazard threatening consumers. Stimulants such as methamphetamine, and depressant substances such as diazepam and dextromethorphan could increase the risk of overdose and other contamination with more adulterants causing death [19,20,22,23].

The overdose deaths between heroin addicts from adulterants, the most common cause was illicitly manufactured drugs commonly containing additional pharmacologically active components such as diazepam, methamphetamine, and dextromethorphan. These components, which are added during the illicit manufacturing process to either increase the bulk of the product or enhance the potency of the primary active component, are known as adulterants or cutting agents and can themselves be toxic [19,23,21].

### 4. CONCLUSION

A total of fifty samples of heroin collected in 2016 and fifty samples of heroin collected in 2017 in powder form, have been analyzed with set of pure standards, in the Forensic Laboratories in the State of Kuwait, by using GC/MS.

By comparing the results of the analysis of heroin samples in 2012, 2016 and 2017, the following conclusions are drawn: -

- **Heroin traded in the State of Kuwait through five years contain papaverine, noscapine, acetylcodene and 6-MAM with very closed values.**
- **The active substance (HER) diacetylmorphine witnessed a change during the five years from 2012 to 2017 by increasing in its concentration % in heroin traded in the State of Kuwait from 20% to 40% in 2012, to 10% to 50% in 2016, and to higher concentration of 30% to 70% in 2017.**
- **Main adulterate substances detected through five years from 2012 to 2017 are paracetamol, caffeine and diazepam, but differ in their % concentrations which are lower in 2016 and 2017 than in 2012collection.**
- **Methamphetamine and dextromethorphan are new adulterate substances detected in heroin 2016 and 2017 samples, with high % concentration, but in low number of samples. Another adulterate substance; namely, methylphenidate has been recorded only in one sample in 2017 collection, but absent in 2016 collection.**
- **The presence of the new adulterate substances in relatively few numbers of samples would suggest the increase in the purity of heroin traded in Kuwait in recent years (2016 & 2017).**

### COMPETING INTERESTS

Authors have declared that no competing interests exist.
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