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Particulates in Injection Solutions of Street Heroin in Israel - Potential Hazard

ABSTRACT

Of the addictive, controlled substances known to be abused in Israel, heroin is one of the more prevalent ones. It is often administered by intravenous injection. In the pharmaceutical industry, solutions for intravenous injection are strictly regulated by pharmacopeial quality assurance standards such as those outlined in Particulate Matter in Injections (USP 788). These standards stipulate pre-marketing tests that intravenous solutions must undergo before being approved. Some of these tests address particulate size and counts.

Much has been written about the dangers of abusing drugs like heroin, such as toxicity, addiction, infectious diseases, and death from overdose. This study highlights an additional hazard of heroin injection: injecting uncontrolled solutions that do not comply with pharmacopeial requirements may expose an injector's circulatory system to large quantities of large-diameter particulate matter.

In this study, heroin samples were prepared copying the methods used by heroin injectors to prepare street heroin for intravenous injection. The samples were diluted and acidified with citric acid, filtered through cotton wool, and then analyzed for quantity and size of particulates in the solutions. This study shows that particle size and quantity in these solutions greatly exceeded the permitted pharmacopeial thresholds for particulate matter in intravenous solutions. In the authors' opinion, this poses a real danger to heroin injectors, in addition to the drug's known toxicological and biological dangers.

Keywords: Forensic Toxicology, Heroin Injection, Particulates, Intravenous Solution, Heroin Injector, Particle Diameter

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INTRODUCTION

Diacetylmorphine is the chemical name of heroin, a semi-synthetic opioid narcotic. Although the medical world had initially welcomed the advent of heroin, it soon came to realize its hazards and recommended that its use and distribution be stopped. In 1914, the Harrison Act was passed, and production and distribution of heroin in the United States was banned [1]. In Israel, possession of any amount of heroin is forbidden by the Dangerous Drugs Ordinance.

Of all morphine derivatives, heroin is one of the most potent. Its physiological effects can be short term (e.g., digestive, respiratory, and central nervous system effects, and a general decline in body function), and its long-term effects include physical and psychological dependence [2-5].

Heroin users in Israel use the drug either by 'chasing' or by injecting. This study focused on the latter route. Chasing means placing some heroin powder on a piece of foil and heating it until the powder melts and forms a bead. By heating it, the bead is guided ('chased') along a creased piece of foil; as it moves it evaporates and the user inhales the fumes. Heroin injectors prepare a solution for injection by dissolving the powder in water so that it can be administered intravenously.

Users who inject heroin into their veins are exposed to the known direct effects of drug abuse (noted above), in addition to biohazards caused by non-sterile preparation conditions, water not specifically approved for intravenous injection, and contaminated needles and syringes [6-10].

The pharmaceutical industry is required to comply with rigorous quality standards as outlined in the three leading pharmacopeias (USP NF, EP, and JP) [11-15].

These standards prescribe tests that intravenous solutions are required to undergo before being approved for marketing. Some of these tests are for particle size. For example, a solution must be clear and may not contain visible particulates (estimated size is 50 μm or larger), and must pass the Light Obscuration Particle Count Test by electronic devices for counting and measuring particle size in solutions to quantify smaller particulates.

Blood corpuscles are ~4.5 μm in diameter and capillaries (the narrowest blood vessels in the human body) are ~5-8 μm in diameter. Theoretically, particulates smaller than this are less likely to cause a blockage (although there remains the risk of granulomas forming). These are the physiological dimensions that were used to establish a permissible particle size in solutions for injection [16].

Foreign particulates in solutions for intravenous injection are insoluble components originating in the drug dose itself or that are introduced when the solution is prepared and include bacteria or impurities from the syringe, stopper rubber, needle, cotton wool,

water, etc. Particulates that are injected directly into a vein can cause inflammation (phlebitis) or infection (abscess), blockages resulting in embolisms, ulcers, necrosis, and in extreme cases even death [6, 7, 9, 17].

Accordingly, and based on the results described here, this study proposes that intravenous injection of a solution, as typically prepared and injected by heroin users, may expose the heroin injector's circulatory system to life-threatening quantities of large-diameter particulates.

The authors obtained the necessary information for reproducing street methods of preparation through police intelligence. Particle counts and dimensions in the sample solutions were measured and compared with the pharmaceutical industry's standards.

MATERIALS AND METHODS

Materials

Heroin from random street doses of heroin seized by the Israeli police and held by the Israel Police National Drug Laboratory

Citric acid (Sigma)

Consumer cotton wool

Filtered water (ULC/MS-CC/SFC) (Bio Lab Israel Ltd.)

Sample Preparation

Five street doses were used to prepare the sample solutions for this study. For each sample, 100 mg of powder from a street dose and 25 mg of citric acid were dissolved in 2 ml of tap water. The mixture was stirred well for one minute. Next, the solutions were filtered through cotton wool and then tested for particulate dimensions and quantity.

For compatibility with the analytical instrument's requirements, the samples were diluted with filtered water to a final volume of 50 ml.

Instrument

Particle dimensions and quantity were measured using a particle counter (Nextar Chempharma Solutions LS-200 LIQUILAZ).

Samples were analyzed by gas chromatography/mass spectrometry (single quadrupole GC/MS; 7890B-5977B, Agilent Technologies).

The solution analysis was carried out by direct injection (1 µl by volume). The split ratio was 25:1. The GC was equipped with a DB-5MS-UI column (15 m x 0.25 mm x 0.25 µm film thickness). The oven temperature was programmed from 120 °C (held for 1 min) to 290 °C (held for 5 min) at 25 °C/min. The helium carrier gas flow was 1.1 ml/min.

The sample inlet port and transfer line were held at 220 °C, MS source at 230 °C, and quadrupole at 150 °C.

RESULTS AND DISCUSSION

The heroin used in this study to simulate preparation and use on the street came from packets that had been seized in Israel during several unrelated police investigations and sent to the Israel Police National Drug Laboratory (see Figure 1). All packets had been analyzed at the laboratory by GC/MS and heroin content was confirmed.

Figure 1: Street heroin packets seized by the police in Israel

In addition to heroin, these typical street doses also contained varying concentrations of common additives and impurities such as caffeine, paracetamol, as well as acetylmorphine, acetylcodeine, and narcotine (noscapine), Figure 2 [18].

Heroin powder on the market can be either in its alkaline form (free base) or the HCl salt. In its alkaline form the heroin powder is not water soluble, so it must be converted to a salt (which is water soluble) before a solution can be prepared. This is achieved by using an acid to protonate the alkaline heroin. Incidentally, street consumers may not be able to tell the difference between the two forms of heroin so they tend to always acidify their dose before injecting. This is most commonly done with citric or ascorbic acid (vitamin C) [16,19-21].

The samples prepared in this study were acidified with citric acid, then dissolved in tap water and filtered through cotton wool [22] which is the preferred street method reported by police informants. The samples were then run through a LS-200 LIQUILAZ particle counter and the data was analyzed and compared with pharmacopeial standards as specified in Particulate Matter in Injection (USP 788) and pharmacopeias (all the pharmacopeias specify identical standards).

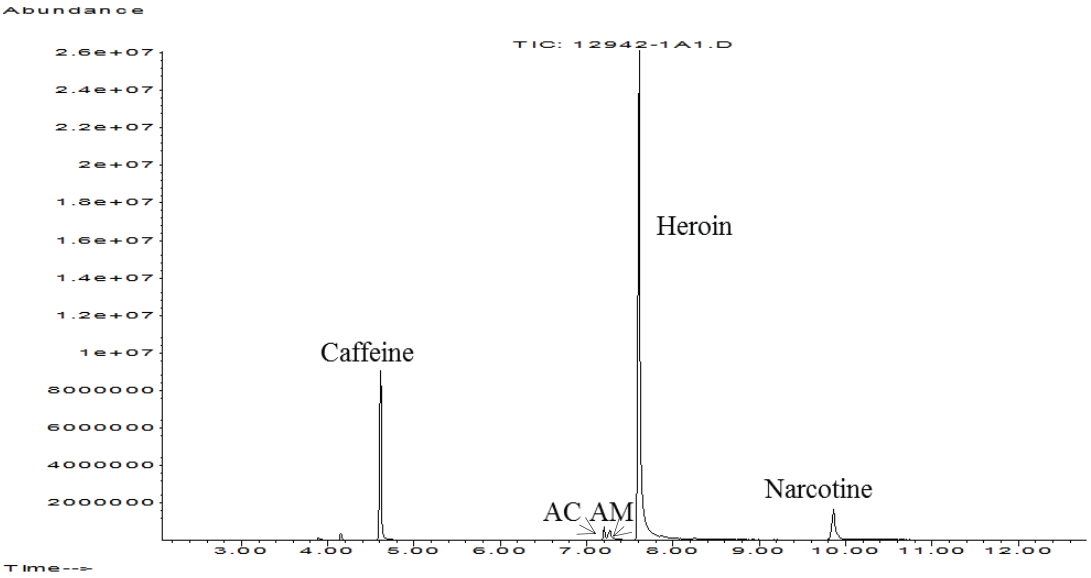

Figure 2: Typical GC/MS chromatogram of an Israeli street dose of heroin showing acetylmorphine (AM), acetylcodeine (AC), caffeine, and narcotine

For solutions of under 100 ml (as are solutions of street heroin injections), the pharmacopeia threshold for particulates of 10 µm in diameter or larger is up to 6000 particulates per container, and up to 600 particulates per container for particulates of 25 µm in diameter or larger (see Table 1).

Table 1: Pharmacopeia standard for intravenous injection solutions of up to 100 ml

Range	≥25 µm	≥10 µm
Number of particulates	600 per container	6000 per container

The cotton wool used to remove coarse particulates from the solution does indeed filter out large particulates, but at the same time is itself a source of particulates in the filtered solution [16]. Note that after this rough-and-ready filtration, visible particulates remained at the bottom of the test tube (see Figure 3), but as the particle counter used in this study decants the vials before scanning them, the deposit at the bottom of the vial is not reflected in the measurements.

Considering that these visible particulates were not counted (as noted above), the implications of our results may be much more serious.

Figures 4 and 5 compare the results obtained from the heroin samples to pharmacopeia standards.

Studies conducted at the National Drug Laboratory in the past have shown that in Israel a street dose weighs 0.8 g on average [18]. The results in Figures 4 and 5 were normalized for this weight.

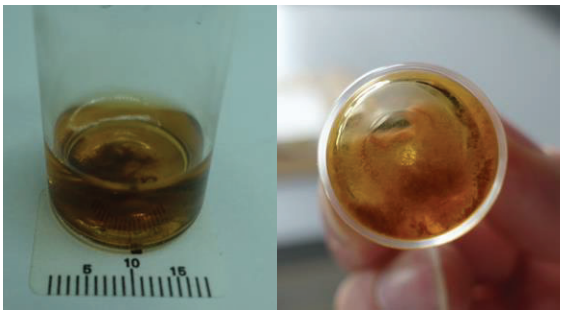

Figure 3: Solution of heroin in water following protonation and cotton wool filtration. Side view of the cloudy solution in the vial (3a); sediment at the bottom of the same vial (3b)

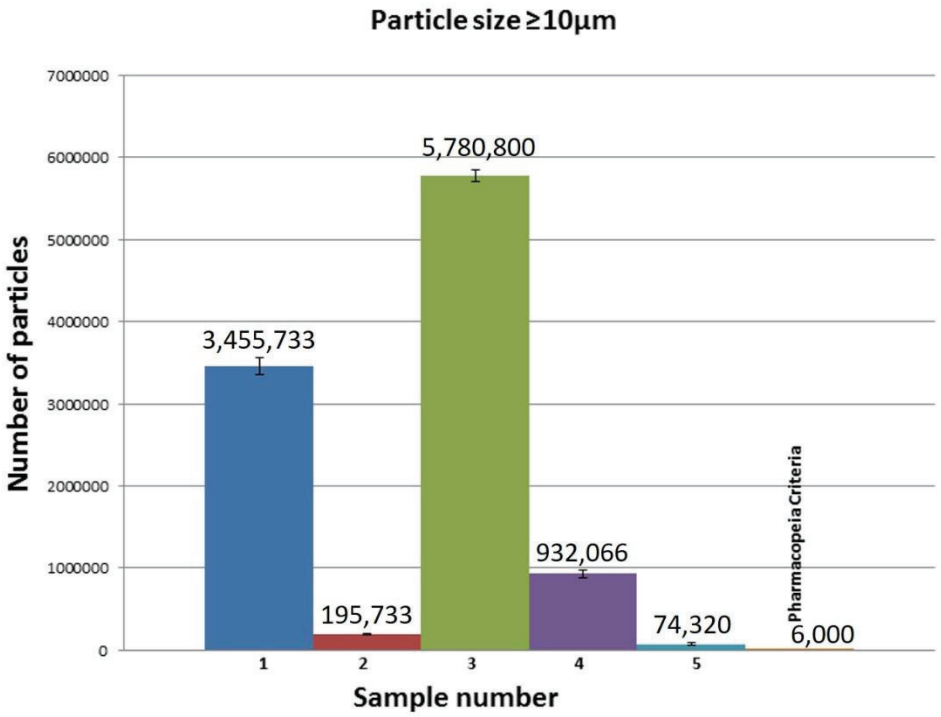

Figure 4: Number of particulates 10 µm in diameter or larger in the heroin samples (samples 1-5) compared with the pharmacopeia standard (right)

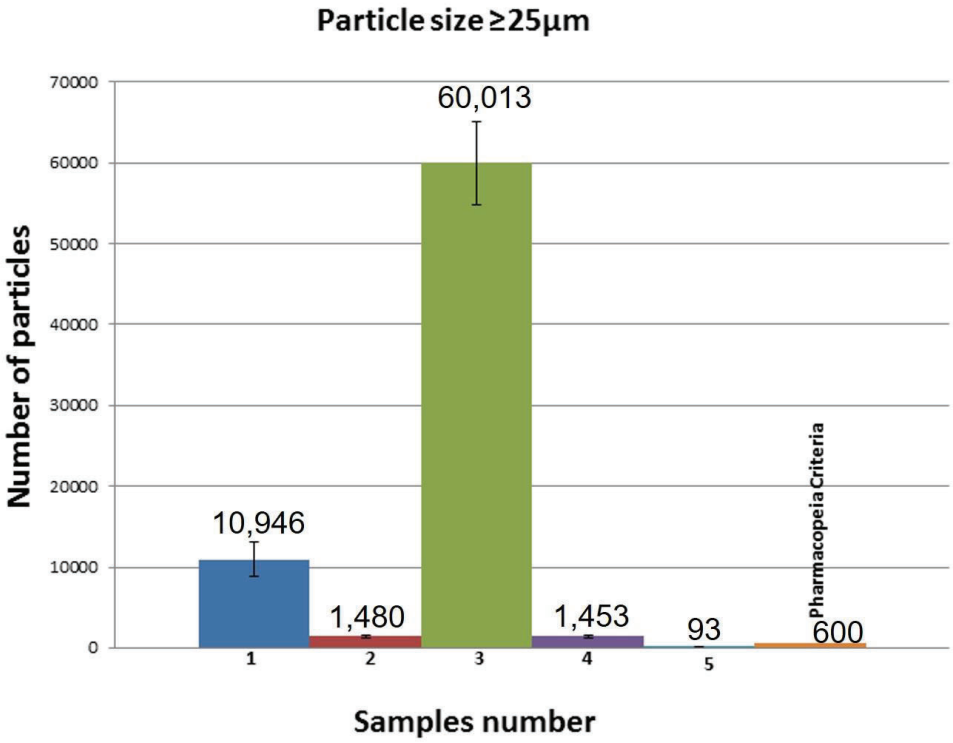

Figure 5: Number of particulates 25 µm in diameter or larger in the heroin samples (samples 1-5) compared with the pharmacopeia standard (right)

As can be seen in these figures, particle number and diameter greatly exceed pharmacopeia standards. For example, Sample 3 in measured 5,780,800 ±66,670 particulates of 10 µm in diameter or larger, where the pharmacopeia threshold is up to 6,000 particulates of this size (Figure 4). This exceeds the standard by 1000 times. The number of particulates measuring at least 25 µm was 60,013 ± 5,152 (see Figure 5), where the pharmacopeia requirement is up to 600 particulates of this size (exceeding the standard by 100 times).

The sample with the largest number of detected particles, Sample 5, still exceeded the pharmacopeia threshold for particles 10 µm or larger by 10 times (see Figure 4).

Sample 5 was the only sample that met the pharmacopeia threshold for particles 25 µm or larger (see Figure 5) but as the thresholds are cumulative, this sample as a whole was non-compliant.

Results show a great degree of variation between heroin doses regarding number of particulates per dose. This variation could be a result of the home-laboratory conditions in which these doses are manufactured (non-GMP, uncontrolled conditions). We note that although variation was great, none of the samples came close to complying with pharmacopeial requirements.

A diameter of 50 µm is huge in terms of physiological dimensions, so for obvious reasons, the pharmacopeias do not address these excessively large dimensions. However, the particle counter used in this study is capable of counting particulates of 50 µm or larger. Accordingly, in Samples 1-3 we found a few dozen particulates of these dimensions which pose an even greater danger to heroin injectors (data not shown). As noted above, these particles are in addition to the visible particulates that were not taken into account due to the way the instrument operates.

CONCLUSIONS

This study simulated the process of preparing a heroin solution for injection as it would have been prepared by a street user. The prepared solutions were acidified and filtered through cotton wool before counting particulates in each sample. Results show that particulate size and quantity in these solutions greatly exceed permitted thresholds for intravenous injection solutions despite filtration through cotton wool. Cotton wool, which is the filter of choice among heroin injectors, is evidently an inadequate filter and does not provide protection from particulate matter in the injected solution. Such inadequately filtered solutions are a real danger to heroin injectors in addition to the known toxicological and biological dangers of drug use itself.

The authors believe that it is advisable on the one hand to raise awareness of this among drug users who inject intravenously and encourage them to filter injected solutions correctly, and on the other hand to encourage authorities to supply drug users with suitable filters, syringes and needles.

A future study of interest to the authors is the examination of a possible correlation between concentration of heroin in a dose and the number of particulates in the solution of injection. A study of the presence of other narcotics in drug solutions for injection is also of interest in this discussion.

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