

Metal Contamination in Illicit Samples of Heroin

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ABSTRACT: We analyzed 198 illicit heroin samples from Andalusia (southern Spain) to determine the contents of various metals (cadmium, calcium, copper, iron, manganese and zinc) with a view to investigating a new aspect of the drug purity and the conditions under which the drugs are used by addicts. Calcium was found in 93.4% of the samples and always at high concentrations, which can be ascribed to adulteration of the heroin by addicts with thinners and excipients containing salts of this metal such as calcium bicarbonate. Also, all samples were found to contain variable amounts of zinc and substantial amounts of iron, probably because it is the most common metal found in metal containers used in the extraction of morphine from the opium poppy. Only cadmium and, to a lesser extent, zinc, copper, and iron, are among the metals detected in heroin that can increase the inherent toxicity of the drug while always taking into account the maximum values.

KEYWORDS: forensic science, heroin, metallics contaminants

One of the aspects to be considered in treating drug addicts, particularly those who use intravenous heroin injections, is determining the amount of drugs they take and their purity (i.e., the composition of the abused substances they use). This is crucial with a view not only to choosing an appropriate treatment for the addict but also to taking effective measures as regards the purely toxicological aspects.

According to the United Nations (1), the substances typically encountered in illicit heroin belong to four different groups, namely:

1. Excipients or thinners, which are usually pharmacologically inactive and used to dilute the drug.
2. Adulterants, which are added to the drug to conceal the scarcity of heroin.
3. Production impurities, the absence of which reveals that the drug was manufactured by specialty chemists.
4. Source impurities, the presence of which is suggestive of a coarser manufacturing procedure.

In addition, heroin may contain other contaminant substances reaching it by accident during its manufacture, adulteration or preparation. These contaminants can be of two types, namely:

1. Non-biotic contaminants, which are chemical substances such as some metals or atmospheric pollutants.
2. Biotic contaminants, the most important of which are bacteria and fungal spores; the microscopic size of which facilitates their spreading by air.

The composition and impurities of clandestine preparations of abused drugs have been studied by many authors in order to identify and distinguish consignments with a view to locating their sources and distribution channels. Studies have dealt with the appearance of the tablets (2), the characteristics of the excipients (3), the dye and additive profiles (4–6), the fungal profile (7,8), and impurities and contaminants (7,9,10–12).

Of special significance in this context is the work of van der Slooten and van der Helm (1), who studied the proportion of heroin, 6-monoacetylmorphine and morphine (HMM), in addition to the more common adulterants, in 32 samples from the black market. They concluded that heroin samples with the same proportion of HMM were from the same source and that those with the same adulterant composition might have gone through the same chain of dealers.

Regarding metals, parenteral administration is one possible vehicle for access to the human body; however, their toxicity is rather variable and more than arguable judging by the results of the few studies performed in this direction. For example, Van Ormer (13) used atomic absorption spectrophotometry (AAS) to determine various trace metals of toxicological interest and praised the advantages of this technique for the intended purpose. Other authors (14) used AAS to quantify lead in 40 heroin samples and noted the significant additional toxic effect of this metal on heroin users.

In one other of the few studies in this area, Garcia-Ferrer (15) examined the presence of aluminum, barium, calcium, copper, iron, lead, magnesium, manganese and zinc in 39 illicit heroin samples and concluded that metal contaminants exert a harmful effect on health that is closely related to the number of doses the addict takes. This toxicity, however, is not due solely to sample contaminants, but also to other factors such as the form of each contaminant, the way it is excreted and individual susceptibilities; as a result, the same contaminant dose can elicit different responses.

For the above reasons, in this work we analyzed illicit heroin from Andalusia (southern Spain) in order to quantify its contents in some metals with a view to examining a new aspect of the conditions under which it is taken by addicts.

Methods

Cadmium, calcium, copper, iron, manganese and zinc were quantified in 198 illicit heroin samples in the form of sachets that were supplied by the provincial offices of the Andalusian Health

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Council of the following provinces of the south of Spain: Cádiz, Córdoba, Granada, Huelva, Málaga and Sevilla. Metal contents were determined by using an atomic absorption spectrophotometer (Perkin-Elmer 370) equipped with appropriate univalent hollow-cathode graphite lamps for each element to be determined.

Samples of this type are usually mineralized either by using a wet procedure (viz. digestion in hot acid) or a dry one (calcination in an electrical furnace at 400 to 600°C). We chose a mixed procedure (14,15), which allowed us to operate at a fairly low temperature below the boiling temperatures for the metals. This avoided their volatilization and allowed us to use low volumes of HNO₃ in order to minimize the effect of the reagent blank. Samples were digested in a microwave acid digestion pump (16) (Model 4781 23 mL trifluoroethylene [Teflon™] reactor, Parr Instruments Co., IL).

The small amount of sample available in some cases precluded the determination of some metals. Also, some samples had to be concentrated in order to detect cadmium or diluted to quantify calcium. The concentration of each metal in each heroin sample was determined by interpolation of its absorbance in a calibration graph previously constructed from standard solutions containing known amounts of the specific metal.

Statistical Analysis

The AAS data obtained were subjected to a statistical treatment by using the BioMeDical Program (BMDP) software package. The variables considered for each sample were source, color and concentration of each metal in micrograms of metal per gram of heroin, and are given in these units throughout. The “source” variable identified the province from which the sample had been obtained (viz. Cádiz, Córdoba, Granada, Huelva, Málaga and Sevilla, which were assigned the numbers 1 to 6, respectively). The “color” variable described the types of heroin: 1 and 2 for samples of the brown and white variety, respectively. After variables were defined, discriminant, 2D univariate and correlation matrix analyses were performed.

Results

Calcium was encountered in most of the samples studied (93.4%); in fact, only 13 of the 198 samples did not contain this metal. The measured calcium concentrations were very high relative to the other metals; as can be seen in Table 1, only the iron levels approached those of calcium, and only in some samples. A fraction, 12.1%, of the samples contained calcium concentrations below 1000 µg/g; among the rest (87.9%) the highest Ca concentration was twenty-nine 924.9 µg/g (Table 1) found in the brown heroin samples.

Albeit at much lower concentrations, cadmium was found in 53.5% of the samples; by contrast 92 samples did not contain it. The maximum concentrations of this metal (548.7 and 531.2 µg/g) were encountered in the brown heroin samples (Table 1).

TABLE 1—Maximum, minimum and average values of metal (in µg) per gram of heroin.

	Ca	Cd	Cu	Fe	Mn	Zn
Minimum, >0	749.1	59.5	100.9	164.3	43.5	30.8
Maximum	29 924.9	548.7	2024.2	5661.9	1003.8	9705.4
Average	4903.6	66.6	173.1	1046.2	267.2	497.6

TABLE 2—Significant values of the correlation analysis between metals.

	Ca	Cd	Cu	Fe
Cu	...	-0.265†
Fe	0.284†
Mn	0.148*	0.239*	-0.155*	-0.144*
Zn	0.202*

* 95% of significance.
 † 99% of significance.

Copper was absent from 38.4% of the samples. Also, 79.5% of the samples that contained it had less than 600 µg/g of this metal. The maximum copper concentration, 2024.2 µg/g (Table 1), was found in brown heroin.

All 198 samples contained iron and in substantial amounts. The maximum and minimum concentrations (5661.9 and 164.3 µg/g, respectively) were found in two brown heroin samples (Table 1).

Manganese was always detected in small amounts. In fact, 12.1% of the samples contained no Mn. Among the others, the maximum and minimum manganese contents (1003.8 and 43.5 µg/g, respectively) were encountered in brown heroin (Table 1).

All the samples contained greater or lesser amounts of zinc, from 30.8 to 9705.4 µg/g, both of which were encountered in brown heroin (Table 1).

We also conducted a correlation analysis, the statistically significant results of which are shown in matrix form in Table 2. As can be seen, there was high, negative correlation between the presence of cadmium and copper, which suggests that the presence of one excludes that of the other. On the other hand, the presence of cadmium is related to that of manganese. Those samples that contain calcium also usually contain iron, manganese and zinc. Finally, the presence of manganese seemingly results in decreased amounts of copper and iron or vice versa.

Discriminant analyses were performed by using each metal in turn as the principal variable. The most significant results are given in Table 3. The purpose was twofold—to quantify the relative significance of the variables in order to classify samples into appropriate groups and, on the other hand, to predict in which group a sample not included in the analysis would fit.

With the cadmium concentrations above and below the mean as the principal variable, the classification function was constructed from three dependent variables: copper, manganese and zinc. The cadmium and copper concentrations in the sample appear to be inversely proportional, whereas that of cadmium, and the zinc and manganese contents, seems to be directly proportional.

The variables included in the discriminant function based on the copper concentration as the principal classifying variable (Table 3) were the calcium, cadmium and zinc concentrations. The copper content was inversely related to those of calcium and cadmium and directly proportional to that of zinc.

The discriminant analysis based on the iron concentration as the principal classifying variable selects calcium, cadmium, copper, manganese and zinc concentrations as potentially classifying variables. As can be seen from Table 3, the iron concentration is directly related to the concentrations of calcium and zinc, and inversely related to those of cadmium, copper and manganese.

The discriminant analysis of manganese selected the cadmium and copper concentrations as classifying variables. The manganese content is directly proportional to the cadmium content and inversely related to the copper content (Table 3).

TABLE 3—Classification function of each one of the discriminant analyses applied to each metal.

Classification Function	Variable	Ca	Cd	Cu	Mn	Zn	Constant
Cd	—	0.00155	0.00624	0.00026	— 1.99498
	+	0.00024	0.00837	0.00076	— 2.92996
Cu	—	0.00027	0.00456	0.00013	— 1.74192
	+	0.00016	0.00054	0.00109	— 1.74192
Fe	—	0.00017	0.00544	0.00262	0.00702	— 0.00026	— 3.08516
	+	0.00037	0.00181	0.00135	0.00349	0.00013	— 2.66809
Mn	—	...	0.00480	0.00215	— 1.66888
	+	...	0.00732	0.00107	— 1.43297
Zn	—	...	0.00600	0.00139	— 1.11901
	+	...	0.01019	0.00429	— 3.09472

Finally, the discriminant analysis based on the zinc concentration selected the cadmium and copper concentrations as classifying variables (Table 3), both of which were found to be directly related to the zinc.

Discussion

Microwave mineralization technology ensures the absence of interferences from the organic matrix of heroin.

The fact that heroin usually is administered intravenously facilitates incorporation of all the metals present in the drug into the bloodstream, free from the constraints of transfer mechanisms across intestinal mucosa. However, based on the concentrations measured in this work and the typical doses used by addicts, the metals will have a limited toxic potential if no concomitant contaminants are involved.

Despite the scarcity of literature pertinent to the topic, our results show that, in some cases, the presence of a given metal in heroin can be related to the presence or absence of another metal (Table 3). Goyer (17) claims that the toxic effects of a metal on an individual are modulated by the presence of, and interactions with, other metals. These data suggest that the metals encountered in heroin samples may interact with one another. Also, one should take into account that the metals are frequently not present in free form, but as salts. As can be seen from Table 2, cadmium is absent whenever copper is present in a sample, and so is manganese if copper or iron is present. This makes us suspect that the presence of one of these metals must therefore somehow control whether the other contaminates the sample. Conversely, the metals in the iron-calcium, manganese-cadmium, manganese-calcium and zinc-calcium pairs require the presence of each other, which suggests that they reach heroin samples via the same routes. However, the presence of some metals in heroin samples is seemingly not sufficient to establish their origin or their pathway to the addict.

The high concentrations of calcium encountered in most of the samples could be explained to their adulteration by addicts, who frequently use thinners and excipients containing salts of this metal (calcium bicarbonate, ascorbic acid, vitamin C), in addition to other substances such as bicarbonate, talcum powder or chalk.

The high concentrations of iron encountered in the samples could be explained because iron is probably the most common metal found in metal containers used in the extraction of morphine from the opium poppy, and then in the further acetylation of morphine to heroin. These metal containers are exposed to very high and very low pH values, and high temperatures in these processes. These extremes will result in leaching of iron and other metals from the processing containers followed by the re-adsorption by the resultant analytical products.

Only cadmium among the metals measured in the illicit heroin samples studied is regarded as toxic (17). Based on this and on our results, we concluded that the potential toxicity of the metals studied at the concentrations found is relatively low. Only cadmium and, to a lesser extent, zinc and copper and always at the highest concentrations found, might add to the intrinsic toxic effect of the drug. In any case, one must always consider the susceptibility of each individual, such as the effects of cumulative doses due to the frequency of the drug's administration. In fact, cadmium accumulates in the body because it cannot be efficiently excreted. On the other hand, zinc and copper may reach the addict at high concentrations but are easily excreted via urine so they will hardly attain toxic levels.

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ERRATA/CORRECTIONS

We have identified a number of instances in which the authors of work published in the Journal of Forensic Sciences have miscited papers originally published in the Journal of the Forensic Science Society as having been published in the Journal of Forensic Sciences.

The known instances of this error for volume 44 of the Journal of Forensic Sciences are detailed/corrected below. We have not checked other volumes for similar errors. The Journal of Forensic Sciences regrets these errors.

Since 1995 (Volume 35), the Journal of the Forensic Science Society has been published under the title "Science and Justice."

The editors of both journals take this opportunity to remind authors of the necessity for ensuring the accuracy of the references they cite in manuscripts submitted for publication. The Instructions for Authors of both journals make it clear that accuracy of reference citation is the responsibility of authors, and good scholarship demands attention to this matter.

A. R. W. Forrest R. E. Gaensslen
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The journal citation in reference 7 in Foreman LA, Smith AFM, Evett IW. Bayesian validation of a quadriplex STR profiling system for identification purposes. should read: *J Forensic Sci Soc* 1992;32:5–14.

The journal citation in reference 5 in Bourel B, Hedouin V, Martin-Bouyer L, Becart A, Tournel G, Deveaux M, Gosset D. Effects of morphine in decomposing bodies on the development of *Lucila sericata* (Diptera: Calliphoridae). should read: *J Forensic Sci Soc* 1991;31:469–72.

The journal citation in reference 8 in Hedouin V, Bourel B, Martin-Bouyer L, Becart A, Tournel G, Deveaux M, Gosset D. Determination of drug levels in larvae of *Lucila sericata* (Diptera: Calliphoridae) reared on rabbit carcasses containing morphine. should read: *J Forensic Sci Soc* 1994;34:95–7.

The journal citation in reference 15 in Hedouin V, Bourel B, Martin-Bouyer L, Becart A, Tournel G, Deveaux M, Gosset D. Morphine perfused rabbits: A tool for experiments in forensic entomotoxicology. should read: *J Forensic Sci Soc* 1991;31:469–72.

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The journal citations in references 4 and 5 in Infante F, Dominguez E, Trujillo D, Luna A. Metal contamination in illicit samples of heroin. should read for 4: *J Forensic Sci Soc* 1979;19:203–9. and for 5: *J Forensic Sci Soc* 1980;20:177–81. [in reference 5 only the volume number is miscited]. And in both references, the lead author's name is "Joyce JR."

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