HEROINE - INSTRUMENTAL METHODS OF QUALITATIVE AND QUANTITATIVE ANALYSIS

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Rezumat

Heroina este un drog foarte puternic, care este răspândit aproape în întreaga lume, disputându-şi întâietatea (în ceea ce priveşte numărul de consumatori clandestini, cantităţile traficate şi câştigurile ilicite realizate de traficanţi) cu cocaina.

Metodele de analiză prezentate sunt legate de proprietăţile fizice şi chimice ale heroinei şi prezintă capacitatea de a face o determinare calitativă şi cantitativă. S-a avut în vedere, atât prezentarea acestor metode din punct de vedere al economicităţii, simplităţii şi a tehnicii de lucru, cât şi prezentarea informaţiilor asupra performanţelor acestora.

Abriss

Heroin ist ein sehr gefährliches Rauschgift, in der ganzen Welt ausgebreitet und zwischen den meist gebrauchten neben Kokain.
Die dargestellten Analysenmethoden erlauben eine qualitative sowie auch eine quantitative Bestimmung. Es wurde beabsichtigt die Sparsamkeit sowie auch die Empfindlichkeit den Analysenmethoden.

Résumé

L'héroïne est une drogue très forte, qui est répandue presque dans tout le monde, en disputant sa primant (concernant le nombre des consommateurs clandestins, les quantités trafiquées et les gains illicites réalises par les trafiquants) avec la cocaïne.

Les méthodes d'analyse présentées sont liées aux propriétés psysique et chimiques de l'héroïne et, présentent la capacité d'en faire une détermination qualitative et quantitative. On a eu en vue aussi la présentation de ces méthodes du point de vue économique, de la simplicité et de la technique de travail que la présentation des informations sur les performances de celles-ci.

Nowadays, one of the most profitable businesses all over the world is the drug dealing. This is because, once the client "seized", he becomes loyal to the product he takes, especially to heroine.

It has been proved that heroine produces physical and psychic dependance in the case of 97% of the addicts, in an interval of up to 21 days from the first snuff. This drug has an addictive influence on the consumer's personality, being five times more toxic than morphine. Actually, it is known that heroine is the most liposoluble opiate substance and, in the same time, it crosses the hemato-encephalic limit at full speed, so, its toxicity is really increased.

At the same time, heroine has, even in small doses, a brutal effect on the organism, and the limits of the overdoses are difficult to establish. That causes and also explains its highest mortality ratio. [Se 98]

Heroine is a semisynthetic drug, resulting from the acetylation of morphine, which, in its turn, is a natural product extracted from the opium latex. It is known that Asia is one of the greatest opium producers in the world, with an impressive seniority comparing to Latin America.

It's no longer a novelty that, after 1989, Romania became a transit territory for the majority of drug – dealers who transported drugs from Orient to Western Europe. Only one

year afterwards, Romania is violently "beset" by the drugs phenomenon, already having drug addicts, channels of drug - dealers, polls of the sale market. [Ţi 03]

Most of the drug addicts take their dose not for obtaining that mood of "well – being", but in order to get rid of the physical and psychic mood that the consumption of these substances produces upon the addict's body.

Heroine's toxic effect and, respectively, its dangerous influence become obvious with a 2 cg dose taken by an individual, while its use in therapy doesn't need more than 2-4 mg. Heroine's toxicity can be explained by its ability to functionally demolish the cells, not only the cerebral ones, but also the other types of cells in the human body.

The physical or psychic perturbations that the heroine's use brings about, as in any other toxicomania, are general, involving the whole body, respectively all the mechanisms of defence and adapting equilibration: psychic, neuro-endocrine, humoral-metabolic mechanisms.

The following reactions can occur in the interval between 2 snuffs: psychomotor excitement, insomnia, perspiration, muscular and articular pain in the limbs, anorexia, nausea, vomiting, diarrhoea, dehydration, tachycardia, high blood pressure, amblyopia (if heroine is mixed up with quinine), lung granulomas (when it is mixed up with talcum), lung oedema, etc. [Se 98]

The methods of instrumental analysis presented before are connected to the physical and chemical properties of heroine and they have the capacity to make a quantitative and qualitative determination. These determinations are very sophisticated and they can be realized from various biological mediums (blood, urine, hair, saliva, tissues, etc), from drinks and mixtures of solid particles.

After oral or injectable administration, heroine is quickly absorbed. In blood, it is quickly hydrolysed to 6-monoacetylmorphine, which is then turned to morphine, this being the major metabolite. From a heroine addict's dose, more than 80% is eliminated in 24 hours through urine. The metabolites that can be detected under these circumstances are: morphine-3-glucoronide; 6-monoacetylmorphine. [Co 95]

Spectrophotometric methods of analysis

1. Spectrophotometry in U.V.

Heroine can be determined through spectrophotometry in U.V., by measuring the absorbance of the solutions containing heroine at the wavelength adequate to the maximums of absorption. That is: in a basic medium, the wavelength suitable to the maximum of absorption is λ=299 nm, in hydrochloric acid 0,1N, λ=278 nm, in sulphuric acid, λ=281 nm and ethanolic solutions λ=281 nm. The values obtained for the absorbance of some test solutions containing heroine are compared to those of some ethanol solutions, with a known concentration, and the value of the sample concentration can be determined through some methods of calculation (the method of the calibration curve, the method of standard addition, etc.). [Pi 99]

2. Spectrophotometry in I.R.

Spectrophotometry in I.R. can be used both to identify and to determine quantitatively the heroine from various types of samples. For example, the samples are analysed by using a Perkin–Elmer-1420 spectrometer. The spectres are registered in the intervals 1800-1500cm^{-1} and 960 - 860cm^{-1}. The registered spectres are stored in the memory of a computer and analysed with a special Perkin-Elmer-Sean-IR soft. This soft allows the

identification up to a value of concentration of 5%. The domain 1800-500cm^{-1} is suitable for the identification of solvents. The technique can be applied to the analysis of the mixtures containing heroine or cocaine. [Lo 95]

3. Spectrophotometry through atomic absorption

The metallic elements can be determined mainly by means of spectrophotometry through atomic absorption. This method will be employed in order to determine the metals in the traces of drugs, in what represents a "print" of the drug. Thus, one can establish the origin of the drug, that is, where the drugs come from and also the labs where the morphine was acetylated. Some examples of metals that can be determined by using this method and their detection limit are shown in table 1:

Table 1

ELEMENTS DETERMINED THROUGH AAS AND THEIR LIMIT OF DETECTION

Crt. no.	Compound	λ (nm)	Detection limit
1.	Aluminium	309,3	48 µg/ kg
2.	Strontium	460,7	17 µg/ kg
3.	Silver	328,1	9,3 µg/ kg
4.	Manganise	279,5	6,9 µg/ kg
5.	Copper	324,8	3,9 µg/ kg
6.	Chromium	357,9	5,8 µg/kg
7.	Nickel	232	32,1 µg/kg
8.	Lead	283,3	31,4 µg/ kg

Spectrometric methods of analysis

1. Mass spectrometry.

The mixtures of alkaloids can be determined directly through mass spectrometry, by ionisation with electrospray. The method suggested shows that the direct the direct analysis through mass spectrometry by electrospray ionisation, without the chromatographic separation of the components, can be used for the quantification of some simple alkaloid mixtures, if an extended version of the Kebarle and Tang methods is used for a mixture of two components (conformity Analytical Chemistry, 1983, 65, 3654). The method was used to determine heroine, 6-O-6-acetylmorphine, acetyl codeine, papaverine and nicotine in heroine samples. The solutions of the samples prepared in methanol 50% are acidulated with acetic acid 1% and are submerged directly inn a ionisation source of a mass spectrometer, with a Finnigan-TSQ-700 treble quadruple, and the analytes are detected by SIM (Selected Ion Monitoring - the pursuit of a single selected ion), where the domains of the M/Z values are: 327,7 and 328,7 for 6-O-6-acetylmorphine; 339,6 and 340,4 for papaverine; 341 and 342,7 for acetylcodeine; 369,7 and 370,2 for heroine and 413,7 and 414,7 for narcotine.

"The efficiency of ionisation"(the constant value from Kebarle and Tang model) presents a dependence having the concentration of the total alkaloids. [Se 98]

2. Mass Spectrometry Inductively Coupled (ICP-MS)

For the preliminary analysis of heroine, one can determine its "print" using the concentrations of the elements in the traces. Thus, 30 mg of sample heroine are weighted in plastic pipes and dissolved in 10 ml of nitric acid 3%. Each sample is blended with an internal

standard solution (5 ppb) in order take into account the fluctuations in the reply of the instrument. The samples are aspired directly in an ICP Perkin-Elmer ELAN-5100 analyser, equipped with a quadruplar mass spectrometer. The minimum detectable concentrations for many elements are of approximately 0,3 ppb. Concentrations larger than 3000 ppb are outside the calibration domain. In order to establish which samples originate in South-Eastern Asia, the analytic data are analysed using logistic models combined with hierarchical clusters, medium K clusters, correlation factors and the analysis of the main components. The predictive values are of 68 –100%.

3. The Analysis Through Diffraction with X Rays

The X rays diffraction spectrum was created for the analysis of heroine. The data resulted show that heroine has an orthorhombic crystallization system, the basic vectors of the primitive cell being of: 8,003; 14,373; 16,092 X 10^{-10}m. Through this method, we can analyse opium, heroine, but also sample in which heroine is impurified with sugar, salt, etc. [Hu 99]

The Electrochemical Methods

From the category of the electrochemical methods of analysis, the specialized literature mentions the *amperometric methods*.

Holt & Co. describe an amperometric study that is used in porder to determine heroine (I), morphine (II) and morphine-3-glucoronide (III). Pheneasyne metasulphate is used as a mediator. Heroine esterase's hydrolyses the acetyl groups from heroine's C_3 and then from heroine's C_6, forming morphine by means of 6-acetylmorphine. Morphine dehydrogenase oxidizes the hydroxyl group from C_6 in the morphine molecule, forming morphinone and NADPH. NADPH reduces the mediator molecule, which is then reoxidized at the surface of the electrode, generating thus a signal.

Freshly made solutions, with a total amount of 100 µl, are used for each study. Morphine-3-gvlucoronide can't be measured directly, but only after preincubation with glucoronydase. The detection limits are: 28; 16,2; 6,8 µg/ml for heroine, morphine-3-glucoronide and morphine. Heroine and morphine give a signal after 2 or 3 minutes, and morphine-3-glucoronide after 10 minutes. [Ho 95]

Heroine can be determined *voltametrically* in powder. Samples of 15 mg are dissolved in 10 ml of $HClO_4$ 10M. A portion of 1 ml of this solution is inserted in an electrolytic cell containing 10ml of Britton-Robinson blotter solution (pH=6). The voltamograms are registered between 5 and 1,3 V at a potential modification speed of 20 mV/ s, using an electrode with carbon paste. The method of standard addition can also be used. The results obtained coincide with the ones obtained through HPLC, but this method has some advantages, such as: it is simple, fast and cheap. [Ba 90]

The chromatographic methods

1. Gas Chromatography

This method is one of the most modern separation methods. The latest experiments in this domain proved that the derivation with N, O-double-trimetylsiliacetamide or double-trimetylsilyl – 2,2,2 – trifluorineacetamide leads to an efficient separation of all the opium components.

Heroine's analysis through gas chromatography raises important problems, owing to the transacetylation between morphine and diacetylmorphine. Nowadays, specialists try to find some shutting off agents in order to prevent transacetylation.

The samples that are analysed in order to emphasize the presence of heroine and its metabolites in the lethal cases are drawn from some tissues (liver, brains, spleen, hair, etc) and from the biological liquids (urine and blood). Through the analysis of the foetus's hair, one can emphasize the exposure to heroine or narcotine during pregnancy. Amounts of 4 - 37mg of hair sample (from the new - born children) and approximately 50mg of hair sample from the mothers are collected for five days from birth. The hair samples are processed and analysed according to the Kintz method (Forensinc SCI. Int., 63, 77, 1993).

The saliva can be used as a "witness" for some drugs, by comparing the heroine concentration in saliva and in blood. Saliva and blood are analysed in order to determine heroine-6-acetylmorphine and morphine, through extraction in solid stage and GC-MS (according to Goldberger method, Clin. Chem., 39, 670, 1993). Through this method, one can represent the excretion profile of the drug administered in different ways. [Je 95]

In order to determine the origins of the heroine samples, one can use the isotope C^{13} analysis. The differences in the C^{13} content of the heroine samples originating in distinct geographical areas occur because the alkaloidic part (morphine) reflects the geographical provenance, and the acetyl part reflects the acetylation source that was used (synthesis).

Thus, the isotopic analysis was applied to the isotopic fractional distillation during the morphine acetylation. The samples of 1 µl are analysed on a DB- column (30 m X 0,25 mm X 0,25 µm), with the following temperature programme: from 180°C (constant for 1 minute), the temperature grows with 40°C/minute up to 300°C (constant for 9 minutes). The carrying gas is the helium (110 kPa) and the detection through ionisation and flame or mass spectrometry, by means of a combustion interface. Through combustion, the organic components are turned into CO_2 and water. The water is condensed using a cryogenic trap at – 100°C± 1°C; CO_2 is analysed through mass spectrometry in the SIM way at the following values of the M/Z report: 44, 45, 46 in order to emphasize the report C^{13}/C^{12}. The results are correlated to the isotopic enrichment given by the acetylation agents used by the drug - dealers. The isotopic differences obtained when different acetylation agents are used, are inserted in a data base, which helps to identify the fraudulent laboratories involved. [Be 97]

In table 2 are emphasized the experimental conditions concerning the column, the temperature system, the mobile phase used, the detection and the samples analysed.

2. Highly Performant Liquids Chromatography (HPLC):

This method is characterized by a sensitiveness superior to chromatography on thin layer. Theoretically, it functions in a column under pressure, filled with a blotter – silica or alumine -, where preparations from the substance that is to be identified are injected. When emerging from the column, the specific elements are detected through various physico-chemical methods.

Certainly, the highly performant liquids chromatography is the most precise and sure method in the drugs analysis. Through this method, one can better separate the opiates, cocaine (even combined with other local anaesthetics), amphetamines, hallucinogens, barbituric derivatives and cannabis. It has to be mentioned that the opiates, the amphetamines, the barbituric derivatives and the cocaine have properties favourable to the detection through gas chromatography, a reason for which, when we take into account such substances, the highly performant liquids chromatography is seldom used.

In table 3 are illustrated some methods to determine heroine through HPLC.

Table 2

METHODS OF DETERMINATION THROUGH GAS CHROMATOGRAPHY

Crt. no.	Column	Temperature regime	Mobile phase	Detection	Sample
1.	HP-5	120°C (constant for 2 minutes) up to 280°C (constant for 10 minutes), at a temperature increase speed of 20°C/ min	helium	MS	watery humour and LCR
2.	DB-1	180°C (constant for 1 minute) up to 290°C (constant 12 minutes), at a temperature increase speed of 30°C/ min	helium	MS	powders
3.	BP-1	150°C (constant for 2 minutes) up to 300°C, at a temperature increase speed of 9°C /min	nitrogen	FID	powders
4.	HP-5	60°C (constant for 1 minute) up to 295°C (constant for 6 min), at a temperature increase speed of 30°C/ min	helium	MS	hair
5.	HP-1	170°C up to 280°C with 10°C/ min	helium	MS	urine
6.	HP-5 MS	–	helium	MS	biological fluids, tissues and hair coming from mother and foetus
7.	TC-1	20°C, starting from 60°C (constant for 0,5 minutes) and getting to 280°C (constant for 5 minutes)	helium	MS	hair
8.	Jand W-DB-5	387°C/ min, between 150°C (constant for 2 minutes) and 200°C, and of 20°C/ min. between 200-290°C (constant for 7 minutes)	helium	MS	hair
9.	methyl-silicone	40°C (constant for 1 min.) up to 200°C, at a temperature increase speed of 25°C/min. and respectively, 4°C/min. up to 300°C (constant 15 minutes)	helium	MS	powders
10.	BP-10	240°C	helium	MS	urine

Table 3

METHODS OF DETERMINATION THROUGH HPLC

Crt. No.	Stationary phase	Mobile phase	Detection	Sample
1.	Lichrosobe PER-60	KH_2PO_4 10mM/heptane sulphonic acid 2mM adjusted to pH= 2,5 with phosphoric acid and acetonitryl (92,5: 7,5)	excitement at 235 nm and emission at 345 nm	blood
2.	LC-18-D13	water/acetonitryl (7:3), containing monosodic phosphate 0,01 M and sodium sulphate lauryl 2 X 10^{-3} M, adjusted at pH= 2,1 with phosphoric acid	254 nm	hair
3.	Ecocarte	ammonium formate 50mM/ acetonitryl (19:1)	MS	biological fluids
4.	Supercosyl	methanol/ acetonitryl/ water/ formic acid (1196: 104: 693: 7)	fluorescence	plasma
5.	C 18 Nova-Pak	acetonitryl/ammonium acetate 2mM (4 :1)	MS	wheat
6.	Hypersyl	dichlormethane/pentane/methanol, containing 0,5 % dietylamine (29,8: 65: 5,2)	U.V. 280nm	urine
7.	Adsorbosphere HS- C18	acetonitryl/ blotter phosphate 0,02 M at pH =7-7,4 (2:3)	amperometric	vapours and aerosols
8.	Partisyl ODS	methanol gradient in blotter phosphate at pH=2, containing sodium sulphate dodecyl 0,02 M	U.V.	powders

Other methods of analysis:

1. Electrophoresis

Heroine's analysis can be made through capillary electrophoresis. Thus, 1,5- 2 ml of blood or 5 ml of urine are submitted to the analysis, extracting in solid phase with 0,3 ml GDX-301 in water/methanol solution by stirring for 20 minutes. The liquid is eliminated, the solid phase is washed with water and dried, and the drugs are eluted with methanol. A portion of eluate is inserted in a column (60 cm X 50µm) and a tension of 25 kV is applied. The blotter solution used is made of NaH_2PO_4 0,1M pH= 4,5, containing 25% of methanol. The detection is made in U.V. at 214 nm. Metamphetamine, ephedrine, cocaine, morphine, triacetylmorphine, heroine and papaverine are very well separated. The extraction on C18 column with inverted phase leads to similar results. The calibration diagrams are linear, the regression coefficients being included in the interval 0,9979 - 0,9999.

The detection limits are 0,3-5 mg/ l. [Me 99]

Another method of analysis through mycellar electrokinetic's chromatography for electrically charged or neutral substances uses standard solutions containing amounts of 100µg/ml procaine, morphine, codeine, heroine, noscapine, papaverine, nicotinamide, caffeine, barbitone, paracetamol, allobarbitone, phenobarbitone and diphenylhydramine (internal standard). The powder samples are dissolved in the blotter solution (0,5 mg/ml) and

the internal standard is added (50 µg/ ml). The samples are hydrodynamically injected in the capillary (65 cm X 50 µm, 60 cm up to the detector). The working tension is of 27 kV. The blotter solution is made of 6-aminocapronic 50mM, 3-N,N-dimetyl-miristyl-aminopropane-sulphonate 50mM, 1-heptane sulphonic acid 5mM and acetonitryl 10%, with the pH adjusted to 4 with phosphoric acid. The detection is realized at 214 nm. Water and methanol are used as electroosmotic markers, and the dodocamphenone as a mycellar marker.

The system realizes a partial separation only for the opiate alkaloids positively charged, and the neuter substances, such as the barbituric substances, caffeine, paracetamol, are not separated in the absence of some surfactants, but a satisfactory separation of all the 12 components is generally produced. [Na 97]

2. *The Flow Injection Analysis- FIA*

This method is used in order to determine codeine, heroine and dextrometorphone. It is based on the detection of the chemiluminescence electrochemically obtained. The results are comparable to those obtained through GC-MS method. [Gr 95]

3.The Radioimmunological Methods (RIA):

The RIA method can be applied in order to determine the morphine distribution in the biological fluids, in the heroine addicts' case. Thus, blood, urine, the glassy humour and the cerebrospinal fluid are directly analysed. The bile samples are alkalised with 1 ml of $NaHCO_3$ saturated solution, extracted with 2 ml CH_2Cl_2/ 2-propanol (9:1) and centrifuged. The organic layer is dried under nitrogen flow at 38^{0}C, and the residue obtained is dissolved in 2ml of serum. We measure an amount of 25 µl from the solution obtained, which is analysed through RIA. [Wa 93]

Another RIA method uses quantities of 50 – 100mg of hair samples, which are incubated for 2 hours at 37^{0}C in 2 ml of hydrochloric acid 0,1M, after which we add 1 ml of blotter solution (formed of 0,1 ml sodium hydroxide 2M and 0,9 ml blotter acetate 1 M, pH=6). The RIA analysis is done using standard Kituri for morphine, Coat a Count Opiates Screen for opiates and Double Antibody 6MAM RIA for 6-monoacetylmorphine. The minimum suitable values are: 4ng morphine/ml eluate and 1ng/ml eluate for 6-monoacetylmorphine. In the analysis of 50 hair samples coming from the patients who haven't taken opiates, the medium values found are: 0,15 ± 0,8ng/ ml of eluate (Kit Opiates Screen) and, respectively, 2,3 ± 8,2ng/ ml eluate (Kit—Morphine). The method is used in order to differentiate the results obtained on hair samples taken from persons who abuse of heroine, in comparison with those who take it in therapeutically dose.

Conclusions

The drugs scourge is one of the most complex, profound and tragic phenomena of the contemporary society. Every year, millions of people fall a prey to the drugs and a percent greater and greater of them are completely lost for the society. Nowadays, when we know to a large extent the incidence of drugs on peoples' health, we are able to become aware of the disastrous consequences of the drug consumption throughout centuries, since the drugs became to be used.

Nobody will ever be able to carry out a statistics of the direct victims of drug abuse, but, on the basis of the existing data, we can qualify this phenomenon as a real calamity of the contemporary world.

The heroinomania has spread so rapidly that, at present, on the basis of the medical and sociological investigations effected by OMS, it is considered that 80% of the world's toxicomaniacs (50 millions) use heroine.

As for the methods of instrumental qualitative analysis, they are based on the chemical properties of heroine, but also on some physico-chemical methods of separation or

identification (chromatography, spectrophotometry, etc). The methods of quantitative determination of heroine from various mediums (biological or non biological) through instrumental techniques, allow us to determine the value of the substances' concentrations with a great selectivity and sensitiveness.

The target of this paper was not only to present these methods from the economy, simplicity and working technique's point of view, but it also contains information on the performances of these methods.

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