

SURFACE IONIZATION MASS SPECTROMETRY. SELECTIVE DETERMINATION OF TRACE AMOUNTS OF OPIOIDS IN URINE

Utkur K. RASULEV¹, Usman KHASANOV¹, Turgun K. ISLAMOV²,
Makhamudjan M. SHAKHITOV³, Dilshod T. USMANOV¹

¹*Arifov Institute of Electronics, Tashkent, Uzbekistan*

²*Republic Forensic Research Center, Tashkent, Uzbekistan*

³*Republic Bureau of Forensic Medicine Expertise, Tashkent, Uzbekistan*

ABSTRACT: In this paper, for the first time, the results of surface ionization-mass spectrometry (SI/MS) of urine samples of the users of poppy juice, poppy “tea”, heroin and others opioids are presented to compare of results the samples have been studied by TLC and GC/MS, the latter with the HP-5890 device. High selectivity and few lines of SI mass spectra make it possible to identify, with the high accuracy, the samples with the sensitivity exceeding that of the well-known methods of analysis and without their chromatographic separation, for toxicological laboratories to work without false-negative results.

KEY WORDS: Surface ionization; Opiates; GC/MS.

Problems of Forensic Sciences, vol. XLIII, 2000, 237–242

Received 9 September 1999; accepted 16 May 2000

INTRODUCTION

Now in Central Asia the volume of illegal turnover of opioid narcotics, especially heroin, has sharply increased where Uzbekistan is used as the transit country. Recently, the use of narcotics has become more frequent. The narcological situation in Uzbekistan strongly requires the development of express and highly sensitive methods of narcotics detection and identification in biological solutions.

It is known that, owing to rapid metabolism in a body, the establishment of the primary structure of abused opioids is a rather difficult problem in analytical toxicology. The difference between medicinal preparations with opioids and abused heroin is considered in [3] where a method of the abused opioid determination by processing GC/MS data for urine was proposed. In spite of intensive studies in this direction, the problem of determination the trace amounts and identification of the abused opioid structure remains unsolved.

Surface ionization of organic and bioorganic compounds as an effective and selective method to ionize nitrogen bases has been proposed relatively recently [4]. Now the general regularities for surface ionization of nitrogen-containing organic

compounds have been established. They allow the prediction of SI mass spectra [2]. The nitrogen base ionization is $\sim 10^2$ effective than the ionization by electrons. Hydrocarbons, alcohol, ketons, aldehydes and other solvents can not ionized by surface ionization. The ion composition is simple and characteristic and contains quasimolecular ions. This allows the analysis of mixture of nitrogen bases without their preliminary separation.

The narcotic compound, according to the established regularities [2], must effectively ionized by surface ionization because in opioids there is one nitrogen heteroatom that is located in the tertiary position. Therefore, SI/MS is very perspective for opiate analysis, allowing not only the establishment of the very low thresholds of the detection of the trace amounts of some psychotropic preparations and narcotics [1], but also the analysis of opiates and their metabolites without their preliminary separation.

The goal of this work is to develop new, express, highly sensitive and selective methods of determination of the trace amounts of opioids in biological solutions, the establishment of the primary structure of abused opioids, because they are rapidly decayed and withdrawn from a human body.

MATERIALS AND METHODS

Experimental and conditions

Experiments were carried out using a standard mass-spectrometer MI-1201V modernized for surface ionization studies. An oxidized tungsten band with the size of $1 \times 12 \times 0.02 \text{ mm}^3$ was used as a thermoemitter. The thermoemitter temperature was scanned in the range of 600–1200 K. The samples were evaporated from the Knudsen quartz cell.

The TLC studies were conducted on a chromatographic plate "Silufol". The GC/MS studies were carried on by Hewlett-Packard HP-6890 (Drug-M) with 5% phenylmethyl siloxane was used. The injector temperature was 280°C, the oven one was programmed from 150°C to 280°C. The helium gas-carrier velocity was 3 ml/min. For EI/MS the electron energy was 70 eV, the emission carrier 0.8 mA.

Extraction procedure

5 ml of urine were mixed with 8 ml of 40% sodium bisulphate solution and then concentrated HCl was added. The mixture was heated in boiling water bath within 30 minutes and then cooled up to the room temperature. Then the 50% solution of trichloroacetic acid was added up to 7%. After the protein substance precipitation in 5–10 minutes the solution was filtrated and neutralized by ammonia up to pH 6.0–7.0, saturated by sodium bicarbonate (0.5 g per 30 ml of the solution) and extracted by the mixture of 1:9 (3 x 20 ml; 5 min). Butanol-chloroform extraction was filtrated by a paper filter with non-water sodium bicarbonate. The filtrate was evaporated at the temperature not over 40%. The remained substance was dissolved in a small quantity of the

butanol-chloroform mixture 1:9. Up to 72% of opiates from urine can be extracted by this method.

RESULTS AND DISCUSSION

One of the characteristic SI spectra for opiates extracted from urine of a narcotics user is presented in Figure 1.

The SI mass spectrum is of a superposition of mass spectra of 6-MAM, acetylcodeine, codeine, morphine and their metabolites. The chromatogram for the same

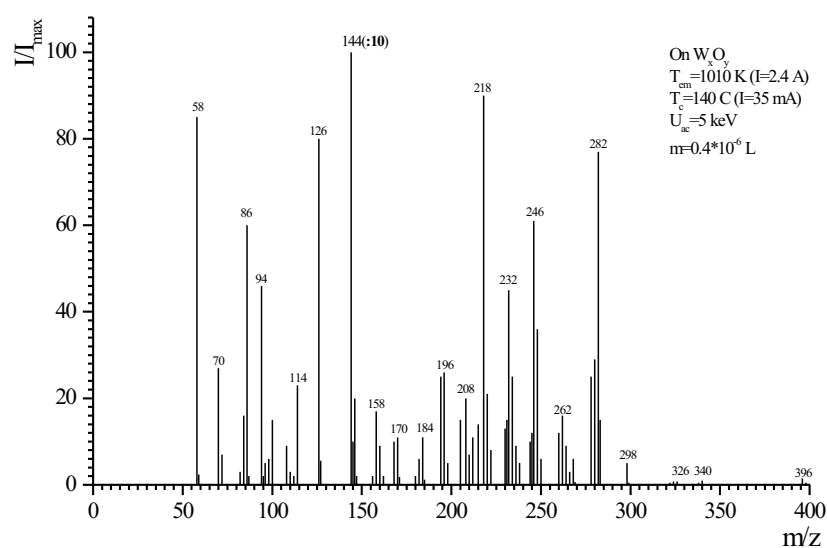


Fig. 1. SI mass-spectra of urine extract.

sample is given in Figure 2a and the mass spectrum of electron impact (EI) in Figure 2b. They are measured by HP-6890 where the identification was made only for 6-MAM. The rest peaks in the chromatogram correspond to hydrocarbons and acids.

It is seen from the mass spectra that opioids and their metabolites are ionized with the high efficiency on the surface of oxidized tungsten. Owing to the high SI selectivity with regard to hydrocarbons, ketons, ethers, spirits and other solvents (10^{-8}) the mass spectrum of urine extract has the small number of lines and can be easily identified. In the mass spectrum the lines of quasimolecular ions of acetylcodeine ($m/z = 340$ a.u.m), 6-MAM ($m/z = 326; 324; 322$ a.u.m), codeine ($m/z = 298$ a.u.m), morphine ($m/z = 284$ a.u.m) are from 0.1 to 5%. The base line is the line of the ion with $m/z = 144$ a.u.m. corresponding to the structure of bensylmethylpiridinium that is the product of the opioid molecule decay on the emitter surface [1], while the base line in the EI mass spec-

Fig. 2. a) The chromatography of urine extract; b) The EI mass-spectra of urine extract ($R_t = 12.353$ min).

trum is the line of an ammonium ion. The ion line with $m/z = 144$ a.u.m. is characteristic of all narcotics with morphine-like structure and it can be served as an indicator of opioids in SI mass spectra. The tentative calculations show that the identification according to this line makes it possible to have the sensitivity level of an order 10 pg/ml for opiates. This sensitivity of detecting the ultra-trace amounts of opiates in biosolutions allows toxicological laboratories to work without false-negative results.

The ion line with $m/z = 396$ a.u.m. is not identified. The question appears whether the transformation of heroine into ethylheroine in a body occurs similar to that of morphine into ethylmorphine

The SI mass spectra of urine extracts with positive and false-negative results obtained by GC/MS show that a character of the intensity distributions of

quasimolecular lines of ions corresponding to acetylcodeine, acethylmorphine and their metabolites is identical. In the case of the false-negative result, the line corresponding to codeine is more intensive (about 6 times).

The line in chromatography in Figure 2a demonstrate that in the case of the positive result only 6-MAM lines can be identified. The rest lines are not identified as opiates. In the case of the false-negative result opiates are not identified at all.

The great number of lines in chromatographs require the preliminary chromatographic separation of samples for EI/MS, while owing to the high selectivity the SI/MS method allows the analysis of the samples without their preliminary chromatographic separation.

CONCLUSION

1. The SI/MS studies of urine extracts of opiates users show that owing to the high selectivity the method allows the direct analysis with no preliminary chromatography of extracts.
2. The SI/MS method, according to preliminary estimations, has the sensitivity of 3 orders higher than the GC/MS one. The high efficiency of the ion formation and the small number of lines in spectra make it possible easily to detect opiates for the very low concentrations (10^{-11} – 10^{-12} g/ml) in urine and identify abused opiates. The analytical possibilities of the SI/MS method for the toxicological analysis are under study.

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