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# SURFACE-IONIZATION MASS SPECTROMETRY OF OPIUM ALKALOIDS

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*Surface ionization of the opium alkaloids morphine, codeine, thebaine, papaverine, and narcotine was investigated by mass spectrometry. It was shown that the alkaloid molecules were ionized with high efficiency through surface ionization. The mass spectra of morphine, codeine, and thebaine exhibited series of lines for quasimolecular ions with elimination of up to nine H atoms from the opiates that was accompanied by heterogeneous aromatization of the rings and their skeletal rearrangement. The results were compared with GC—MS data from electron ionization.*

**Key words:** surface ionization, thermoemitter ions, mass spectrometry, morphine, codeine, thebaine, papaverine, narcotine.

Various physicochemical methods are used to detect and identify traces of opium alkaloids in various samples, including complex solutions [1]. The most sensitive methods involve ionization, for example, GC—MS with electron ionization [2]. However, the detection limits for analysis of opiates by traditional ionization methods (electrons, photons, ions, fast atoms, etc.) are seriously limited owing to a lack of selectivity due to inefficient ion production and chromatographic separation of samples.

Surface ionization [3, 4] (SI), in contrast with traditional methods, is not so common but is highly selective relative to the particle ionization potential V. Thus, if V of two particles differs by 1 eV, the effectiveness of their SI can differ by up to $10^5$ times. On the other hand, the ionization efficiency for particles with a low potential can reach the limiting values where each analyzed molecule reaching the surface emitter is ionized, for example, with an efficiency up to 0.2, whereas mass spectrometry with electron ionization can produce up to one ion per $10^3$ molecules.

At present, classes of organic molecules that are effectively ionized by SI have been defined. The basic principles of ion formation (molecular adsorption schemes, heterogeneous transformations on the emitter surface, dependences of the molecule ionization efficiency on the electrochemical properties of substituents, etc.) have been established. These enable a prediction of the ion composition and an estimate of their current density [3, 4].

SI of organic compounds, thanks to the high efficiency and simplicity of implementation, is widely used in organic analysis, especially of N-containing organic bases [5-7].

Mass spectra from SI of N,N-heterocyclic compounds consist of a set of lines for the ions $[M - H]^+$, $M^+$, $[M - H - 2nH]_\beta^+$, $[M - R]_\beta^+$, and $[M - R - 2nH]_\beta^+$ (where H is a hydrogen atom; M, the molecule; and R, a radical), which are also characteristic of simpler amines. With the exception of $M^+$, they do not contain unpaired electrons and can be represented as ions with saturated bonds and a positively charged tetravalent N atom with $sp^2$ hybrid orbitals.

The lines for $[M - H - 2nH]_\beta^+$ ions, which are formed by aromatization of the rings, can be stronger than those for $[M - H]^+$ ions in mass spectra of N,N-heterocyclic compounds, in contrast with simple amines, because aromatization of the rings is an energetically favorable process. The number of H atoms eliminated is related to the number of saturated bonds in the heterocycles. For example, SI of allomatrine [8], where formation of ions by elimination of up to 13 H atoms is theoretically possible, produces a mass spectrum in which all lines for the $[M - H - 2nH]_\beta^+$ ions are observed, from $[M - H]^+$ to $[M - 13H]^+$, which corresponds to complete aromatization of all rings. The base peak in the SI mass spectrum of allomatrine is $[M - 5H]_\beta^+$. Its current density under the optimal regimes is $I = 1 \cdot 10^{-8}$ A/cm$^2$.

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TABLE 1. Mass Spectra of SI Base Peaks of Opium Alkaloids

| Compound | $M^+$, amu | Base peak of ion, *m*/*z* | Current density, $A/cm^2$ | Temperature | | Heat of sublimation, eV |
|---|---|---|---|---|---|---|
| | | | | thermoemitter, K | vaporizer, $T_{vap}$ °C | |
| Morphine | 285 | 144 | $1.4 \cdot 10^{-10}$ | 780 | 120 | 1.25 |
| Codeine | 299 | 144 | $6.1 \cdot 10^{-10}$ | 780 | 100 | 0.87 |
| Thebaine | 311 | 174 | $1.5 \cdot 10^{-9}$ | 1020 | 90 | 0.77 |
| Papaverine | 339 | 339 | $5.7 \cdot 10^{-9}$ | 1180 | 100 | 1.07 |
| Narcotine | 413 | 220 | $2.2 \cdot 10^{-9}$ | 1080 | 100 | 1.07 |

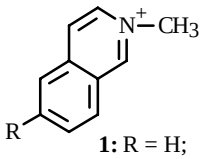
The opium alkaloids are N,N-heterocyclic compounds. It is expected that they also will be ionized by SI with high efficiency. The use of an SI detector for GC detection of codeine in human body fluids was reported [9]. The detection limit was ~100 pg per column, which is approximately an order of magnitude greater than that using thermionic N—P detectors.

The SI mass spectra of opium alkaloids should consist of ions produced by heterogeneous dehydrogenation reactions with aromatization of the rings accompanied by cleavage of various bonds and formation of particles with energetically more favorable structures.

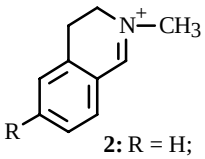
SI mass spectra of the opiates morphine, codeine, and thebaine consist of lines for the ions $[M - H]^+$, $[M - H - 2nH]^+$, and $[M - H - 2nH - R]_\beta^+$. Ionization of these alkaloids by SI is highly efficient (Table 1). Their mass spectra are nonlinear by comparison with electron-impact mass spectra. Ionization of opium alkaloids on the surface of oxidized tungsten, like that of heterocyclic compounds, produces lines for ions formed by elimination of the maximum possible number (up to nine) of H atoms and cleavage of various bonds.

The strength of the quasimolecular ion $[M - H]^+$ with *m*/*z* 284 in the SI mass spectrum of morphine is 0.5%; for codeine with *m*/*z* 298, ~1%; for thebaine with *m*/*z* 310, ~5.2%. The series of lines for $[M - H - 2nH - 16]^+$ and $[M - H - 2nH - 32]^+$ in the mass spectra of these alkaloids, which are formed by dehydrogenation and aromatization of the rings with elimination of O and OH, are rather strong and reach 20-40% of the base peak.

Changing the hydroxyl in morphine to methoxy in codeine and thebaine leads to a substantial redistribution of line strengths within the series $[M - H - 2nH]^+$ and $[M - H - 2nH - R]^+$. Among these, the strongest lines for morphine are those for $[M - 9H]^+$, $[M - H_2O - 7H]^+$, and $[M - O - H_2O - 7H]^+$ with the maximum achievable degree of dehydrogenation whereas for codeine and thebaine, the strongest lines are those for $[M - H]^+$, $[M - H_2O - H]^+$, and $[M - O - H_2O - H]^+$ with the lowest degree of dehydrogenation. A doublet series with *m*/*z* 144 and 146 is the base peak in the mass spectra of morphine and codeine. The second methoxyl (locant 6) in thebaine is situated on the double bond. As a result, the base peak changes in the SI mass spectrum of thebaine to the series of lines for ions with *m*/*z* 174 and 176. These ions form through cleavage of the bonds β to the N heteroatom. Despite the existence of three $\beta$-bonds, cleavage of only one of them leads to formation and desorption of ions with a saturated bond and tetravalent positively charged N atom. The structures of the base peaks in SI mass spectra of morphine and codeine with *m*/*z* 144 and 146 correspond to N-phenylmethylpyridine (**1**) and N-methylphenyldihydropyridine (**2**). For thebaine, the lines with *m*/*z* 174 and 176 correspond to N-methoxyphenylmethylpyridine (**3**) and N-methoxyphenylmethyldihydropyridine (**4**).




**1:** R = H;
**3:** R = $OCH_3$




**2:** R = H;
**4:** R = $OCH_3$

Figure 1a shows some ion currents for morphine and thebaine as functions of temperature. It can be seen that the yields for forming quasimolecular ions through heterogeneous reactions are shifted to high emitter temperatures whereas the yields for forming fragment ions dominate at relatively low temperatures. This is explained by the fact that the molecule lifetime on the emitter surface at high temperatures is substantially shorter and comparable with the duration of the dehydrogenation reaction, which is accompanied by bond cleavage and molecule fragmentation on the surface. Therefore, they manage to desorb intact during this time. At low emitter temperatures, the molecule lifetime on the emitter surface is sufficient for their complete dehydrogenation and fragmentation. This trend of temperature dependences is typical of N-heterocyclic compounds like opiates, in contrast with simple amines.

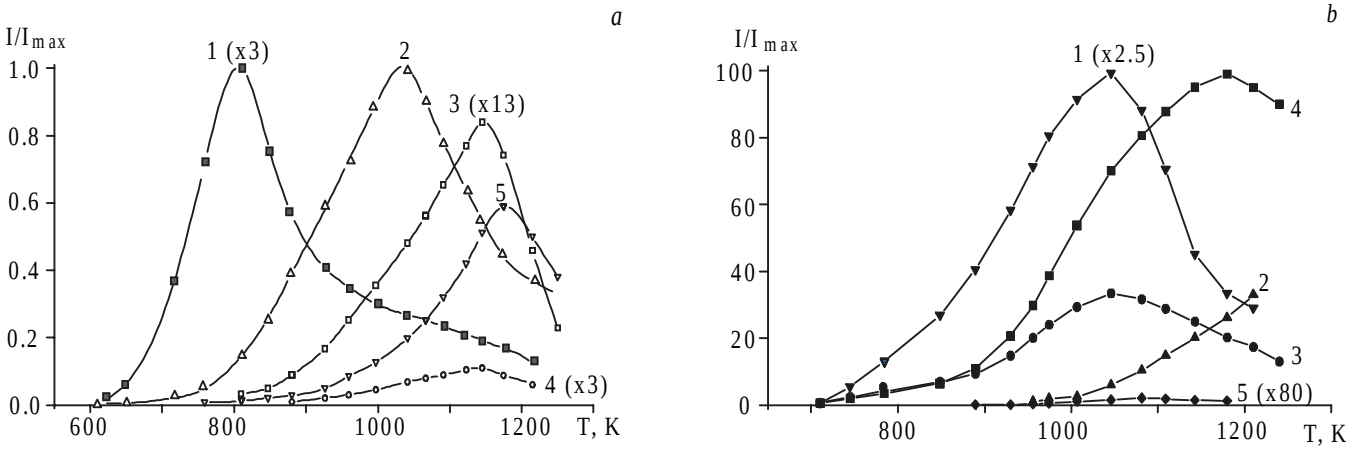
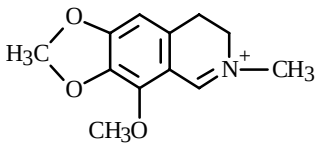



Fig. 1. Temperature dependences of ion currents of morphine and thebaine (a) and papaverine and narcotine (b). 144 (1), 174 (2), 268 (3), 284 (4), 310 (5) (a); 220 (1), 323* (2), 338 (3), 339 (4), 412 (5) (b).

The representatives of benzylisoquinoline derivatives among the studied opium alkaloids, papaverine and narcotine, are also highly efficiently ionized by SI (Table 1). The SI mass spectra indicate that they are nonlinear and consist of $[M - H]^+$, $[M - H - 2nH]^+$, and lines of fragment ions.

The structures of the SI and EI mass spectra agree in the region of quasimolecular masses with the exception of a few lines. The strengths of the molecular $M^+$ (papaverine) and quasimolecular $[M - H]^+$ ions (narcotine) differ substantially in the SI mass spectra owing to their structural features. The line for the molecular ion $M^+$ with *m*/*z* 339 is the base peak for papaverine whereas the strength of the quasimolecular ion $[M - H]^+$ with *m*/*z* 412 for narcotine reaches hundreths of a percent. The base peak in the SI mass spectrum of narcotine is the fragment ion with *m*/*z* 220, which corresponds to hydrocotarnine:




It is formed by a heterogeneous aromatization reaction of the N-ring with elimination of a meconine radical.

The mass spectra and temperature dependences of the ion currents (Fig. 1b) lead to the conclusion that papaverine is the most stable molecule of the isoquinoline opiate derivatives in the studied emitter temperature range (650-1250 K). The temperature dependences of the ion currents for $M^+$ and $[M - H]^+$ of papaverine are bell-shaped and reach a maximum at high emitter temperatures of ~1000 and 1200 K, respectively, and have different decomposition patterns.

Heterogeneous aromatization reactions of narcotine, which form fragments on the emitter surface, begin to yield products at relatively low emitter temperatures (650-700 K) and reach a maximum at T = 1000 K, for example, for the base peak with *m*/*z* 220.

Lines for $[M - H - 2nH]^+$ and $[M - H - 2nH - R]_\beta^+$ observed in SI mass spectra of opiates represent products of heterogeneous aromatization reactions and molecule dissociation on the hot emitter surface. However, the opiate molecules may also be destroyed in the Knudsen cell to form particles of structure $[M - R]_\beta^+$ that then aromatize on the emitter surface. In order to determine the origin of $[M - H - 2nH]^+$ and $[M - H - 2nH - R]^+$ for the studied opiates, we compared the dependences of the logarithm of the relative current change for these ions on inverse vaporizer temperature $T_{vap} = f[\log(I/I_{max})] = 5040/T$. The resulting slopes of the curves are identical for various ions at various $T_{vap}$. This indicates that all ions in the mass spectra of opiates are produced from starting molecules reaching the surface. We present as an example the Arrhenius curves (Fig. 2) for some morphine ion currents with *m*/*z* 144, 232, 260, and 284. The results were also confirmed by GC—MS investigations of opiate samples before and after experiments with heating in vacuum of a Knudsen cell over the range 40-160°C. No changes of opiate composition were observed in the chromatograms. The heats of sublimiation of the opiates were calculated from the slopes of the curves (Table 1). The heats of sublimation of the opiates increase from thebaine (0.77 eV) to morphine (1.25 eV) and correlate with their structural features, which are related to the successive replacement of OH by methoxy group.

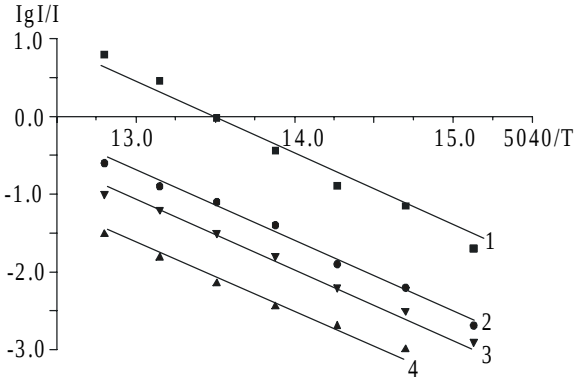


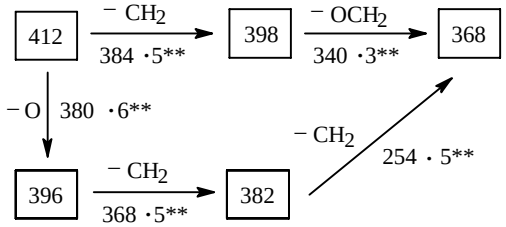

Fig. 2. Arrhenius curves for determination of heats of sublimation of morphine. 144 (1), 260 (2), 232 (3), 284 (4).

As noted above, multiatomic particles desorb from the hot emitter surface in a vibrationally excited state. The energy accumulated among the vibrational degrees of freedom is estimated as $E = (3N - 5)\cdot k\cdot T$, where N is the number of atoms in the molecule, k is Boltzmann's constant, and T is the temperature.

The energy is rather high at the emitter temperatures (1000 K) and increases from morphine (10.5 eV) to narcotine (15.0 eV). However, lines for ions corresponding to monomolecular decompositions are not observed in the mass spectra of morphine, codeine, and thebaine at 600-1250 K (on oxidized tungsten). They are found in the SI mass spectra of papaverine and narcotine. Lines for ions with *m/z* 323* and 308* in the SI mass spectrum of papaverine are formed in the MS field space whereas weak lines with *m/z* 308.6** and 280.6** are formed in the fieldless space of the mass spectrometer during monomolecular decompositions of the parent ion $[M - H]^+$ with *m/z* 338 that occur along two different channels with loss of methyl and $OCH_2$ groups according to the following scheme:


As the emitter temperature increases from 950 to 1000 K, the strength of the $[M - H]^+$ ions of papaverine decreases (Fig. 1b). Papaverine begins to decompose. The strength correlates with the decrease of current from the parent ion. Decompositions of the molecular ion $M^+$ are not observed over the emitter temperature range. The decrease of current from $M^+$ is explained by a change of the emitter oxide layer at high temperatures.

The SI mass spectrum of narcotine exhibits multistepped decompositions of the quasimolecular ion $[M - H]^+$ with elimination of $CH_2$, O, $OCH_2$ from the parent ion according to the scheme:




Such a multistepped decomposition scheme for the parent ion $[M - H]^+$ of narcotine is explained by the magnitude of the accumulated energy among its vibrational degrees of freedom and structural features. The number of decompositions in the SI mass spectrum of narcotine range from $5\cdot10^{-3}$ to $1\cdot10^{-2}$% and is comparable with the strength of the quasimolecular ion $[M - H]^+$ with *m/z* 412. The heats of sublimation of the isoquinoline opiate derivatives determined from the Arrhenius curves were equal at 1.07 eV.

Thus, the opiate alkaloids morphine, codeine, thebaine, papaverine, and narcotine were studied for the first time by SI mass spectrometry. It has been found that these alkaloids are highly efficiently ionized by SI. Their mass spectra are

nonlinear and can detect trace quantities with high sensitivity. These compounds can be analyzed in various complex solutions, including biological ones. The detection limits for SI mass spectrometry of opium alkaloids was ~$10^{-12}$-$10^{-10}$ g, which is two orders of magnitude and more greater than those for GC—MS with electron ionization.

## EXPERIMENTAL

Experiments were performed using a MX-1320 static magnetic mass spectrometer upgraded for SI research [10]. The thermoemitter was an oxidized tungsten wire of length 58 mm and diameter 200 μm. The molecular current of the studied compounds was directed at the emitter with a standard quartz vaporizer introduced into the ionization chamber through an SVP-5 system. The thermoemitter temperature for $T_e > 800$ K was measured with a VIMP-015M optical micropyrometer; for $T_e < 800$ K, by extrapolation of the emitter temperature dependence on its ohmic resistance.

Mass spectrum (SI morphine, $T_{vap} = 120°C$, $U_{mult} = 3$ kV, $T_{em} = 1000$ K), $m/z$ ($I_{rel}$, %): 284 $[M - H]^+$ (0.5), 282 (2), 280 (1.4), 278 (2.8), 268 (1.9), 276 (5.2), 266 (2.7), 264 (8.4), 262 (10.8), 260 (20), 252 (1), 250 (4), 248 (20.4), 246 (14), 236 (10.4), 234 (6), 233 (9.2), 232 (16), 224 (5.2), 220 (6.6), 218 (5), 214 (25.2), 210 (1.6), 208 (3.2), 205 (1.5), 198 (2), 196 (5), 186 (1), 166 (1), 158 (2), 146 (30), 144 (100), 122 (2.6), 108 (1.6), 100 (1.6), 96 (1.8), 94 (19), 86 (6), 82 (24), 72 (1), 70 (19), 58 (13.6).

Mass spectrum (SI codeine, $T_{vap} = 100°C$, $U_{mult} = 3$ kV, $T_{em} = 1000$ K), $m/z$ ($I_{rel}$, %): 298 $[M - H]^+$ (1), 296 (0.3), 294 (0.2), 292 (0.25), 290 (0.13), 282 (27.6), 280 (5.5), 278 (3.7), 276 (1.2), 268 (0.12), 266 (1.2), 264 (2.5), 262 (2.3), 260 (1.8), 250 (1.3), 248 (5), 246 (7.5), 244 (1.1), 238 (1.6), 236 (1.4), 235 (3), 234 (4.2), 232 (5.8), 228 (2.5), 220 (1.2), 218 (6), 208 (1.2), 205 (3.4), 196 (1.4), 158 (3), 146 (22), 144 (100), 108 (1.3), 100 (2.2), 94 (9.3), 72 (1.5), 70 (21), 58 (6.6).

Mass spectrum (SI thebaine, $T_{vap} = 90°C$, $U_{mult} = 2.8$ kV, $T_{em} = 1000$ K), $m/z$ ($I_{rel}$, %): 310 $[M - H]^+$ (5.2), 308 (0.66), 306 (0.2), 296 (0.5), 294 (0.66), 292 (0.4), 290 (0.4), 282 (1.3), 280 (0.6), 278 (28.8), 276 (2), 266 (1.5), 264 (1.6), 262 (20.4), 255 (1), 250 (0.8), 248 (1.5), 246 (0.4), 238 (0.13), 236 (0.3), 235 (1.3), 234 (0.53), 232 (0.73), 226 (1.3), 214 (0.53), 198 (0.16), 176 (2), 174 (100), 158 (0.6), 146 (1.3), 144 (10.5), 70 (1.3), 58 (1.3).

Mass spectrum (SI papaverine, $T_{vap} = 100°C$, $U_{mult} = 3$ kV, $T_{em} = 1000$ K), $m/z$ ($I_{rel}$, %): 339 $M^+$ (100), 338 (61.4), 323* (5.7), 308.6* (2.5), 308* (2), 296 (0.14), 294 (0.4), 292 (0.3), 282 (0.15), 280.6** (0.22), 100 (0.3), 86 (0.6), 58 (0.2).

Mass spectrum (SI narcotine, $T_{vap} = 100°C$, $U_{mult} = 3$ kV, $T_{em} = 1000$ K), $m/z$ ($I_{rel}$, %): 412 $[M - H]^+$ (0.02), 398* (0.1), 396* (0.015), 384.5** (0.07), 382* (0.08), 380.6** (0.01), 368.5** (0.03), 368* (0.03), 354.5** (0.01), 340.3** (0.01), 276 (0.007), 266 (0.015), 264 (0.01), 252 (0.5), 234 (1.8), 232 (8.8), 220 (100), 218 (33), 205 (3.5), 203 (1.1), 192 (60), 180 (2.2), 178 (3), 168 (3.3), 148 (17.7), 146 (3), 114 (1.1), 113 (1.3), 112 (1.4), 108 (0.7), 100 (1.3), 96 (1.8), 86 (0.71), 72 (2.5), 70 (1.5).

GC—MS of opiates were recorded on an HP-6890 at ionizing-electron energy U = 70 eV.

Mass spectrum of morphine (EI, 70 eV), $m/z$ ($I_{rel}$, %): 285 $M^+$ (72), 284 (15), 283 (4), 282 (5), 281 (11), 280 (3), 278 (2), 276 (1), 274 (1.5), 272 (1), 271 (0.7), 270 (0.7), 269 (3), 268 (5), 267 (11), 266 (9), 265 (3), 264 (4), 262 (0.7), 261 (0.7), 259 (3), 258 (3), 256 (2), 242 (10) series, 215 (35) series, 197 (20) series, 181 (34) series, 173 (40) series, 160 (55) series, 152 (52) series, 148 (30) series, 142 (30) series, 131 (90) series, 124 (32) series, 115 (96) series, 104 (42) series, 94 (64), 91 (60) series, 81 (54) series, 77 (46) series, 69 (56), 67 (41) series, 57 (100) series.

Mass spectrum of papaverine (EI, 70 eV), $m/z$ ($I_{rel}$, %): 339 $M^+$ (74), 338 (96), 324 (100), 322 (12), 308 (24), 296 (4), 294 (10), 293 (15), 292 (12), 281 (6), 280 (8), 278 (7), 266 (8), 264 (8), 262 (4), 253 (5), 252 (4.5), 251 (2.5), 250 (6.4), 249 (4), 248 (4), 246 (0.5), 240 (0.7), 239 (1), 238 (4.5), 237 (3.5), 236 (6), 235 (4), 234 (4), 233 (3), 232 (2), 227 (1), 224 (1.5), 223 (4), 222 (5), 221 (5), 220 (7), 212 (0.5), 211 (1), 210 (5), 209 (4), 208 (5.5), 207 (6.8), 206 (4), 205 (3), 204 (4.5), 203 (3), 202 (3.2), 196 (2), 195 (4), 194 (5), 192 (4), 191 (6), 178 (6) series, 169 (5) series, 154 (12), 152 (3), 151 (5), 139 (4.5) series, 123 (3) series, 107 (5) series, 89 (6) series, 69 (3) series, 51 (5) series.

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