The investigation of ionization conditions in the trace amounts detection of heterocyclic compounds by ion mobility spectrometry and mass spectrometry

Y R Shaltaeva¹, A A Sysoev¹, S S Poteshin¹, K I Negru², S S Grishin², V V Trefilova², M I Zuev² and E P Baberkina²

¹National Research Nuclear University MEPhI (Moscow Engineering Physics Institute), Kashirskoe shosse 31, 115409 Moscow, Russian Federation
²D. Mendeleev University of Chemical Technology of Russia, Miusskaya sq. 9, 125047 Moscow, Russian Federation

Corresponding author e-mail address: shaltaeva@yandex.ru

Abstract. The first part of paper is devoted to the detection of New Psychoactive Substances by ion mobility mass spectrometry study. In the second part of the paper presents a promising approach to prevent the spread of narcotic substances, consisting in the use of field-portable ion mobility spectrometers and finding the correlation between the peaks of the spectrograms of ion mobility and the chemical structure of the compound.

1. Introduction

The spread of narcotic substance one the major problems in the modern world. A growing number of New Psychoactive Substances (NPS) are reported every year by a large number of countries and territories throughout the world. Between 2008 and 2014, a total of 569 NPS were reported to be on the market [1]. The formula of synthetic drugs is constantly changing, making it difficult to interdiction "spice", as each time specific formula is entered in the register of prohibited substances [2-4]. As a result, sales of the mixture is, in fact, legal until restriction of its use.

The second major problem is the difficulty of identifying and traffic restraint [5-7]. Most of the narcotic substance are transported by public transport (trains, planes, etc.) and can be hidden under clothing, in hand luggage, in checked baggage. The first part of paper is devoted to the detection of NPS by ion mobility mass spectrometry study. In the second part of the paper offers a promising approach to prevent the spread of narcotic substances, consisting in the use of field-portable ion mobility spectrometer and finding the correlation between the peaks of the spectrograms of ion mobility and the chemical structure of the compound.

2. Detection of synthetic drugs by Ion Mobility Spectrometry

The six synthetic drugs and cocaine is studied by ion mobility time-of-flight mass spectrometry (IMTOFMS) with atmospheric pressure chemical ionization (APCI) and electrospray ionization (ESI) [8]. It were determined characteristic ion mobility mass spectrometry (IMMS) data, reduced mobility, and limits of detection (S/N=3) for the drugs (figure 1).
Figure 1. APCI ion mobility mass spectra in a mixture of 8 μM methylone, 5 μM 4-MEC, 8 μM 3,4-MDPV, 6 μM JWH-210, 4 μM JWH-250, 9 μM JWH-203, 7 μM cocaine, and 1 μM 2,6-DtBP in acetonitrile. Adapted from Ref. [8] with permission.

Absolute reduced mobilities in nitrogen were 1.35, 1.28, 1.41, 1.30, 1.18, 0.98, 1.09 and 1.07 cm²·V⁻¹·s⁻¹, for methylone (M-H)+, methylone (M+H)+, 4-MEC (M-H)+, 4-MEC (M+H)+, 3,4-MDPV (M+H)+, JWH-210 (M+H)+, JWH-250 (M+H)+, and JWH-203 (M+H)+, respectively (Table 1).

### Table 1

| Substance name | Monoisotopic mass, M (Da) | The characteristic ions | \( K_0 \), cm²/(V·s) | The limit of detection |
|---------------|--------------------------|-------------------------|----------------------|-----------------------|
|               | APCI-M, M (Da)           | ESI-M, M (Da)           |                      | Relative, mol / l     | Absolute, g          |
| Metilon       | 207.09                   | 206.08                  | 208.10               | 3×10⁻⁷                | 7×10⁻¹⁰              |
|               | 208.10                   |                         |                      |                       |                      |
| 4-MEC         | 191.13                   | 190.12                  | 192.14               | 1.5×10⁻⁷              | 4×10⁻¹⁰              |
|               | 192.14                   |                         |                      |                       |                      |
| 3,4-MDPV      | 275.15                   | 276.16                  | 276.16               | 1.8×10⁻⁷              | 1.5×10⁻¹⁰            |
| JWH-210       | 369.21                   | 370.22                  | 370.22               | 4×10⁻⁷                | 1.7×10⁻⁹             |
| JWH-250       | 335.19                   | 336.20                  | 336.20               | 2.3×10⁻⁷              | 7×10⁻¹⁰             |
| JWH-203       | 339.14                   | 340.15                  | 340.15               | 3×10⁻⁷                | 1.2×10⁻⁹             |
| Cocaine       | 303.15                   | 304.15                  | 304.15               | 4×10⁻⁹                | 1.4×10⁻¹¹            |

The application allows one to consider IMTOFMS as a good candidate for a method for fast determination of recently appeared designer drugs marketed on the internet as "bath salts," "spice" and "herbal blends." Nevertheless, IMTOFMS stay expensive dimensional laboratory equipment.

The basis of designer drugs is the chemistry of heterocyclic nitrogen compounds, which is the main reason for the paper, presented an investigation of ionization conditions in the trace amounts detection of heterocyclic compounds. The alternative way to massive IMTOFMS consist in the use of field-portable ion mobility spectrometers and finding the correlation between the peaks of the spectrograms of ion mobility and the chemical structure of the compound.
The main reason for the significant interest in the indoles and their derivatives is their wide range of manifestations of the biological activity. Tryptophan is an essential amino acid, which is included in most proteins. In animal organisms, two hormones are produced from tryptophan, related in chemical structure. One of them is serotonin, which is closely associated with the central nervous system activity, regulates motility and secretion of gastric juice, and the second - melatonin is involved in the control of the change of day and night rhythm of physiological functions. β-indoleacetic acid, which is also produced from tryptophan, is a hormone belonging to flora regulating plant growth. Among the indole derivatives with significant potential physiological activity are hallucinogenic drugs such as lysergic acid diethylamide (LSD), indole alkaloids are widely used in medicine. It should be called reserpine, which has anxiolytic properties, vincristine - drugs used to treat leukemia and cause uterine contractions, ergotoxine alkaloids group, including ergotamine, also used as a remedy for a migraine.

One of the devices operating on the method of ion mobility spectrometry is the Kerber IMS, produced by JSC "Yuzhpolymer-Holding", Russia. This device detects trace amounts of low-volatile and volatile organic compounds of explosives and narcotic substances in the air, on the surface of various objects on the skin and clothing of people. The preliminary exploratory studies were conducted by the Kerber IMS.

3. Results
The dissolved in acetonitrile heterocyclic compounds is detected in low ppb range from evaporated sample (Table 2).

| Substance name                   | Monoisotopic mass, M (Da) | \(K_0, \text{cm}^2/(V\cdot s)\) | \(K_0, \text{cm}^2/(V\cdot s)\) | \(K_0, \text{cm}^2/(V\cdot s)\) |
|---------------------------------|---------------------------|-------------------------------|-------------------------------|-------------------------------|
| imidazole                       | 68                        | 1.715333                     | 1.506                         |
| 1-methyl imidazole              | 82                        | 1.61                         |                               |
| 4-methyl imidazole              | 82                        | 1.569                        |                               |
| 2-phenyl imidazole              | 144                       | 1.674                        | 1.2                           |
| 1,2-dimethyl imidazole          | 96                        | 1.446                        |                               |
| benzimidazole                   | 118                       | 1.793                        | 1.293                         |
| 2-methyl benzimidazole          | 132                       | 1.751                        | 1.313                         |
| 2-formyl benzimidazole          | 146                       | 1.64                         |                               |
| 1-methyl-2-formyl benzimidazole | 160                       | 1.621                        |                               |
| 1,4-diphenyl-5-methylimidazole | 234                       | 1.309                        | 0.8625                        |
| indazole                        | 118                       | 1.4035                       |                               |
| Benzene                         | 78                        | 1.6435                       |                               |
| Aniline                         | 93                        | 1.79                         | 1.4635                        |
| pyridine                        | 79                        | 1.974                        |                               |
| indole                          | 117                       | 1.7836                       |                               |
| 3-formylindole                  | 145                       | 1.6365                       | 1.34325                       | 1.13325                       |
| 3-acetylindole                  | 159                       | 1.608                        | 1.18                          | 1.076                         |
| 3 nitriindol                    | 142                       | 1.427                        |                               |
| Methyl 3-carb. acid             | 175                       | 1.4585                       |                               |
| 1-pentyl-3-formylindol          | 215                       | 1.649                        | 1.319                         | 0.829333                      |
| Grameen                         | 174                       | 1.504                        | 1.3064                        | 1.1284                        |
| 2-methylindole                  | 131                       | 1.73                         |                               |
| 2-phenylindole                  | 193                       | 1.4725                       | 1.33                          | 1.192                         |
Investigated indole derivatives give clear signals on the ion mobility spectrometer Kerber produced by "Yuzhpolymermetal-Holding" (YPH) LLC, Russia. The spectrometer has corona discharge ion source. The nature of the spectrogram signal is substantially dependent only on the mass, but the electron density distribution in the molecule under the influence of substituents.

4. Results
The experimental spectrums of studied heterocyclic compounds (dissolved in acetonitrile) shows characteristic peak in reduced mobility range from 1.5 to 1.7 cm$^2/(V\cdot s)$. During the experiment and analyzing the results, it is suggested that the particles could be formed, protonated at a specific position of the ring or on a particular atom and complex ions clustered between π- aromatic ring system and reactant ion. It is found that this cluster ion appears on spectrogram more mobile field measurements $K_o = 1.6-1.9$ cm$^2/(V\cdot s)$. The formation and stability of cluster ion are affected by the chemical structure of substances.

5. Conclusion
The article presents retention times of synthetic drugs and their heterocyclic constituents on ion mobility spectrometers and mass spectrometers. The study of the chemical structure of synthetic drugs will improve the means of combating the spread of the illicit substances. It is necessary to conduct a detailed study with machine learning processing of the chemical reactions in the corona discharge ionization chamber for improvement of the methodology and rapid detection of drugs.

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