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Heat assisted sample introduction and determination of cannabinoids by dielectric barrier discharge ionization mass spectrometry

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ABSTRACT

DBDI-MS equipped with an appropriate sample heater was employed to analyze directly 8 seized synthetic cannabinoids in botanical matrices. The heater allowed for a pronounced increase of the quality of acquired spectra, allowing for much easier identification of cannabinoids, as compared to standard DBDI source without heating device. A few hundred micrograms of herbal material was sufficient for easy detection of cannabinoids content in the samples. These designer drugs are difficult to identify in a conventional way due to their association with complex plant matrices during manufacturing (to mask active and illicit ingredients) and so requires time consuming extraction and sample preparation before analysis. The ability for fast and direct analysis of the so-called "legal highs" can be a useful supporting tool for an initial and rapid identification of compounds present in this type of species, and can partially replace GC/MS technique for fast screening.

1. Introduction

In recent years, many herbal mixtures containing new cannabis alternatives have been introduced to the illegal drug market, mainly through Internet [1,2]. Many countries have taken legal actions to control this market, but new derivatives or analogs are constantly introduced, circumventing legal regulations, and thus are coined as "legal highs" or "designer drugs". Synthetic cannabinoids are known by a variety of names, such as "Spice" or "K2," and sometimes are referred to as "synthetic marijuana" or "fake marijuana" because they are sold with claims that their effects mimic those of marijuana. Synthetic cannabinoids are usually sprayed onto the surface of herbal products, and sold in that form. They have been reported to cause a variety of side effects like anxiety [3], vomiting [4], tachycardia [5], hallucinations [6], nonresponsiveness [7], and many others [8]. The routine screening tests are not currently designed for identification of synthetic cannabinoids and this causes high demand for analyses of this type of compounds. Synthetic cannabinoids have been studied by many mass spectrometry methods, such as GC–MS [9], LC–ESI-MS [10], MALDI [11] or DART [12]. Each method has its own advantages or drawbacks. The main advantage of the method used in the present study is a possibility for direct and rapid analysis of cannabinoids in herbal matrices. Original construction of the heat assisted DBDI allows to obtain MS and MS/MS data of a very good quality within seconds and without derivatization or presence of any solvent. From this point of view, only DART MS can be comparable with DBDI source. DBDI source has been developed in 2007 [13] and since then it has been used for many applications. It was applied for pesticide testing [14], for detection of amino acids, water-soluble vitamins, and nonpolar compounds like polycyclic aromatic hydrocarbons and functionalized hydrocarbons [15], explosives [16], and to detect both minor and trace components (free fatty acids, phenolics and volatiles) in raw, untreated olive oil [17]. DBDI was also coupled to HPLC for detection of pesticides, polycyclic aromatic hydrocarbons,

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Table 1
Structures of all cannabinoids analyzed and proposed formulas for the main fragmentation ions.

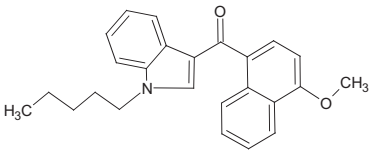
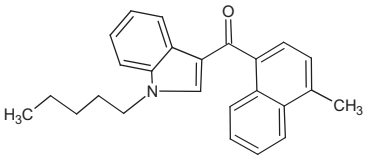
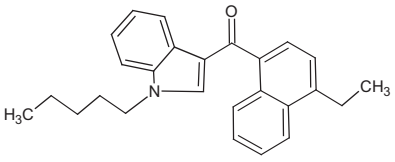
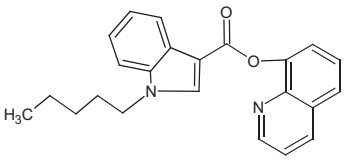
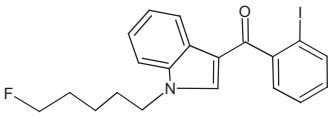
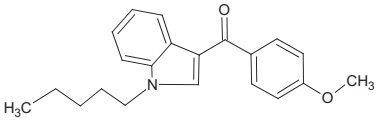
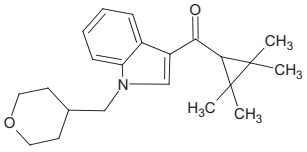
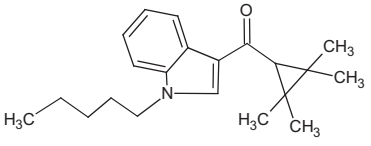
Name Formula M_w [Da]	Structure	MS/MS fragments (observed m/z)	Proposed formula of the fragment
JWH-081 $C_{25}H_{25}NO_2$ 371.19		157.1 185.1 214.1	$C_{11}H_9O^+$ $C_{12}H_9O_2^+$ $C_{14}H_{16}NO^+$
JWH-122 $C_{25}H_{25}NO$ 355.19		141.1 169.1 214.1	$C_{11}H_9^+$ $C_{12}H_9O^+$ $C_{14}H_{16}NO^+$
JWH-210 $C_{26}H_{27}NO$ 369.21		155.1 183.1 214.1	$C_{12}H_{11}^+$ $C_{13}H_{11}O^+$ $C_{14}H_{16}NO^+$
PB-22 $C_{23}H_{22}N_2O_2$ 358.17		214.1	$C_{14}H_{16}NO^+$
AM-694 $C_{20}H_{19}FINO$ 435.05		230.9 309.1	$C_7H_4IO^+$ $C_{20}H_{20}FNO^+$
RCS-4 $C_{21}H_{23}NO_2$ 321.17		135.2 186.1 265.0	$C_8H_7O_2^+$ $C_{13}H_{16}N^+$ $C_{17}H_{15}NO_2^+$
A-834,735 $C_{22}H_{29}NO_2$ 339.22		125.3 242.1 322.2	$C_8H_{13}O_2^+$ $C_{15}H_{16}NO_2^+$ $C_{22}H_{28}NO^+$
UR-144 $C_{21}H_{29}NO$ 311.22		125.1 214.0 294.2	$C_8H_{13}O_2^+$ $C_{14}H_{16}NO^+$ $C_{21}H_{28}N^+$

Fig. 1. Schematic diagram of DBDI source with sample heater.

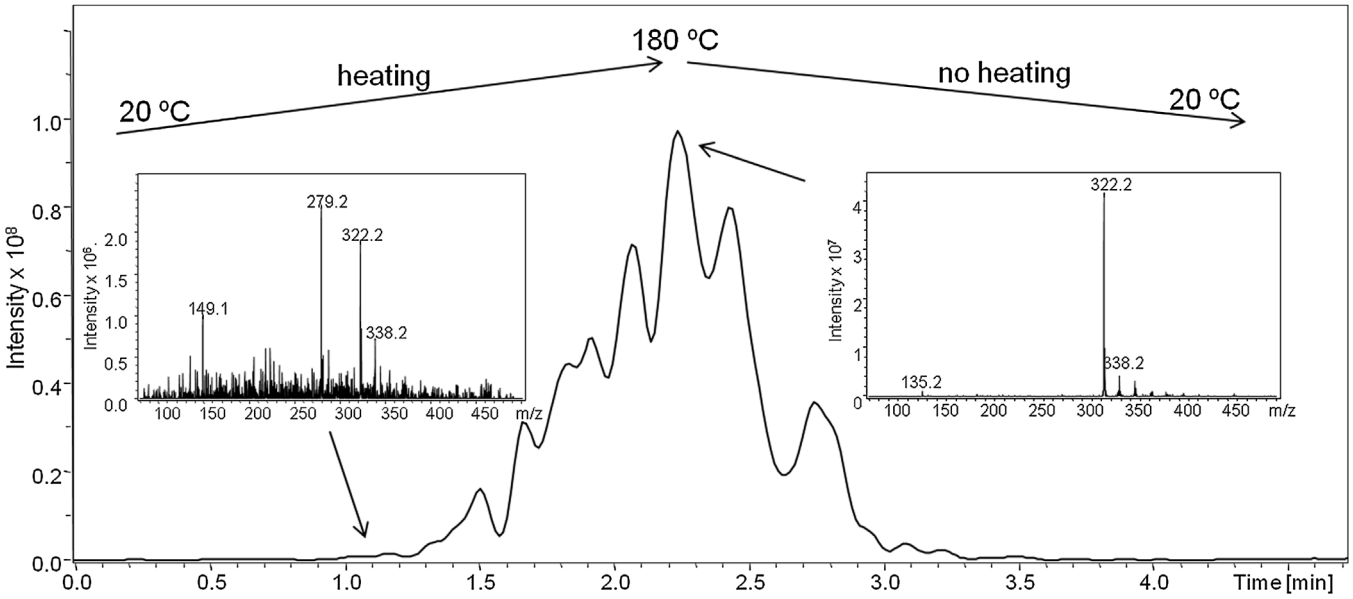


Fig. 2. Extracted ion chromatogram for the ion at *m/z* 322.2 corresponding to protonated RCS-4. Heating of the sample causes an increase of signal intensity. The inserts represent mass spectra of RCS-4 obtained at ca. 80 °C (spectrum on the left) and 180 °C (spectrum on the right).

organochlorine species, pharmaceuticals, personal care products, and drugs of abuse [18].

2. Experimental

2.1. Reagents and chemicals

All cannabinoids (collected in Table 1) were obtained from the Institute of Forensic Research (Krakow, Poland). No solvents were used except for rinsing DBDI heater after each measurement. In this case, methanol (methanol p.a., Avantor, Gliwice, Poland) was used. Helium (purity 99.996%, Air Liquide Poland) was used as a discharge gas.

2.2. Mass spectrometry

The ionization of all compounds was achieved with a homemade (Wroclaw University of Technology, Wroclaw, Poland) helium-based dielectric barrier discharge ionization (DBDI) source. The source (without heating device) has been described in detail elsewhere [19]. Briefly, the DBD plasma source consists of quartz capillaries (O.D. 0.7 mm and I.D. 0.5 mm), a ring high voltage electrode on the surface of a quartz tube and a grounded (25 μm diameter) platinum needle concentric with the tube. A glow discharge is formed between the needle and outer electrode. The quartz tube makes a barrier for direct current flow between both electrodes. Piezoelectric transformer based on a high voltage power supply generates AC voltage (3 kV_{pp}, 70 kHz), which is adequate to ignite the discharge in helium (flow rate 1 L/min, purity 99.996%). The source works fully automatically in a fixed current mode with output overvoltage and short circuit protection. The needle source operates with DC voltage (between 6 and 12 V) and consumes a very low amount of power (approx. 2.5 W). Sample heating was conducted by the heater equipped with aluminum well (1 mm I.D., 1 mm deep hole) for sample deposition. The thick-film heater consists of platinum heating layer and gold electrodes deposited on Al_2O_3 ceramic substrate. The heater was driven by Keithley 2400 source meter (Keithley, USA) in current control mode with resistance readout. The temperature was determined from heater resistance. Heater and aluminum well were placed in a Teflon case. The maximum temperature achievable by the heater was 220 °C. The schematic diagram of the source is shown in Fig. 1. For each experiment the small amount of the herbal product has been taken with tweezers and placed in the heater. The average mass of the analyzed herbal sample was approximately a few hundred of micrograms. For all compounds MS and MS/MS spectra have been acquired.

A Bruker Esquire 3000 quadrupole ion trap mass spectrometer (Bruker Daltonics, Bremen, Germany) was used for all measurements. The typical ESI-MS source settings were found to be optimal also for the DBDI source, with the exception of the mass spectrometer entrance glass capillary voltage, where lower potential (1 kV) compared to the standard ESI setting (4.5 kV) was used. The temperature of the glass capillary was set to 200 °C, the drying gas flow was maintained at 3 L/min, and the nebulizer gas (N_2) was not applied. The scan range was set from 80 to 500 *m/z*. For MS/MS experiments the isolation width was set to 1 *m/z* and the fragmentation amplitude was in the range of 0.5–0.8 unit.

3. Results and discussion

A series of eight cannabinoids have been analyzed utilizing DBDI source equipped with the sample heater. The representative example of the relationship between heating and intensity of the signal is shown in Fig. 2. The signal increases up to the highest temperature used (180 °C) and falls down when heating has been switched off. MS and MS/MS spectra of all compounds tested are shown in Fig. 3. MS/MS spectra allowed for identification of the active components of herbal highs. The collection of main MS/MS ions for all tested cannabinoids is summarized in Table 1 as well as in Fig. 3. All spectra were obtained at elevated temperature (160–180 °C, depending on the compound).

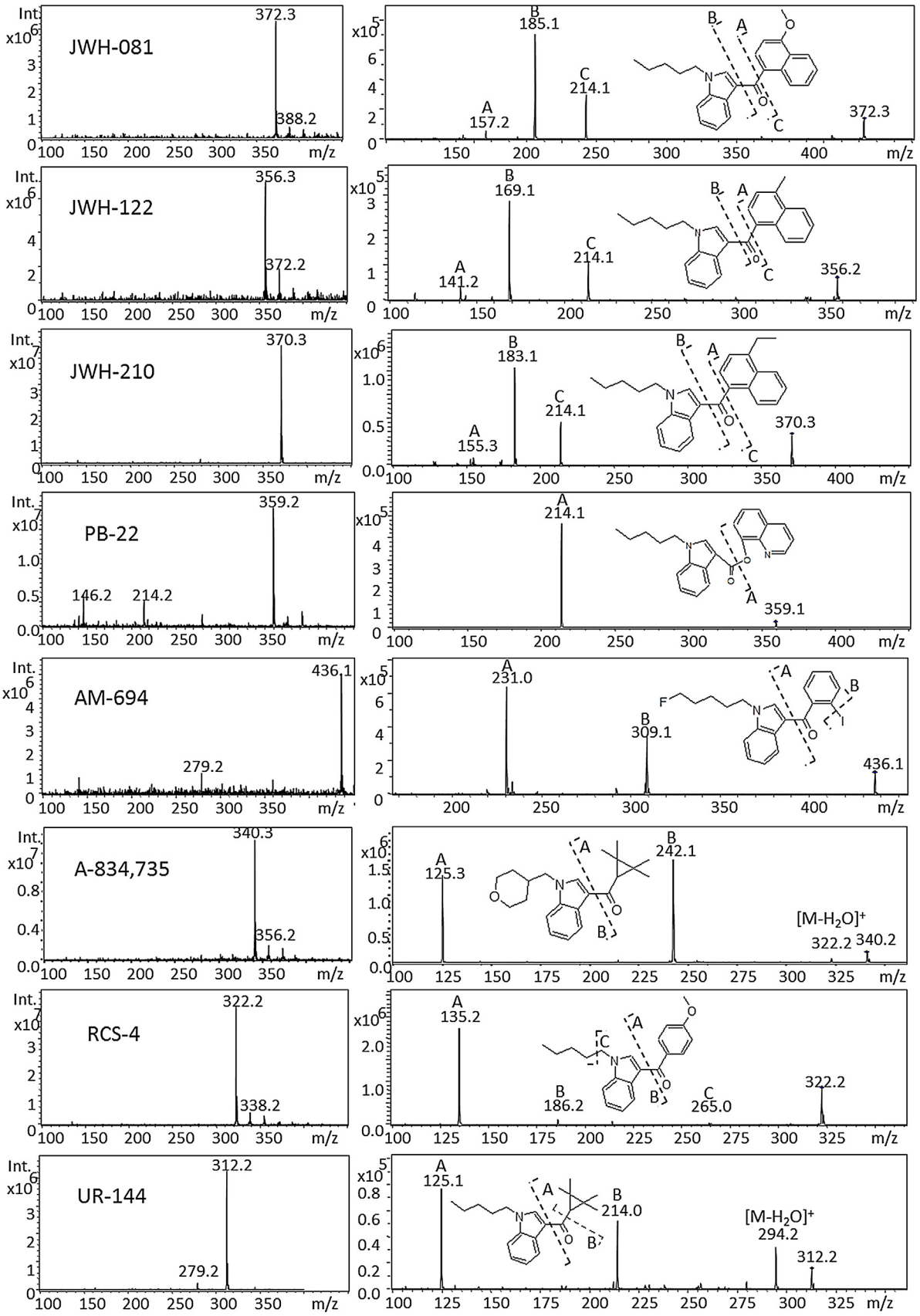


Fig. 3. MS and MS/MS spectra of all cannabinoids tested with proposed fragmentation pattern.

4. Conclusions

Dielectric barrier discharge ionization mass spectrometry has been successfully used for the analysis of eight seized synthetic cannabinoids present in herbal material. Introduction of the sample heating device allowed for the significantly increased quality of the obtained MS and MS/MS spectra, allowing for higher sensitivity and easier spectra interpretation. The method was suitable for direct and rapid analysis of all tested compounds. No sample preparation was necessary, neither were solvents used. The method can be used for the initial, fast identification of compounds, directly from herbal matrices.

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