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Spectral identification of cannabinoids

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Abstract
The combination of infrared spectroscopy and chemometrics has become a popular method of detection and / or identification of illicit substances. This review paper highlights the most frequently used analytical tools in this research area, focusing on the identification of synthetic or natural cannabinoids.

Keywords: cannabinoids, spectroscopy, chemometrics, ATR – FTIR, GC- FTIR.

1. INTRODUCTION

Due to dynamics of the new hallucinogens found on the black market, the identification and detection of these compounds represent a very important issue for the fight against illicit laboratories. From this point of view, infrared spectroscopy and chemometrics became the two most important analytical methods. Spectroscopy studies how to record, measure and interpret the emission and absorption spectra of different compounds. Chemometrics applies mathematical methods and models in physics and chemistry in order to process very large analytical data, such as that provided by spectroscopy. The aim of this paper is to review the principal methods of detection of illicit drugs based on their chemical and physical properties.

2. EXPERIMENTAL

In order to review the main methods applied for drugs identification, open science databases (such as PubMed, Wiley) were searched. They indicate that the main methods used for the qualitative and quantitative analysis of cannabinoids are Attenuated Total Reflection coupled with Fourier Transform Infrared Spectroscopy (ATR-FTIR), Gas chromatography coupled with Mass Spectrometry (GC-MS), Gas Chromatography coupled with Fourier Transform Infrared Spectrometry (GC-FTIR), High-Performance Liquid Chromatography (HPLC), and two-dimensional Gas Chromatography (GC x GC) that is recommended for complex mixtures, especially cannabis extracts [1].

FTIR spectroscopy is the process by which the functional groups present in molecular structures irradiated with electromagnetic radiation are identified. Following the interaction between the substance and the radiation, the molecules absorb photons that have the energy necessary to generate spectral transitions [2]. The absorption spectrum of a chemical compound consists of absorption bands that are characteristic to the chemical groups present in the analyzed molecule. The interactions between the radiation and the groups of vibrating atoms give each spectrum its individuality [3].

GC is one of the most widely used methods in the quantitative analysis of cannabinoids. IN this case, GC is usually performed at temperatures up to 300°C and is completed in less than 20 minutes [1].

The utility of MS arises from the fact that the ionization process splits the analyzed molecule into fragments whose mass distribution is characteristic to the specific compound (parent species) [4]. GC coupled with MS is often used to detect and quantitatively analyze cannabinoids. MS allows the use of libraries of spectra to compare the spectrum of the sample with those of known compounds. The GC-MS chromatograms show on the X-axis the retention time and on the Y-axis the concentration or peak intensity. The active peaks correlate each component of the cannabinoid to the time when they reach the detector [5]. HPLC coupled with MS may also be successfully used for the quantitative identification of cannabinoid compounds [6].

To elude the law, illicit laboratories seek to synthesize new analogues of known drugs by slightly altering their chemical structure [7]. The increasing number of synthetic molecules constantly found on the illicit market has led to the development of multiple techniques with increased separation and identification powers. GC-FTIR is one of the main techniques that are very efficient for the separation and identification of new compounds, as it provides very specific information about the chemical structure of the analyzed sample [8].

For a better understanding these identification techniques, two synthetic cannabinoids (JWH-019 and JWH-081) were selected from the naphthoylindoles group and their spectra were compared. Their physico-chemical properties are presented in Table 1.

Table 1. MlogP and LogP values of the JWH-019 and JWH-081 synthetic cannabinoids [9]

Compound identifier	**Molweight**	**MLogP**	**Aqueous solubility**	**CACO-2 permeability**
JWH-081	371.47	4.7	-3.6207	1.3397
JWH-019	355.47	5.26	-3.7983	1.1806

The 2D molecular structures of the two compounds were drawn by using the *KnowItAll Informatics System* and the 3D molecular structures were drawn with ACD/ Chem Sketch software (see Fig. 1).

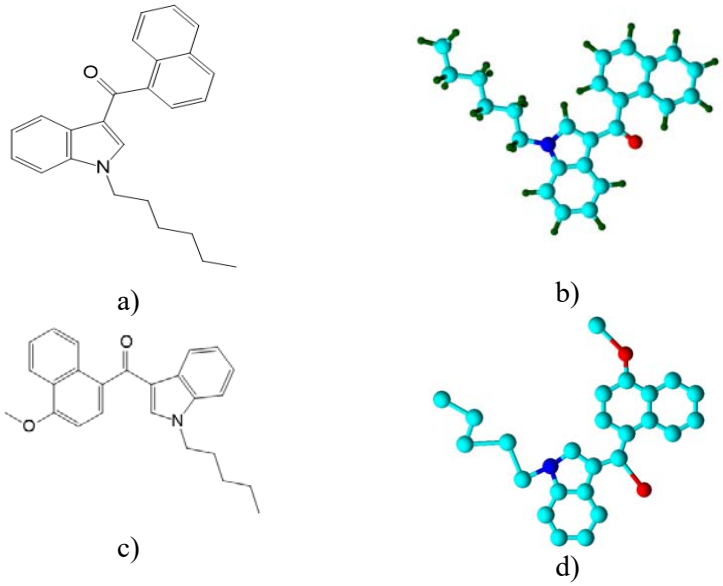


Fig. 1. a) 2D structure of JWH-019; b) 3D molecular structure of JWH-019; c) 2D structure of JWH-081; d) 3D molecular structure of JWH-019

3. RESULTS AND DISCUSSION

Starting with the compound name and molecular structure, and by using the *KnowItAll Informatics System*, the spectrum of the two synthetic cannabinoids were obtained and analyzed. Fig. 2 and 3 present the ATR- FTIR spectra of JWH-019 and JWH-081, which were recorded by performing 32 scans at a resolution of 4 cm^{-1}.

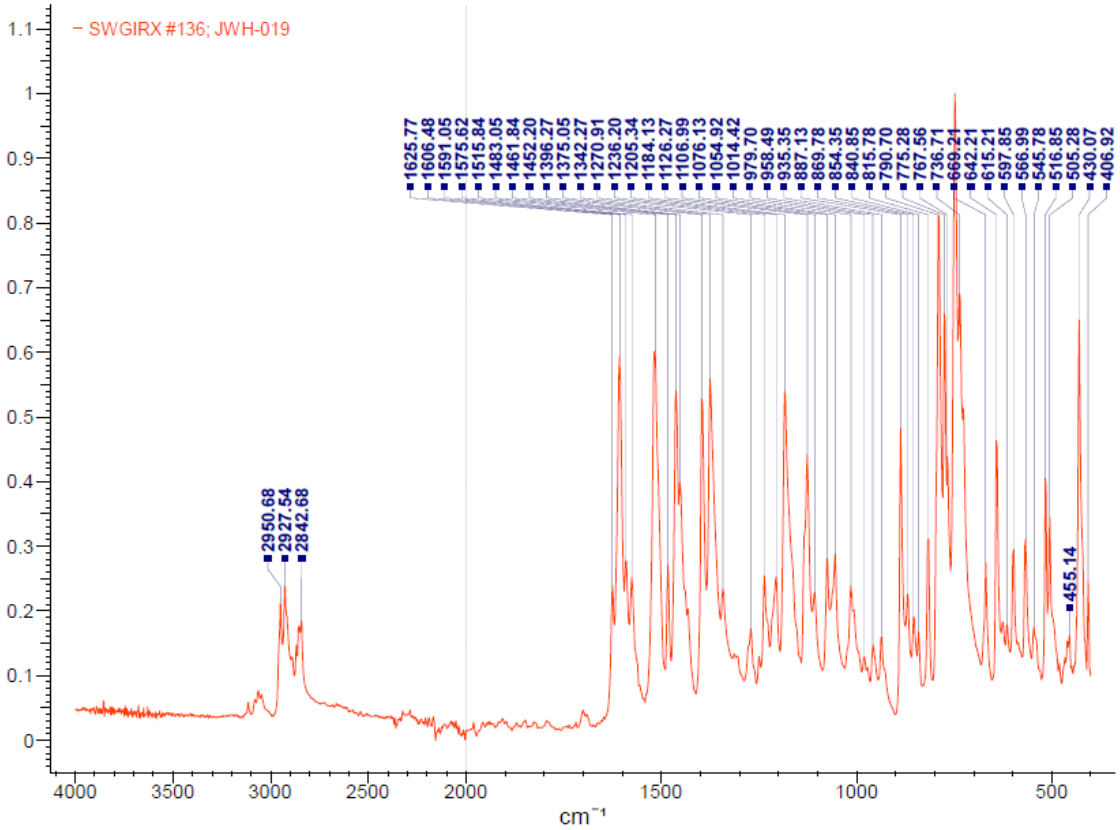


Fig. 2. ATR-FTIR spectrum of JWH-019, as obtained by using the KnowItAll software

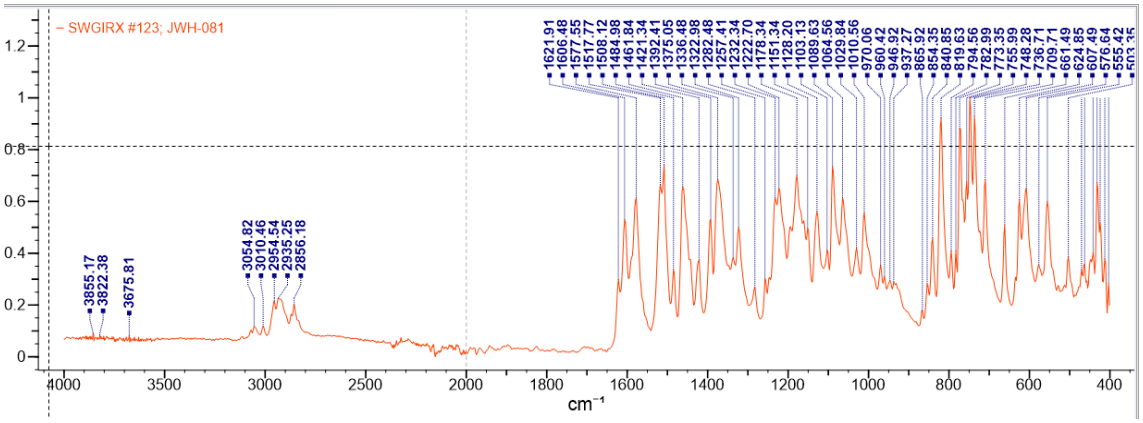


Fig. 3. ATR-FTIR spectrum of JWH-081, as obtained by using the KnowItAll software.

The overlaid spectra of JWH-019 and JWH-081 (see Fig. 4) have been analyzed in order to detect the common absorption bands specific to the two compounds, which are indicating the spectral similarities of these two synthetic cannabinoids. Fig. 5 highlights the spectral similarities of JWH-019 (green line), JWH-081 (blue line) and Δ9 THC (red line), their natural counterpart.

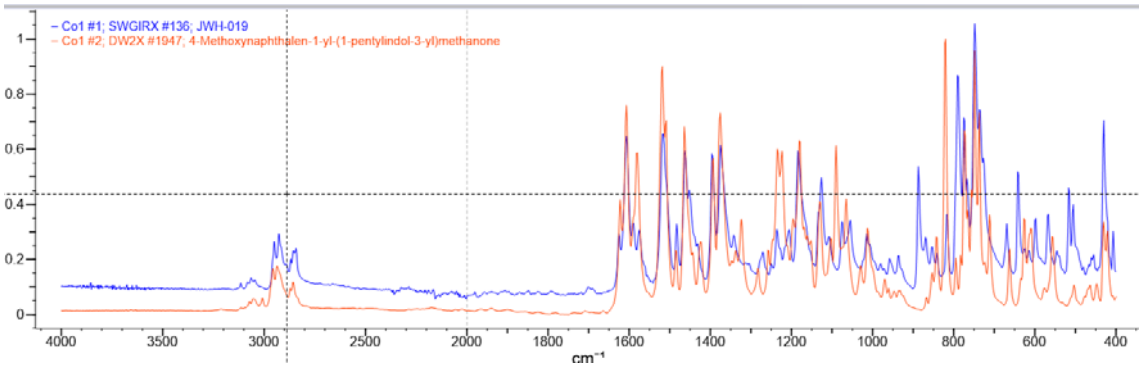


Fig. 4. Overlaid spectra of JWH-081 and JWH-019, as obtained by using the KnowItAll software

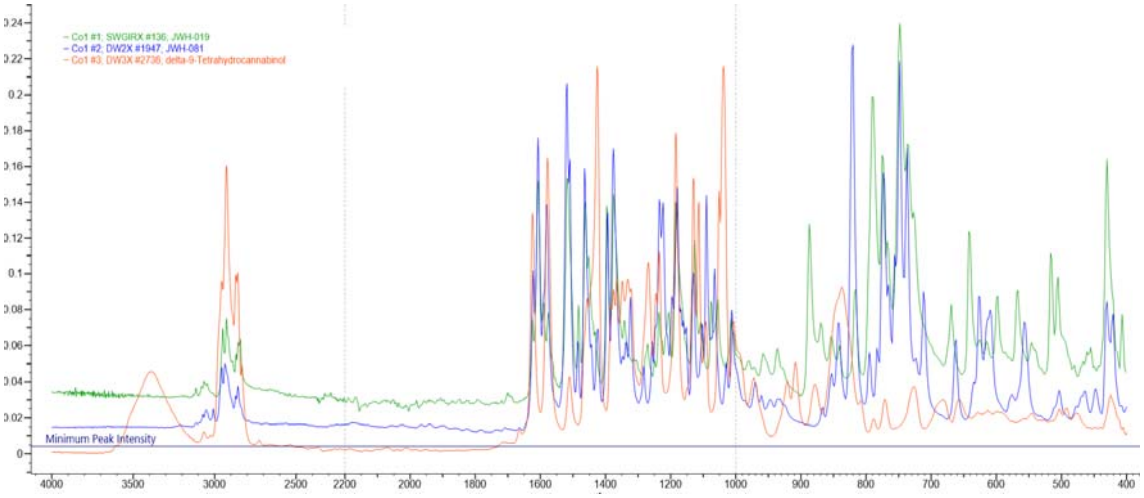
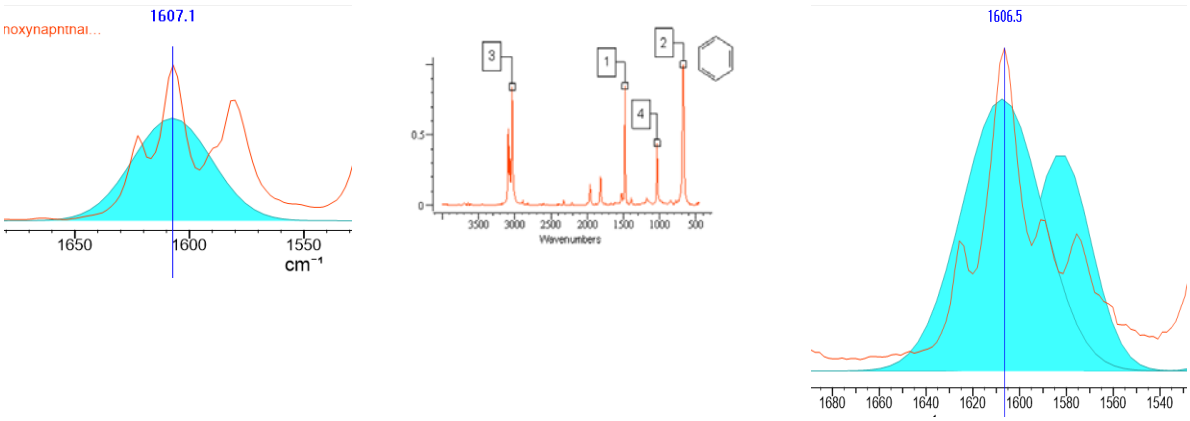


Fig. 5. ATR-FTIR spectra of the synthetic cannabinoids JWH-019 and JWH-081in comparison with the spectrum of Δ9 THC, their natural counterpart (as obtained by using the KnowItAll software).

For example, the absorption band specific to the aromatic compounds (see Fig. 6a) is found in the spectrum of Δ^9 THC in the 1625-1590 cm^{-1} region. The same functional group is present in the spectrum of JWH-019 (see Fig. 6b) and JWH -081 (see Fig. 6c) spectra.



a) *b)* *c)*

Fig. 6. Identification of the aromatic functional group: a) according to the Sadtler handbook; b) in the spectrum of JWH-019; c) in the spectrum of JWH-081 (as obtained by using the KnowItAll software)

The second analyzed technique is GC-MS. The analyte was diluted in $CHCl_3$, and the carrier gas was Helium at 1 ml/min. The injection temperature was 280°C [10]. Fig. 7 shows the GC-MS spectrum of JWH-019 and Fig. 8 the GC-MS spectrum of JWH-081.

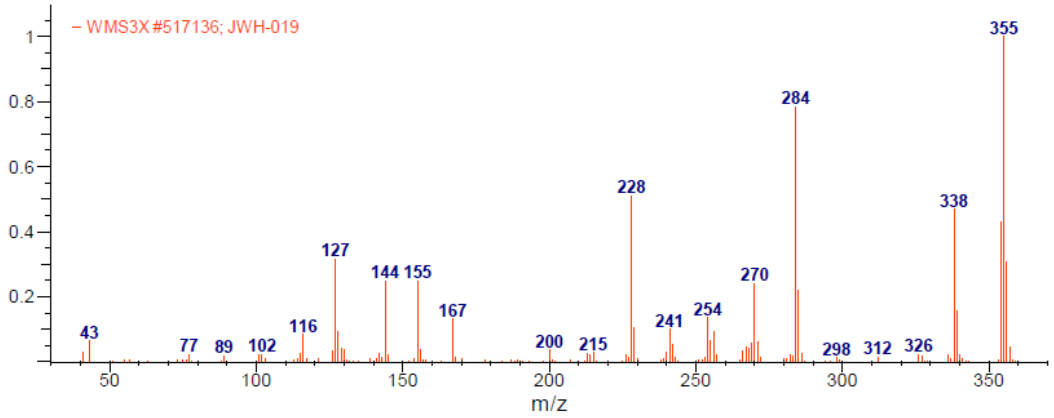


Fig. 7. GC-MS spectrum of JWH-019

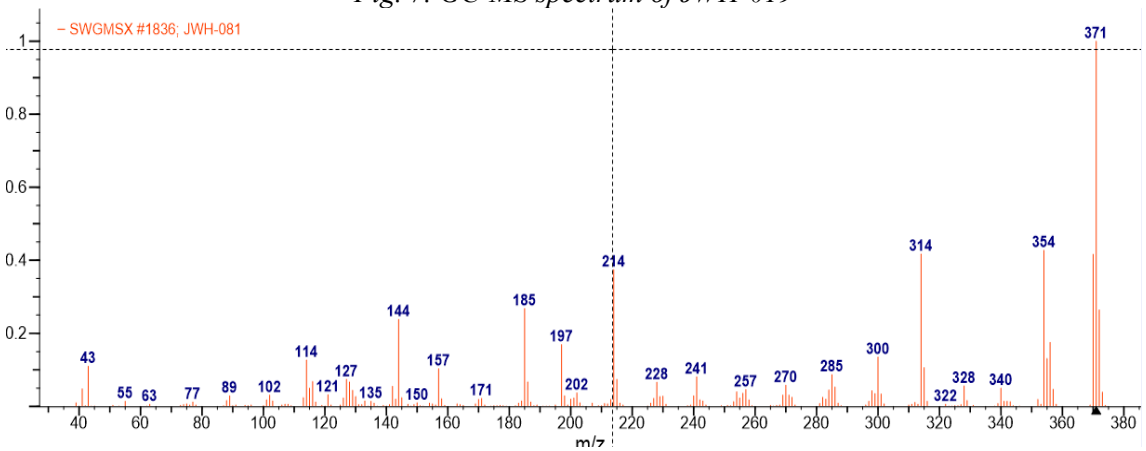


Fig. 8. GC-MS spectrum of JWH-081

The common peaks that appear in the two GC-MS spectra and which can therefore be used to recognize the class of synthetic cannabinoids are: 43, 77, 89, 127, 144, 228, 241, 270 m/z (marked in green in Table 2). The main peaks that are specific for JWH 019 are 338, 355 m/z and for JWH -081 are 314, 371 m/z (see Table 2).

Tabel 2. Identification of the common ions

JWH-019	43			77	89		116		127		144		155		167				200		
JWH-081	43	55	63	77	89	114		121	127	135	144	150		157		171	185	197		202	214
JWH-019	215	228	241	254		270	284		298		312			326		338			355		
JWH-081		228	241		257	270		285		300		314	322		328		340	354		371	

4. CONCLUSIONS

Analytical tools with increased separation and identification powers are required for the identification of cannabinoids. The most frequently used techniques from this point of view are GC-FTIR and GC-MS, although it is necessary to obtain volatile derivatives to avoid decarboxylation of cannabidiol acid.

The results indicate that in the case of these compounds, GC-FTIR spectroscopy provides more detailed spectral information that can be used for the characterization of the analyzed samples.

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