Synthetic cannabinoids: analytical methods

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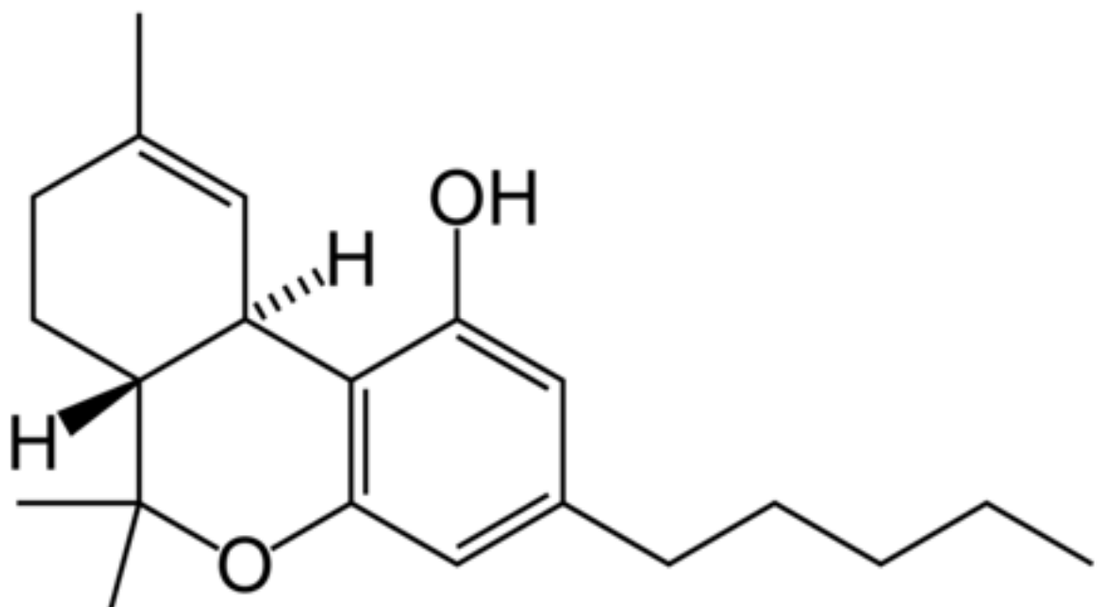
Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

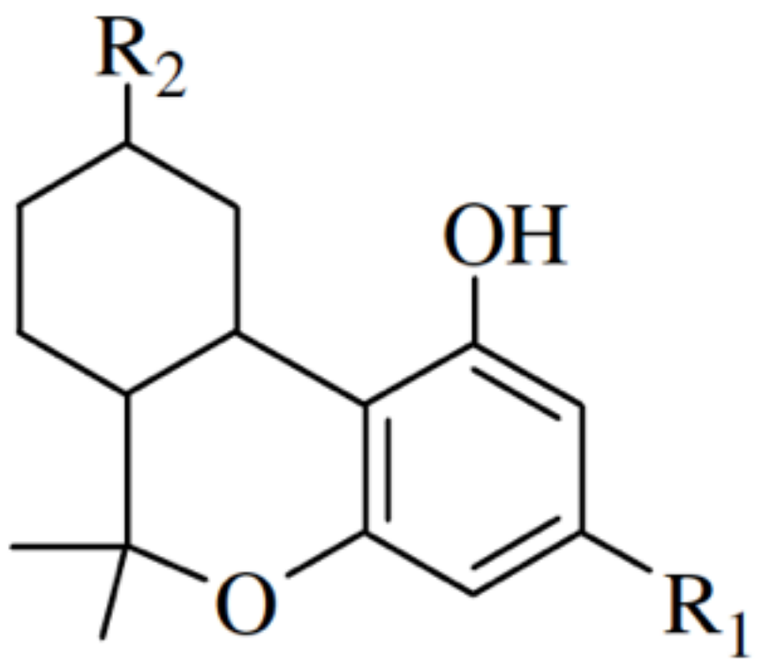
The term « **synthetic cannabinoids** » covers all synthetic substances binding to one of the two known cannabinoids receptors (CB1 or CB2) and their structural/chemical analogues:

- Classical cannabinoids
- Nonclassical cannabinoids
- Aminoalkylindoles
- Eicosanoids
- Others

■ Classical cannabinoids



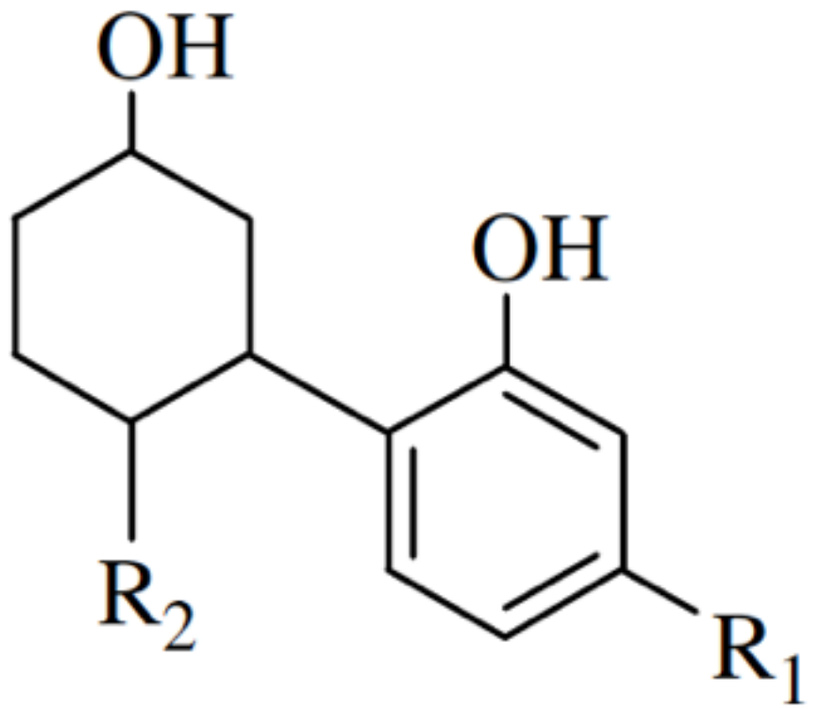
THC



HU-210 R_1 = 1,1 dimethylheptyl
R_2 = hydroxymethyl

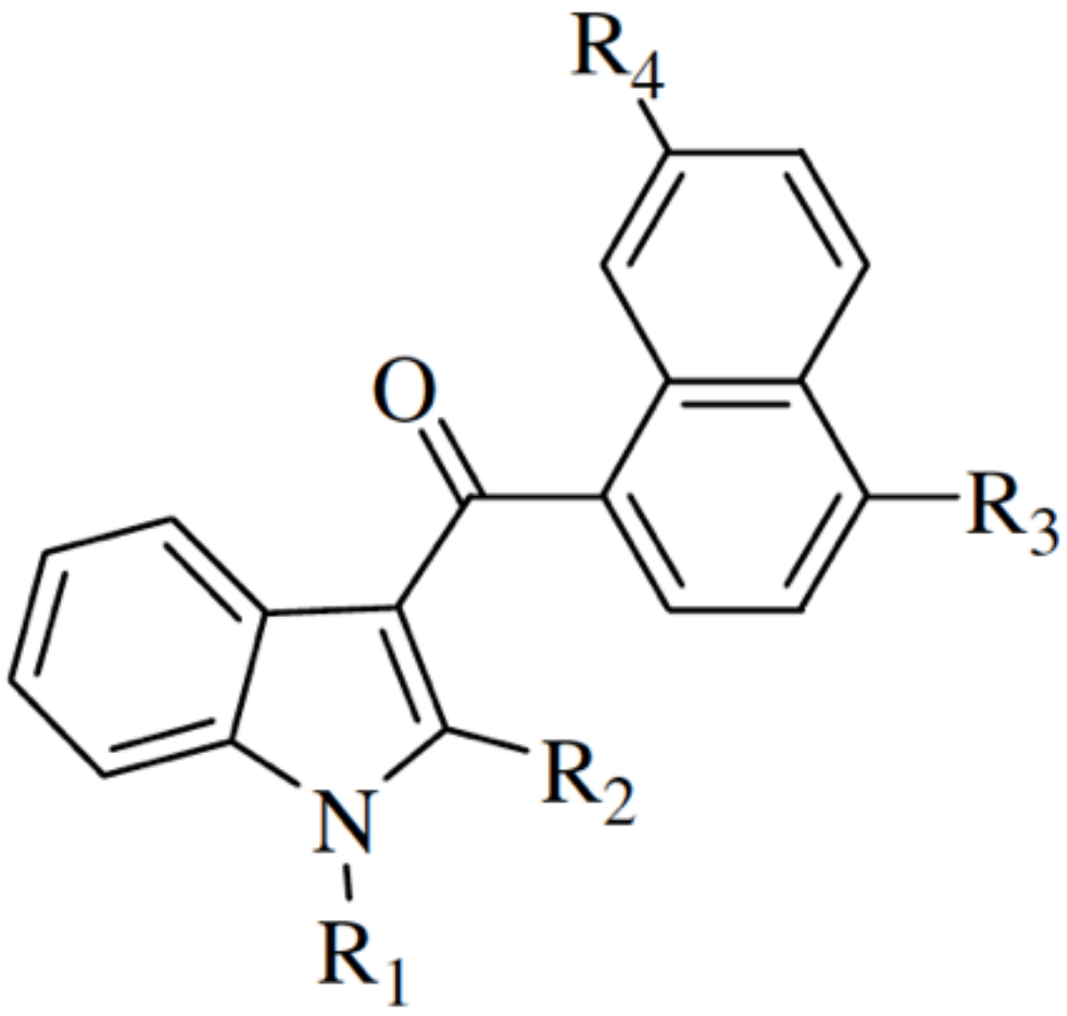
Nabilone R_1 = 1,1 dimethylheptyl
R_2 = keto

■ Cyclohexylphenols



CP47,497	R_1 = 1,1 dimethylheptyl
Cannibicylohexanol	R_1 = 1,1 dimethyloctyl
CP55,940	R_1 = 1,1 dimethylheptyl
	R_2 = hydroxypropyl

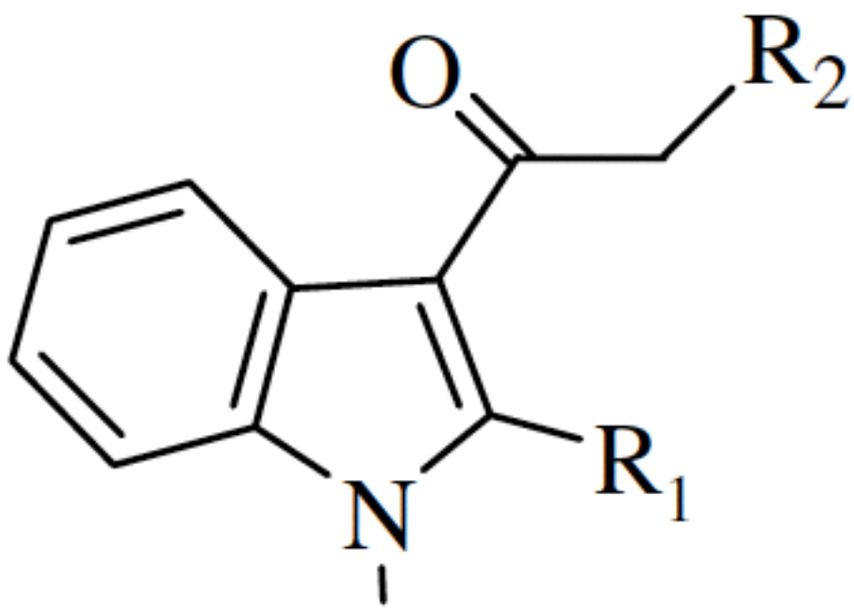
■ Naphtoylindoles



JWH-015 R_1 = propyl R_2 = methyl
JWH-018 R_1 = pentyl
JWH-019 R_1 = hexyl
JWH-073 R_1 = butyl
JWH-081 R_1 = pentyl R_3 = methoxy
JWH-122 R_1 = pentyl R_3 = methyl
JWH-200 R_1 = morpholinylethyl
JWH-210 R_1 = pentyl R_3 = ethyl
JWH-387 R_1 = pentyl R_3 = Br
JWH-398 R_1 = pentyl R_3 = Cl

(R=H unless specified)

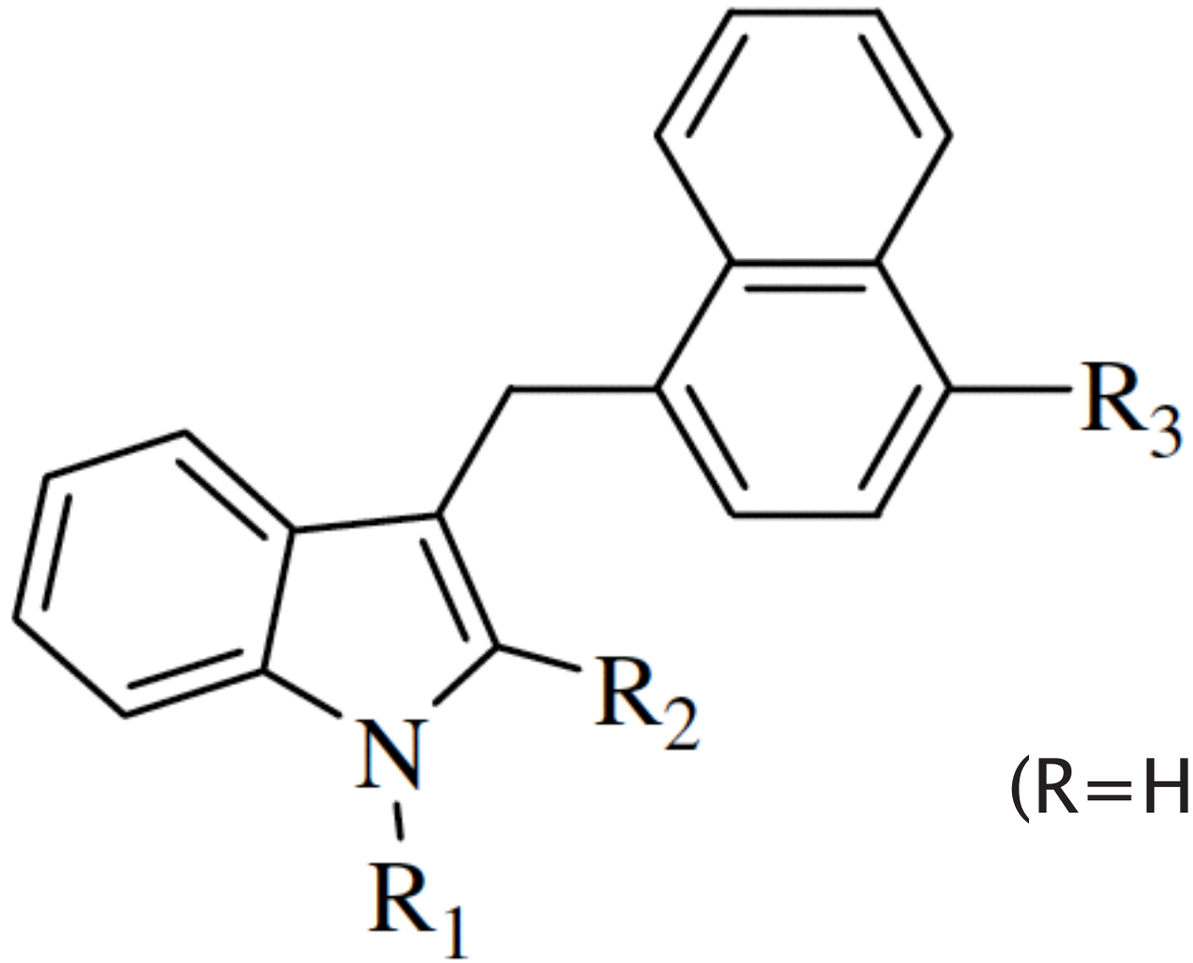
■ Phenyacetylindoles



(R=H unless specified)

JWH-250 R_2 = methoxyphenyl
JWH-253 R_1 = methyl
R_2 = methoxyphenyl

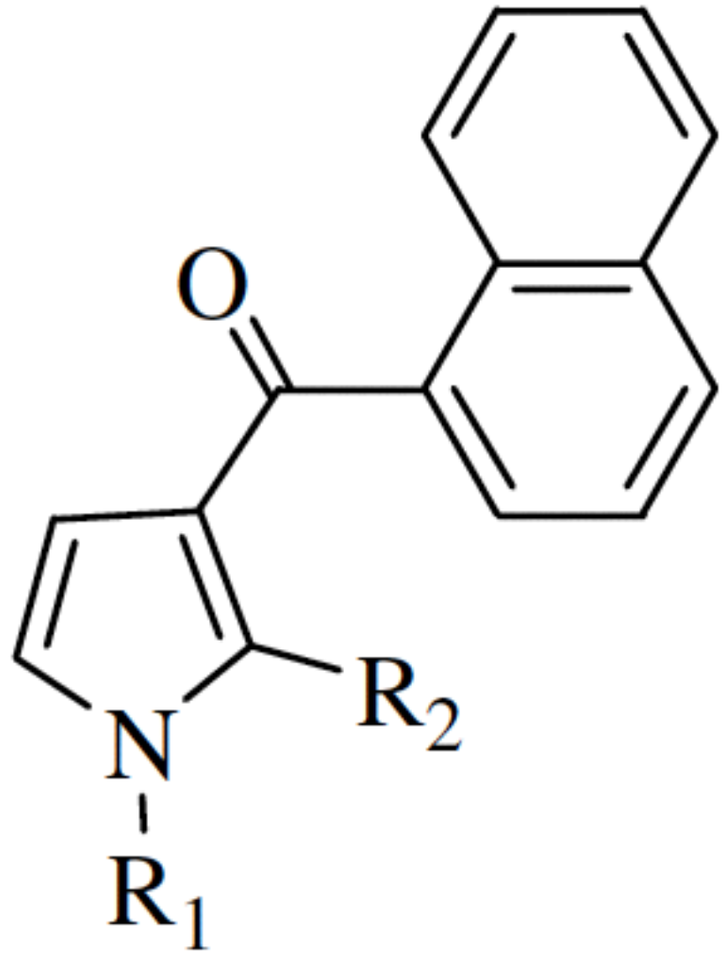
■ Naphtylmethylindoles



(R=H unless specified)

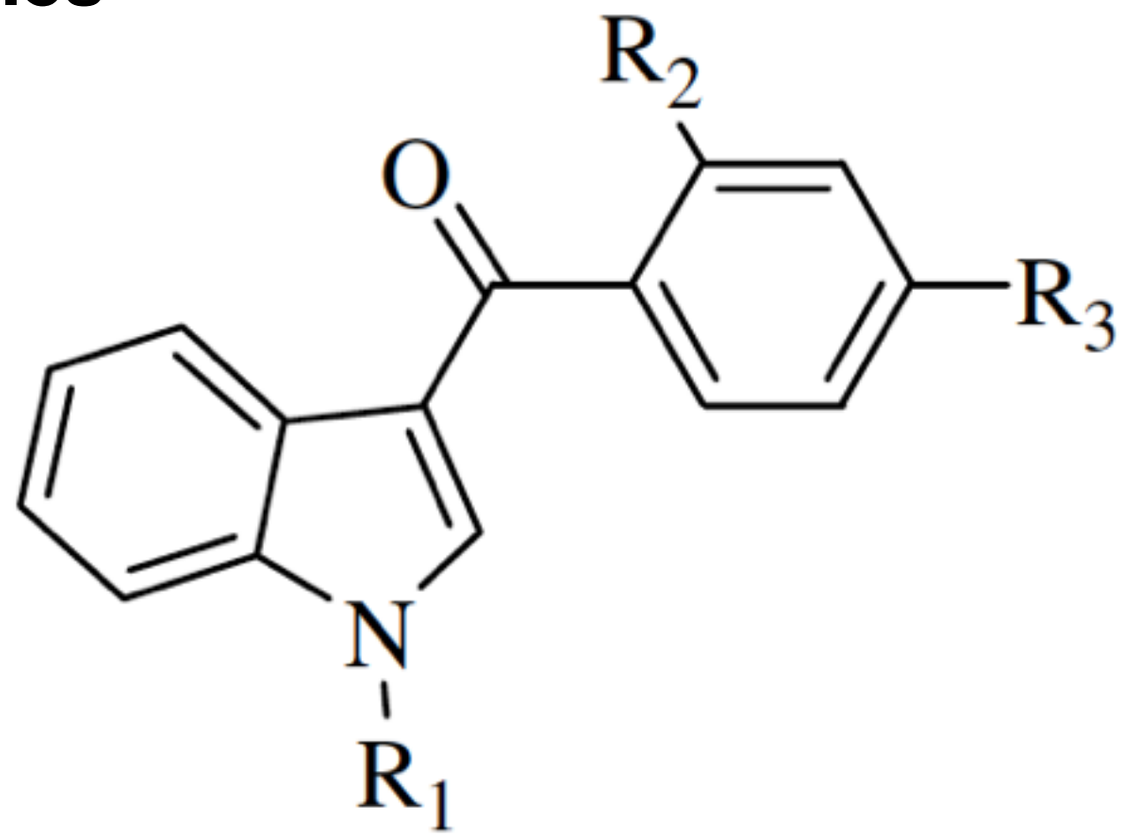
JWH-184 R_1 = pentyl R_3 = methyl

■ Naphtoylpyrroles



JWH-146 R_1 = heptyl R_2 = phenyl

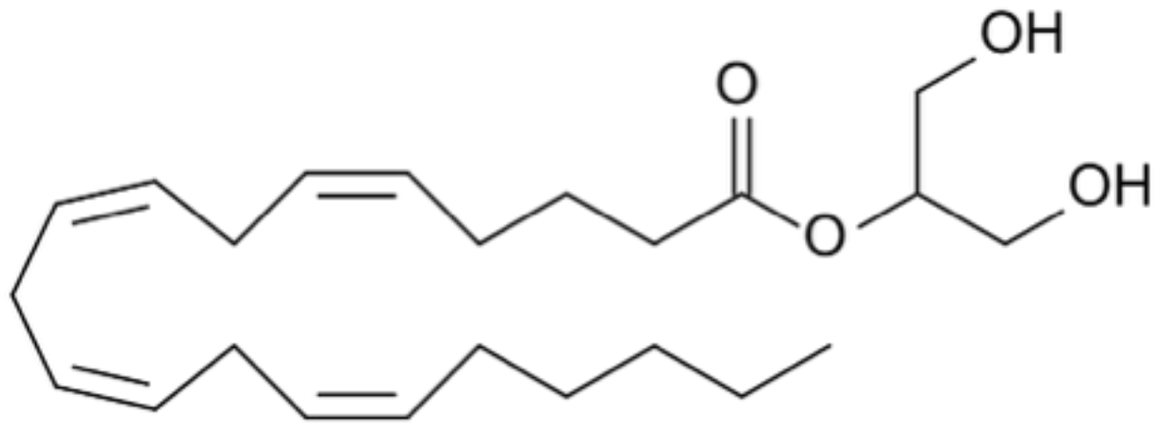
■ Benzoylindoles



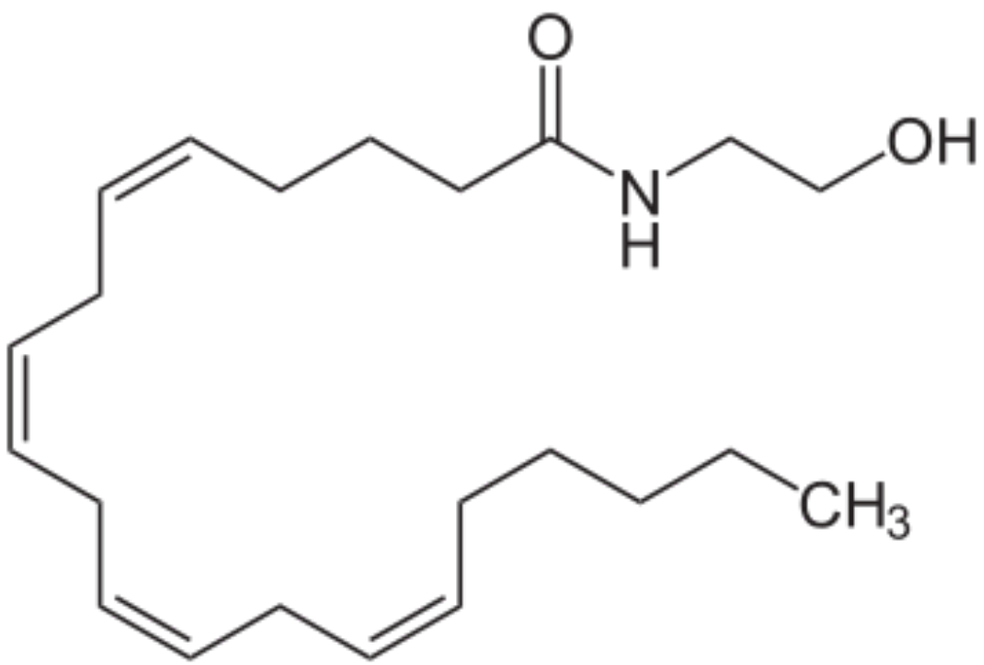
AM-694 R_1 = 5-fluoropentyl
R_2 = I

RCS-4 R_1 = pentyl
R_3 = methoxy

■ Eicosanoids



2-arachidonoylglycerol



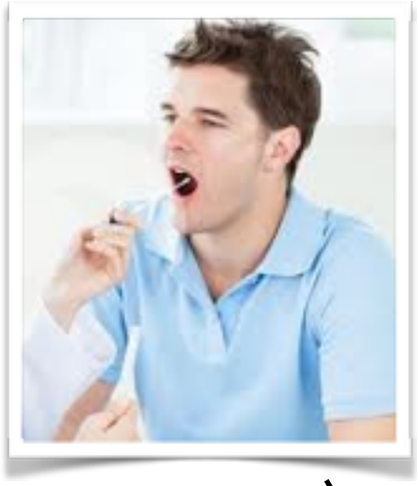
anandamide

NON-BIOLOGICAL MATERIAL

HERBAL BLENDS

BULK POWDERS

ORAL FUID



URINE

HAIR

BLOOD / SERUM

BIOLOGICAL MATERIAL

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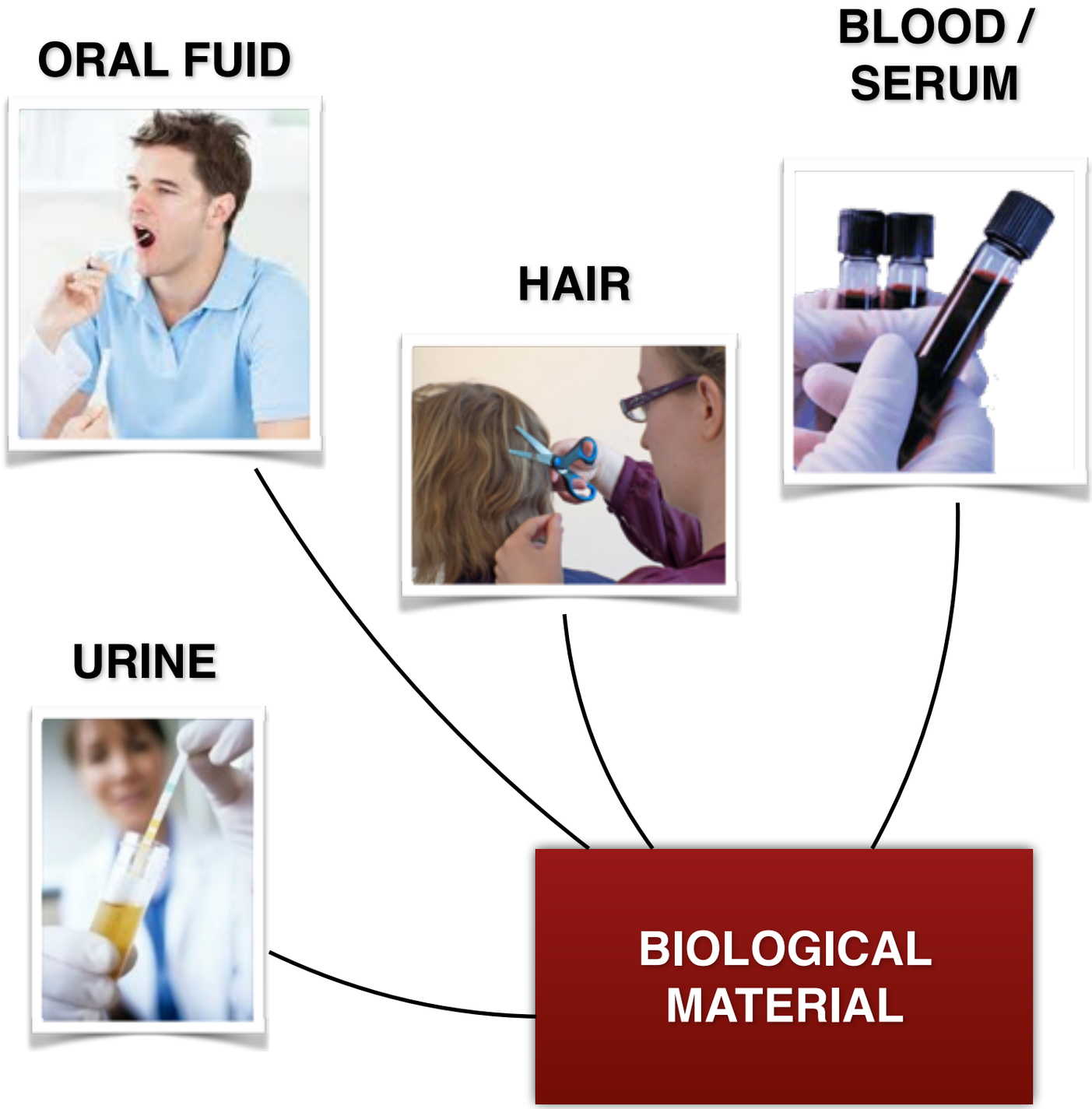
NON-BIOLOGICAL MATERIAL

HERBAL BLENDS

BULK POWDERS


ORAL FUID
HAIR
BLOOD / SERUM
URINE
BIOLOGICAL MATERIAL

Reference material

- Reliable identification and particularly quantification of synthetic cannabinoids in herbal products and their metabolites in biological specimens of users requires the use of **reference material**.

- However, due to the immense variety of synthetic cannabinoids in the market, reference material for **most of these compounds is currently unavailable**.

Reference material

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NON-BIOLOGICAL MATERIAL

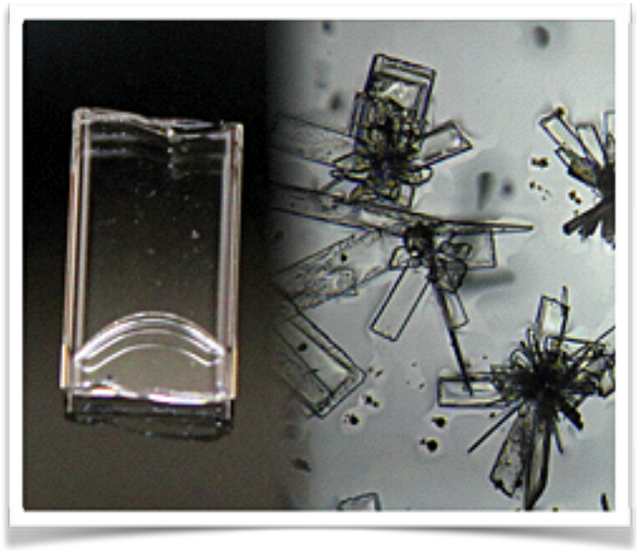
HERBAL BLENDS

BULK POWDERS

Presumptive test

COLOUR TESTS

MICROCRYSTAL TESTS



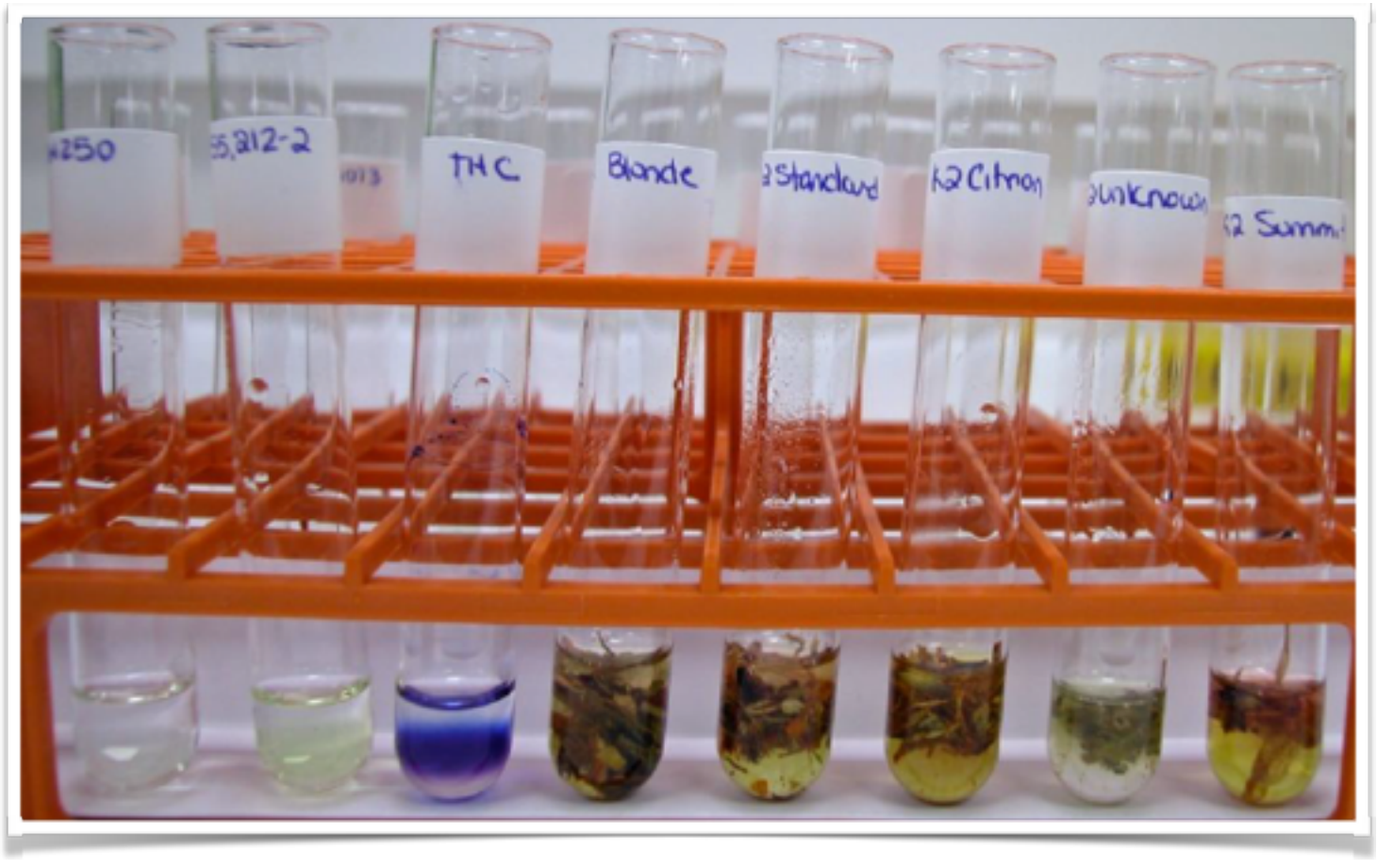
Presumptive test

COLOUR TESTS

Reagents :

- Duquenois–Levine
- Liebermann
- Marquis
- Mecke
- Mandelin

■ Duquenois-Levine



No purple color for synthetic cannabinoids

■ Liebermann

Reference	Cannabinoid Chemical Class	Source	Color
JWH-307	Naphthoylpyrrole	Reference Collection	Dark Yellow
AB-001	Adamantoyl indole	Reference Collection	Dark Yellow
CB-13	Dinaphthlyene methanone	Reference Collection	Dark Green
JTE-907	1,2-Dihydroquinoline-3-carboxamide	Reference Collection	Black (Bubbling)
UR-144	Tetramethylcyclopropanoylindole	Reference Collection	Dark Red
URB597	FAAH inhibitor	Reference Collection	Yellow-Brown
URB602	FAAH inhibitor	Reference Collection	Dark Brown
URB754	FAAH inhibitor	Reference Collection	Light Brown
AM-1248	Adamantoyl indole	Reference Collection	Dark Yellow
AB-034	Tetramethylcyclopropanoylindole	Reference Collection	Red-Orange>Dark Red
A-796, 260	Tetramethylcyclopropanoylindole	Reference Collection	Red-Orange>Dark Red
A-834-735	Tetramethylcyclopropanoylindole	Reference Collection	Red-Orange>Dark Red
FUR-144	Tetramethylcyclopropanoylindole	Reference Collection	Dark Red
AKB48	Adamantyl amidoindazole	Reference Collection	No color change
JWH-073	Naphthoylindole	Cayman Chemical	Yellow-Brown
JWH-018	Naphthoylindole	Cayman Chemical	Yellow-Brown
JWH-200	Naphthoylindole	Cayman Chemical	Dark Yellow-Brown
AM-2201	Naphthoylindole	Cayman Chemical	Yellow-Brown
JWH-203	Phenylacetylindole	Cayman Chemical	Yellow-Orange
RCS-4-C4 homolog	Benzoylindole	Cayman Chemical	Brown
AM694	Benzoylindole	Cayman Chemical	Dark-Yellow
MAM2201	Naphthoylindole	Cayman Chemical	Green-Brown
AM2233	Benzoylindole	Cayman Chemical	Yellow
STS-135	Adamanty lamidoindole	Reference Collection	Brown

■ Marquis / Mecke / Mandellin

JWH-018, JWH-073, JWH-081
Marquis - Yellow quickly changing to brown
Mecke - Brown/Yellow
Mandellin - Dark brown

JWH-200
Marquis - Yellow/orange
Mecke - Yellow
Mandellin - Dark red-brown

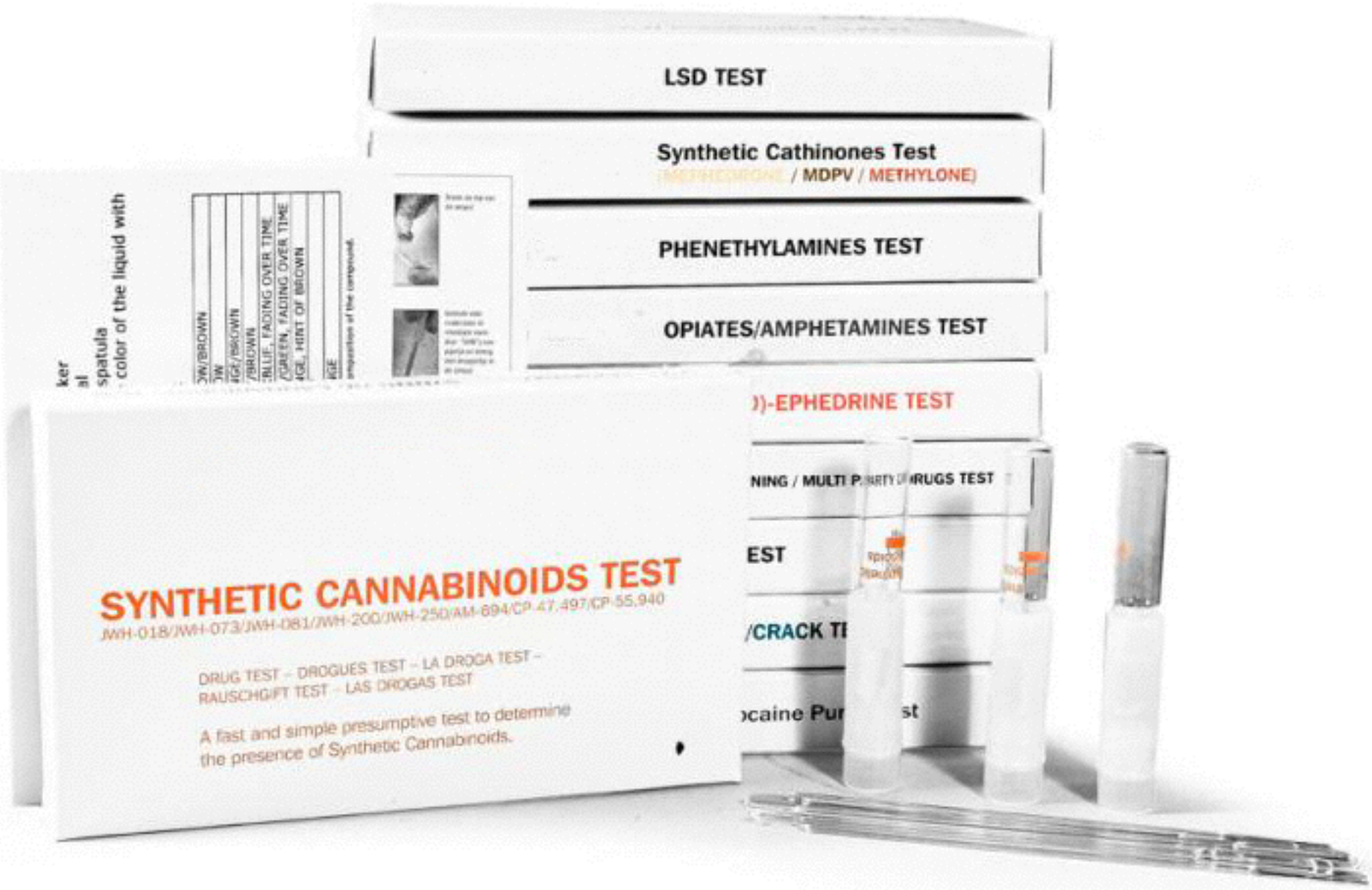
JWH-250
Marquis - Red, fading to orange over time
Mecke - Orange
Mandellin - Dark grey-brown

AM-694
Marquis - Brown/yellow, hints of green
Mecke - grey/brown
Mandellin - Dark red-brown

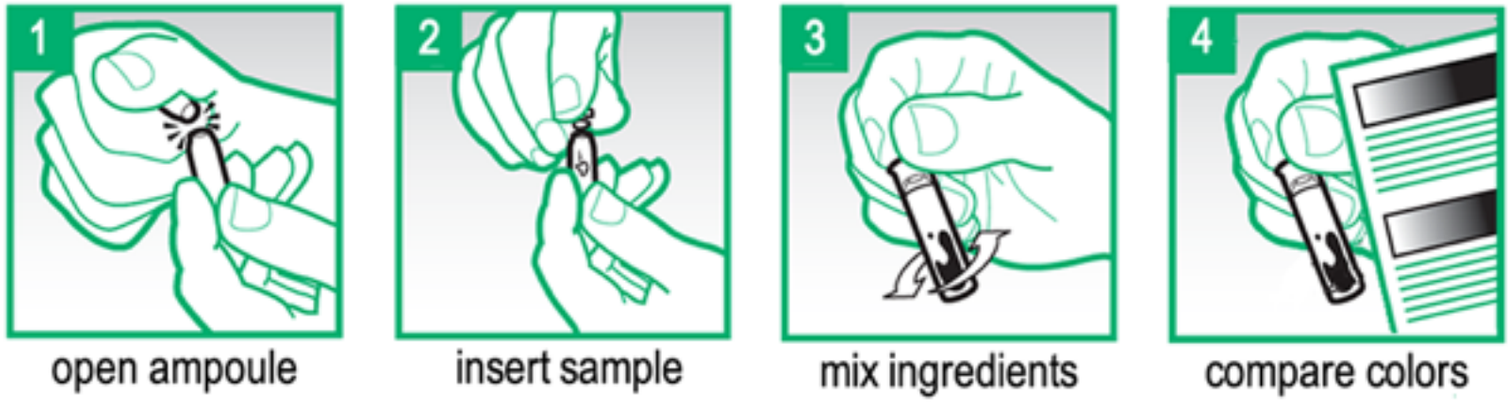
CP-47,497
Marquis - Red/orange
Mecke - Blue, fading over time.
Mandellin - Brown

CP-55,940
Marquis - red/orange
Mecke - Blue-green, fading over time
Mandellin - Brown

■ Available commercial kits



■ Available commercial kits



JWH-018, JWH-073, JWH-019, JWH-122, AM2201	YELLOW / BROWN	
JWH-200, AM2233, RCS-4	YELLOW	
AM-694	GREY/BROWN	
CP-47,497	DARKBLUE, FADING OVER TIME	
CP-55,940	BLUE/GREEN, FADING OVER TIME	
JWH-081	BROWN	
URB-597	YELLOW CHANGING INTO GREY	
JWH-250	GREY	
RCS-4	ORANGE	

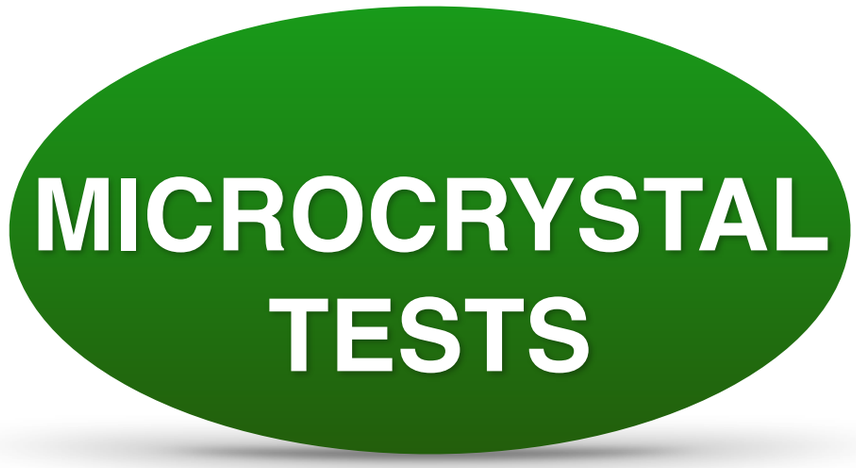
Presumptive test

COLOUR TESTS

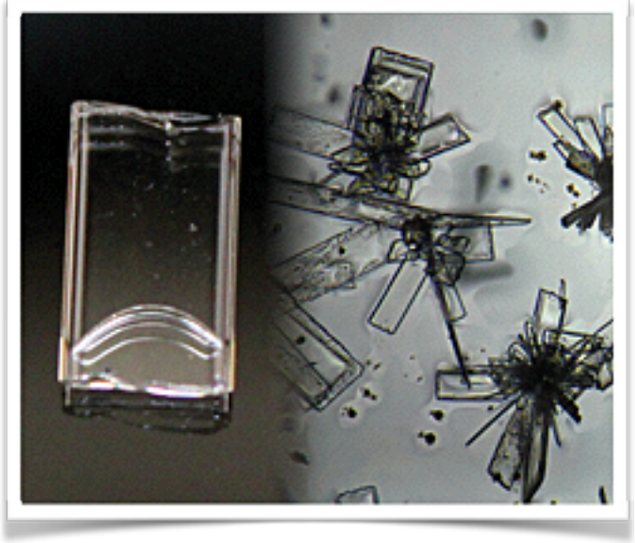
- Lack of specificity
- No tests cover the whole range of synthetic cannabinoids

Not appropriate

Presumptive test



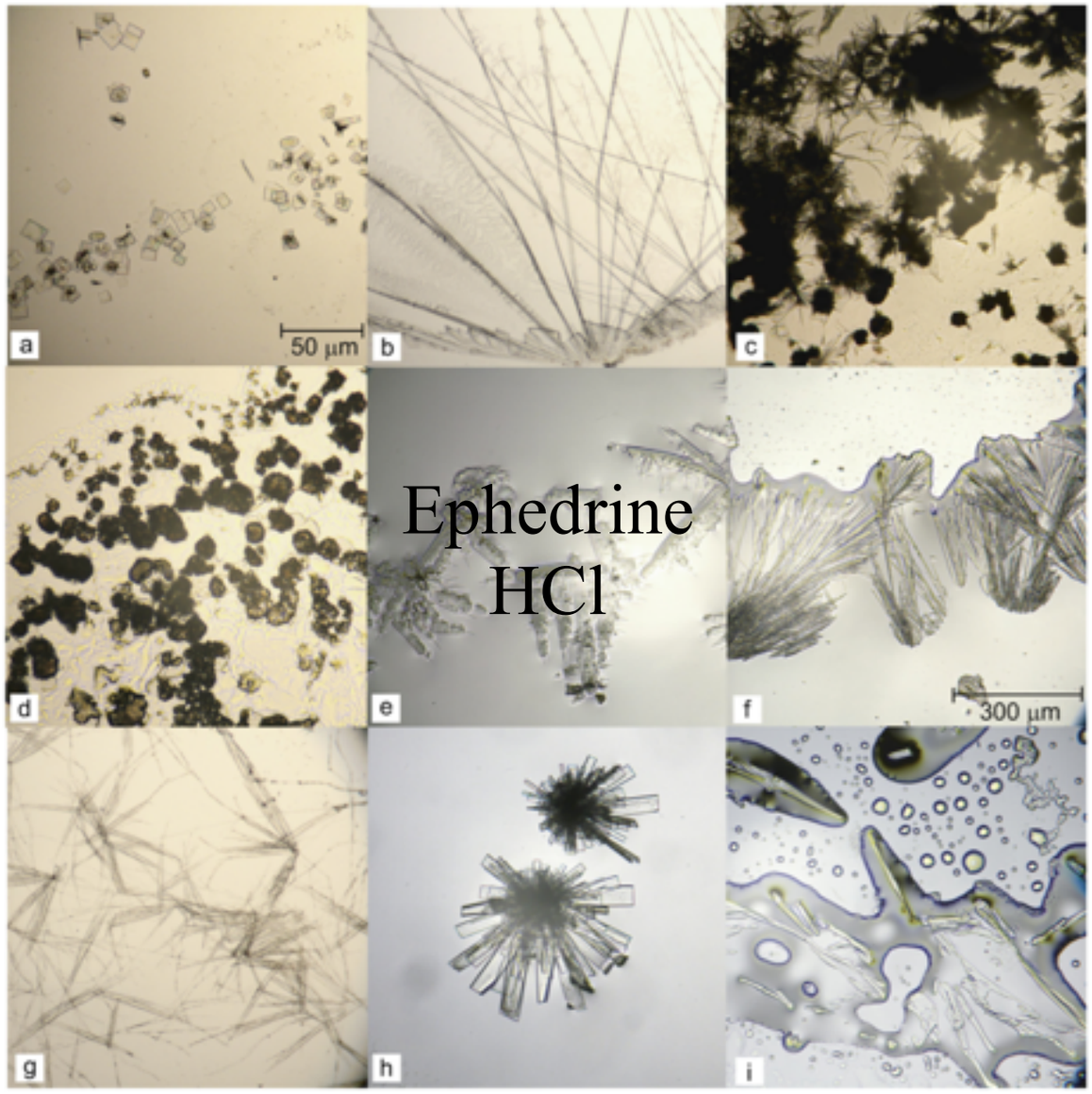
- Reaction with mercury chloride
- Observation with a microscope
- Visual comparison with reference material



■ Exemples with other drugs

BZP

Caffeine



D-amphetamine

DL-amphetamine

Ephedrine sulfate

MDAI

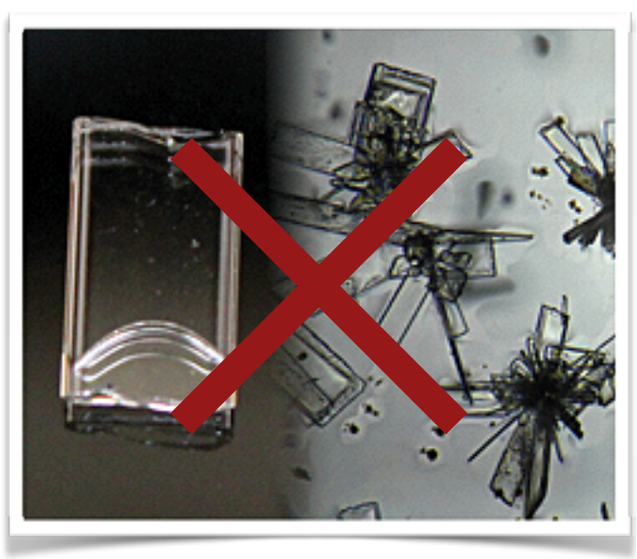
Mephedrone

Metamphetamine

Presumptive test

- Low concentration of synthetic cannabinoids in herbal material
- Possible interference by the sample matrix

MICROCRYSTAL TESTS



Not appropriate

TLC

Thin-layer chromatography

- Commonly used technique for the separation and detection of illicitly manufactured drugs

- Inexpensive, rapid and flexible in the selection of both the stationary and mobile phase and amenable to a wide variety of substances

TLC

Thin-layer chromatography

- Classical and non-classical cannabinoids (e.g. HU-210 and CP-47,497-C8) can be selectively and sensitively detected with **UV light, Fast Blue RR reagent, iodine** as well as **iodoplatinate**

- Aminoalkylindoles (e.g. JWH-018, JWH-081, JWH-210) can be detected with **UV light, iodine or iodoplatinate**.

TLC

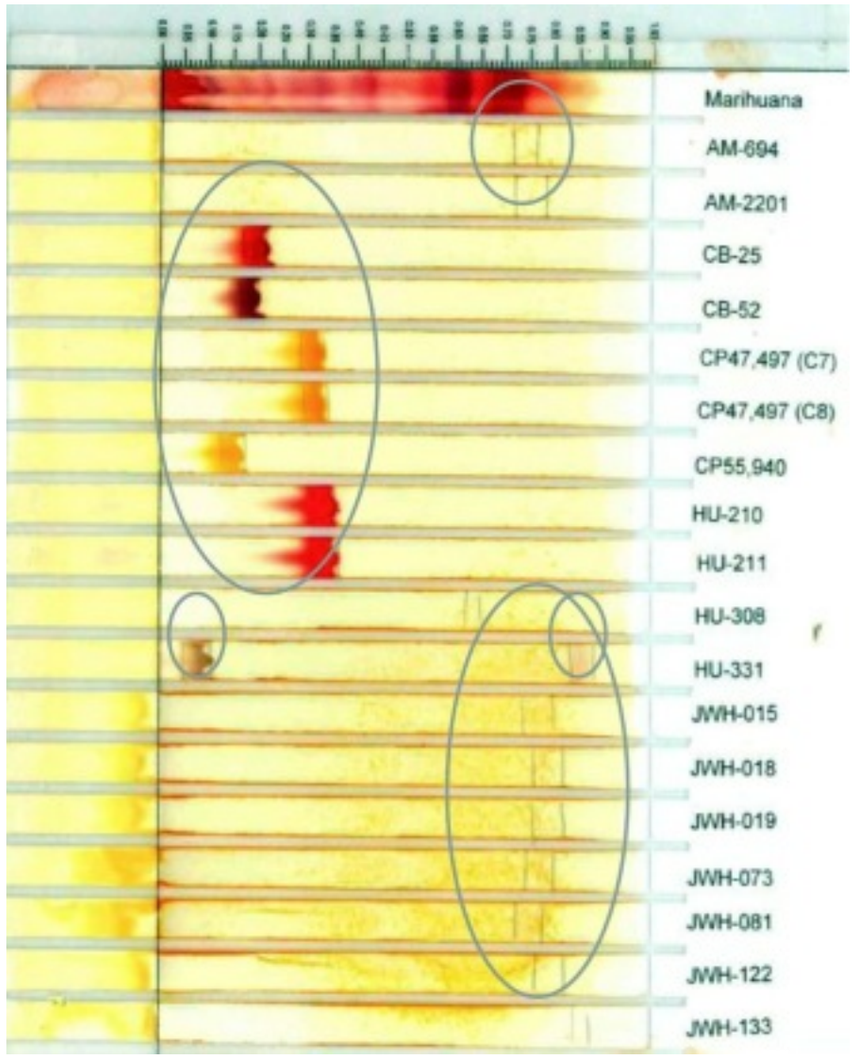
Thin-layer chromatography

Solvent System:
9:1 Toluene:Diethylamine

Visualization Spray:
Fast Blue B Spray

Distinct red/orange bands for Cannabinoids, CP & most HU compounds

Obvious 254 nm UV absorbance for AM, JWH & WIN compounds



TLC

Thin-layer chromatography

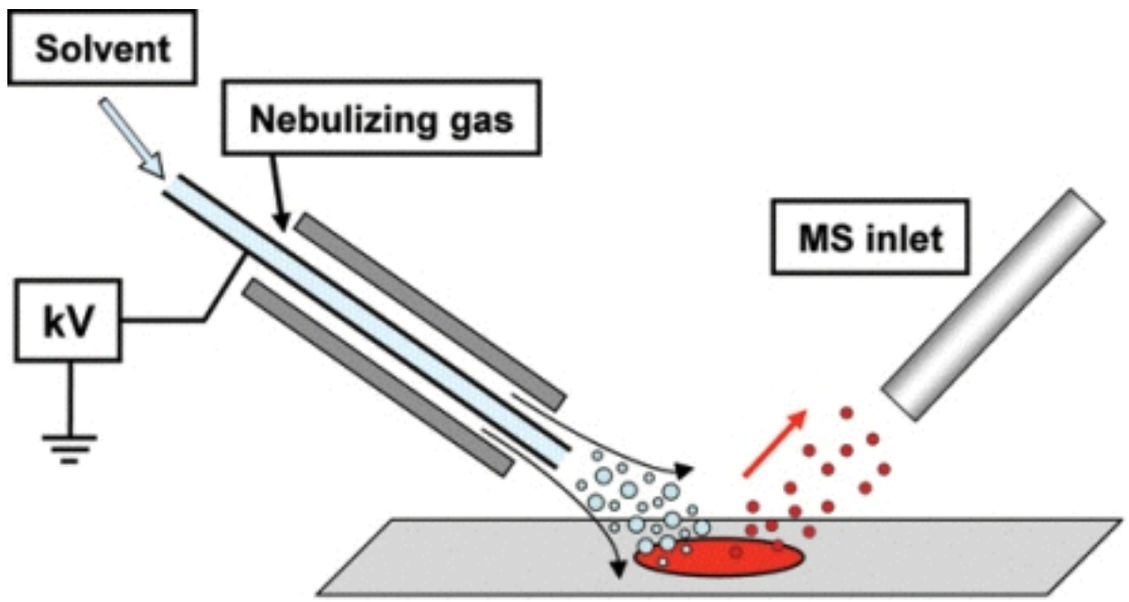
$$Rf = \frac{\text{Migration distance}}{\text{Development distance}}$$

- Reference standards must be run simultaneously on the same plate.
- GC-MS or GC-IRD must be used to confirm substances with close Rf

DESI-MS

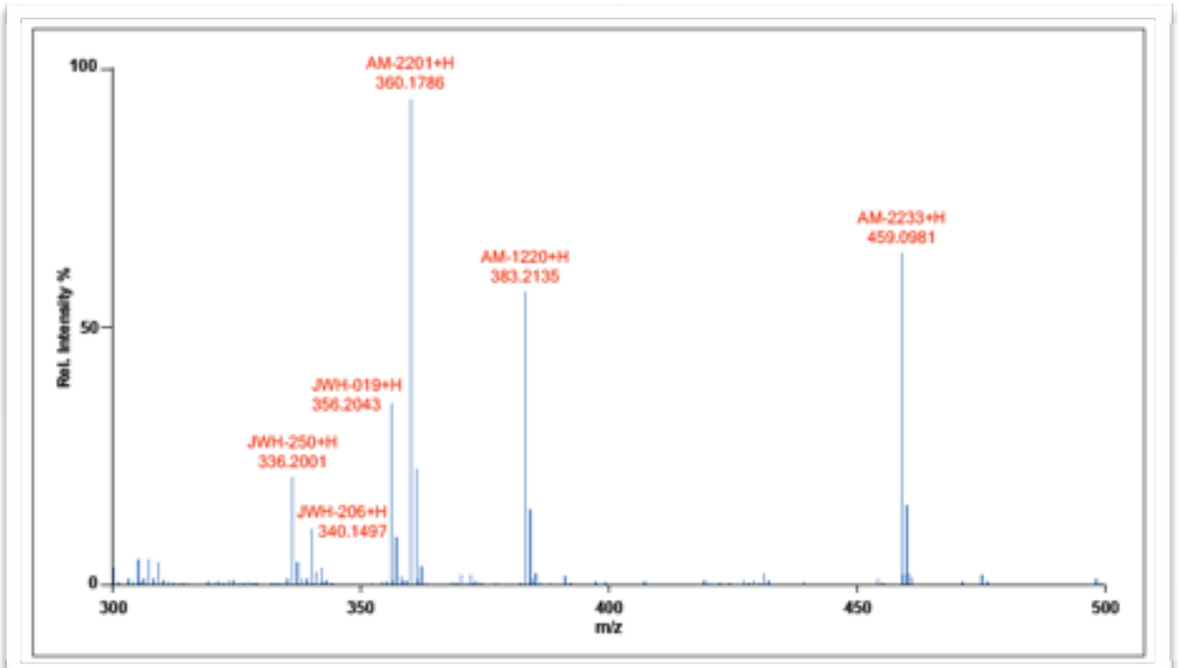
Desorption ElectroSpray Ionization

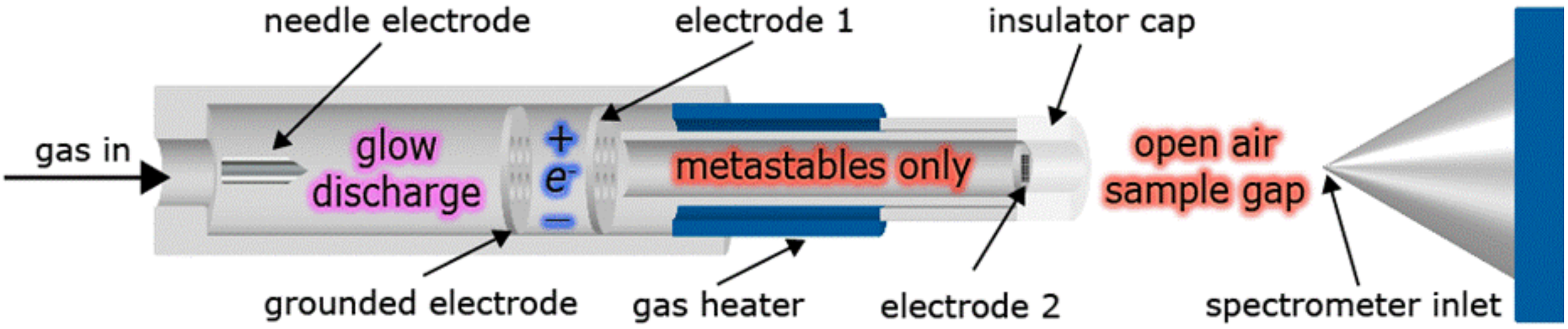
- DESI-MS could be employed to the plant material without the need for extraction and sample preparation.
- DESI-MS could also be used in combination with TLC.



DART-MS

Direct Analysis in Real Time





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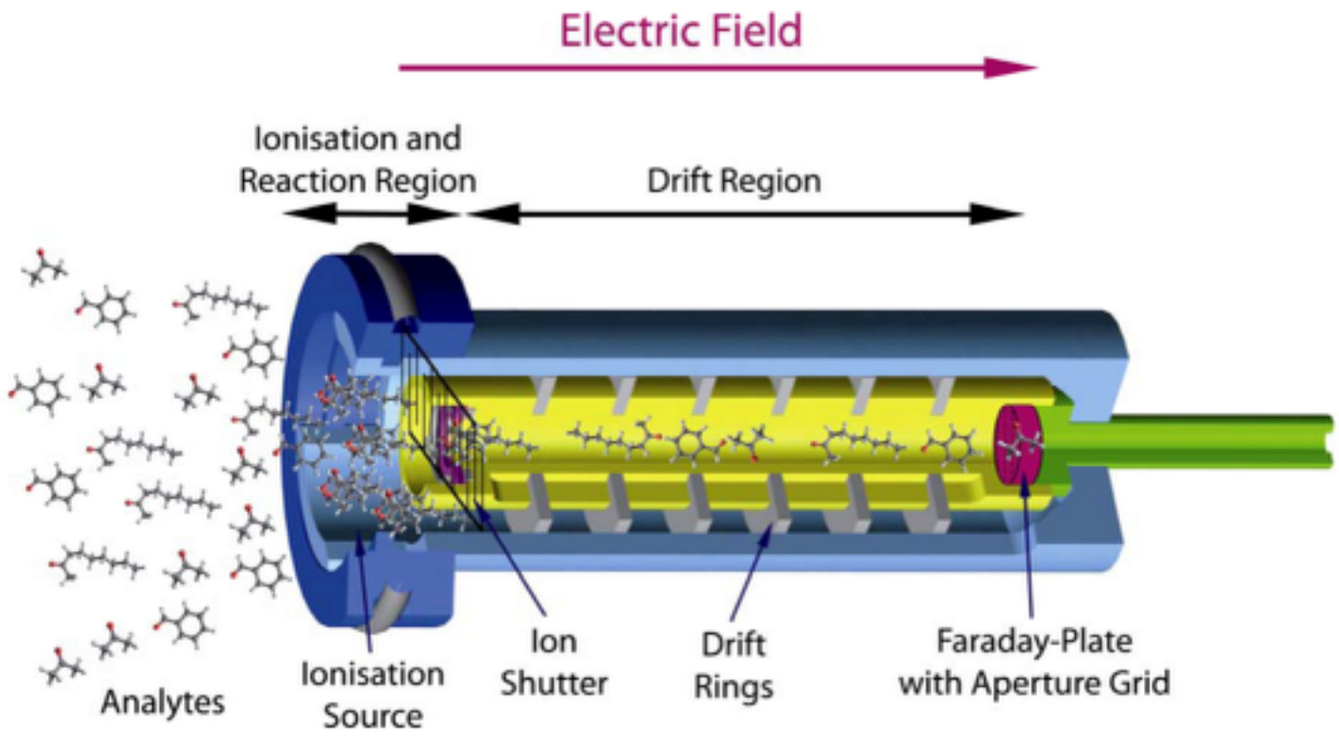
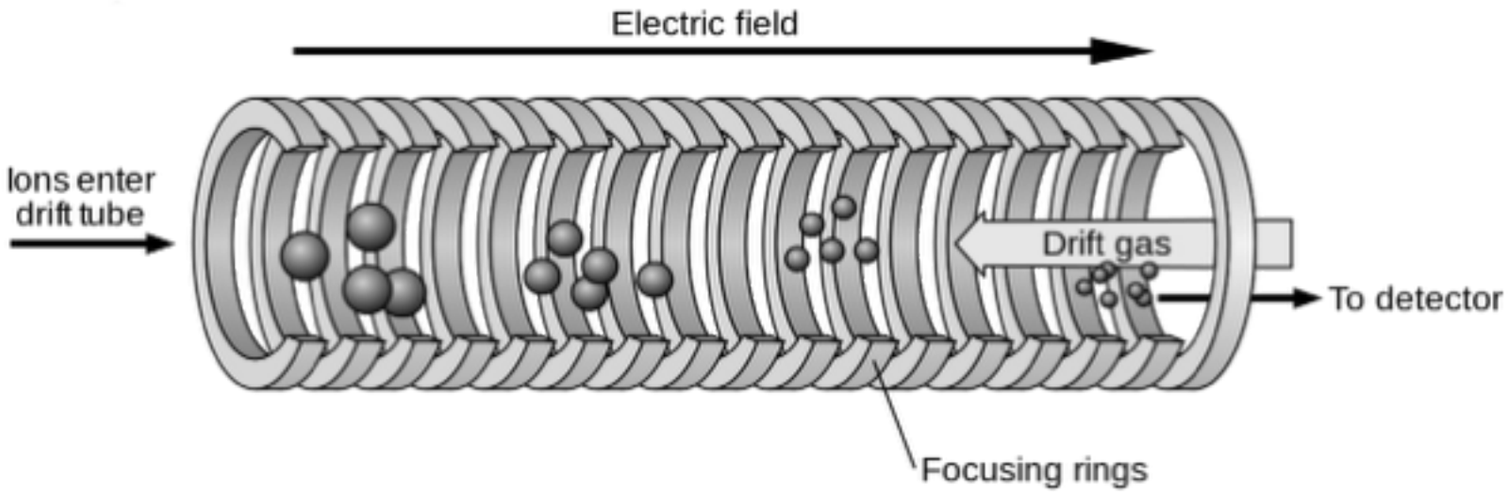
IMS

Ion-mobility spectrometry





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IMS

Ion-mobility spectrometry

- Suitable for the detection of trace organics under atmospheric pressure conditions.
- **Rapid screening technique** for many drugs of abuse including synthetic cannabinoids.
- Easy sampling and handling
- Portable IMS systems commercially available
- Operate in positive (aminoalkylindoles) and negative ion modes (e.g. CP-47,497-C8).

IMS

Ion-mobility spectrometry

$$K_{0_{analyte}} = \frac{K_{0_{cal}} \times t_{d_{cal}}}{t_{d_{analyte}}}$$

- Limited selectivity
- GC-MS must be used to confirm substances with close K_0 values

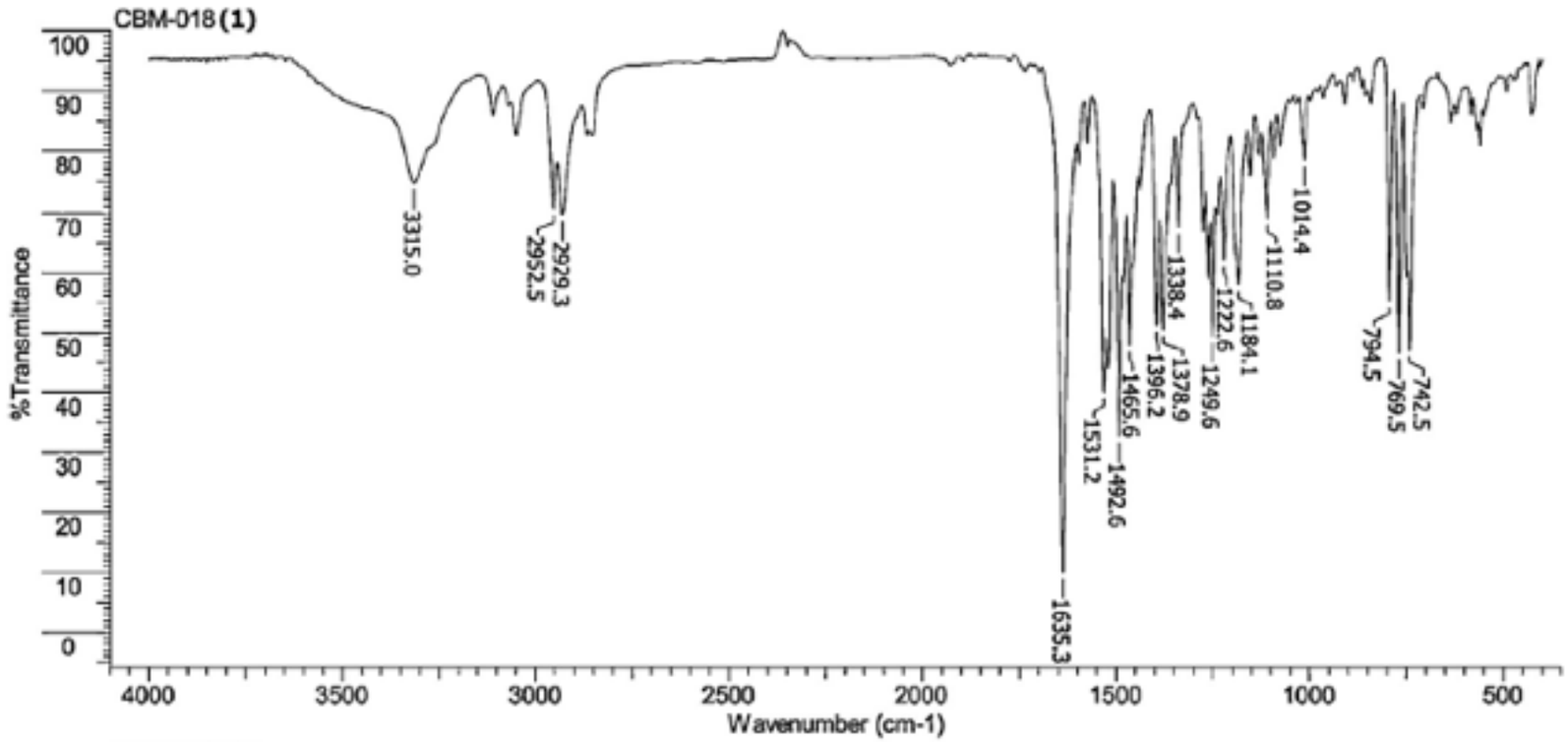
ATR-IR / FT-IR

Fourier Transform - Infrared Spectroscopy

- IR techniques may be applied to solid material containing pure substances
- If there is only a single synthetic cannabinoid in the seized sample, identification of the compound by IR is also possible with extracts of herbal mixtures after evaporation of the solvent on the ATR diamond cell

ATR-IR / FT-IR

Fourier Transform - Infrared Spectroscopy



- Structure elucidation / Isomers differentiation

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GC-IRD

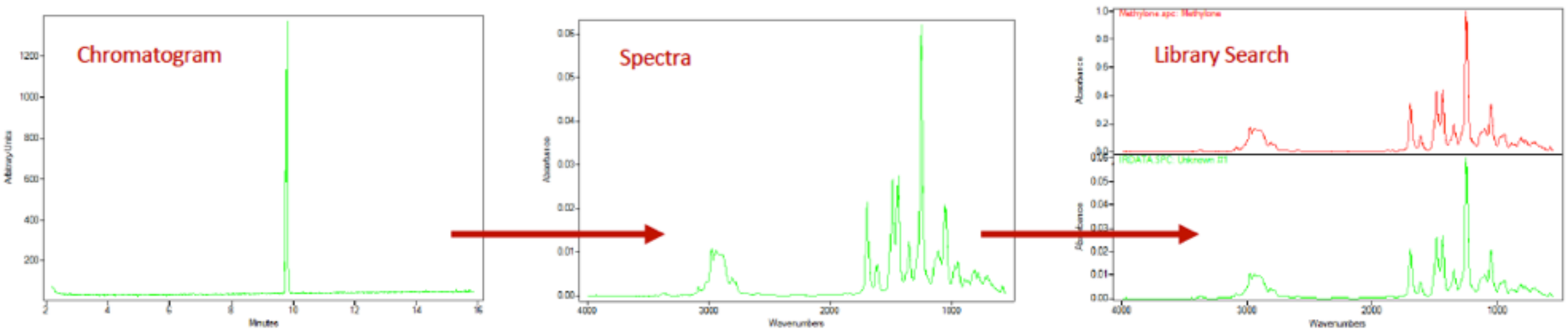
Gas chromatography with infrared detection

- The fractions containing single components are directed into an FTIR spectrometer, to provide the infrared spectrum of the sample.

- GC-IR method is particularly useful for identifying regioisomers, diastereoisomers and other isobaric molecules

GC-IRD

Gas chromatography with infrared detection



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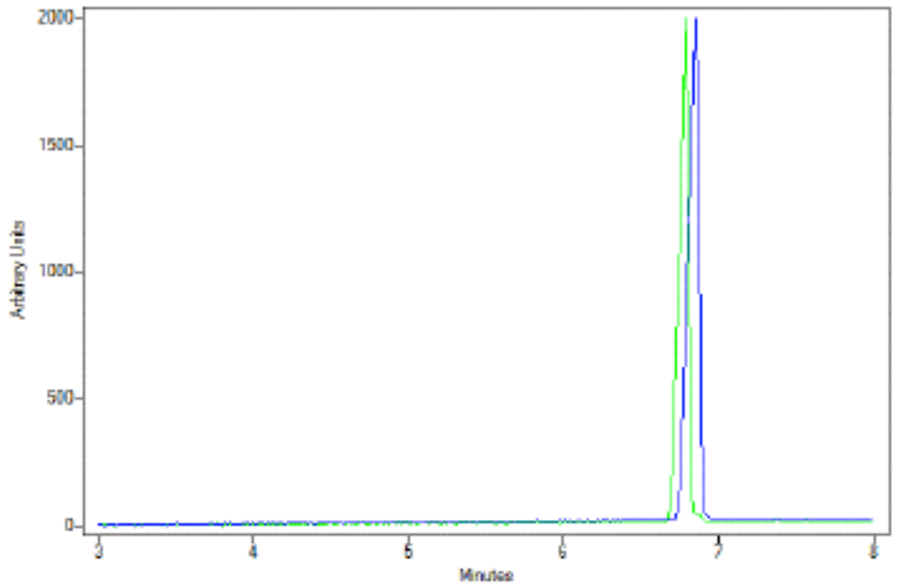
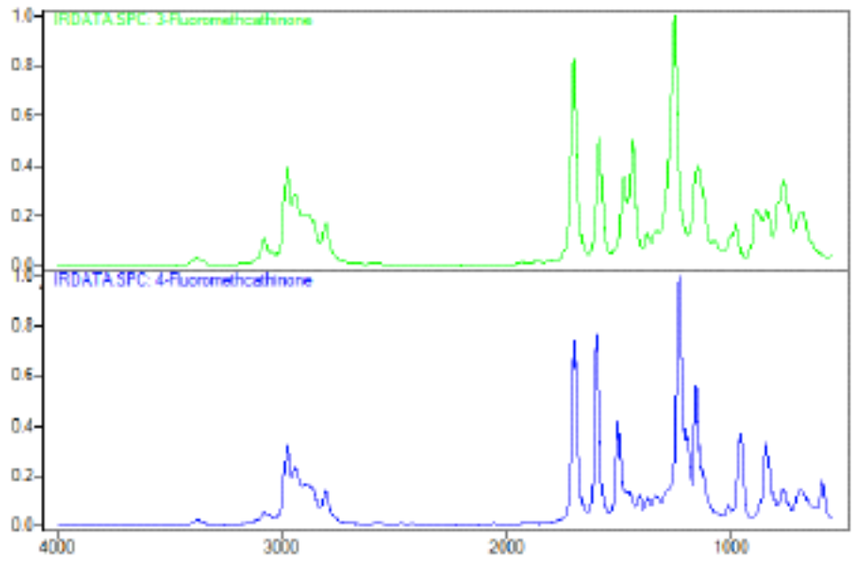
GC-IRD

Gas chromatography with infrared detection





3-FMC

4-FMC

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GC-MS

Gas chromatography–mass spectrometry

- **Gold Standard**
- Excellent chromatographic resolution
- Identification by RT and EI-MS spectra

GC-MS

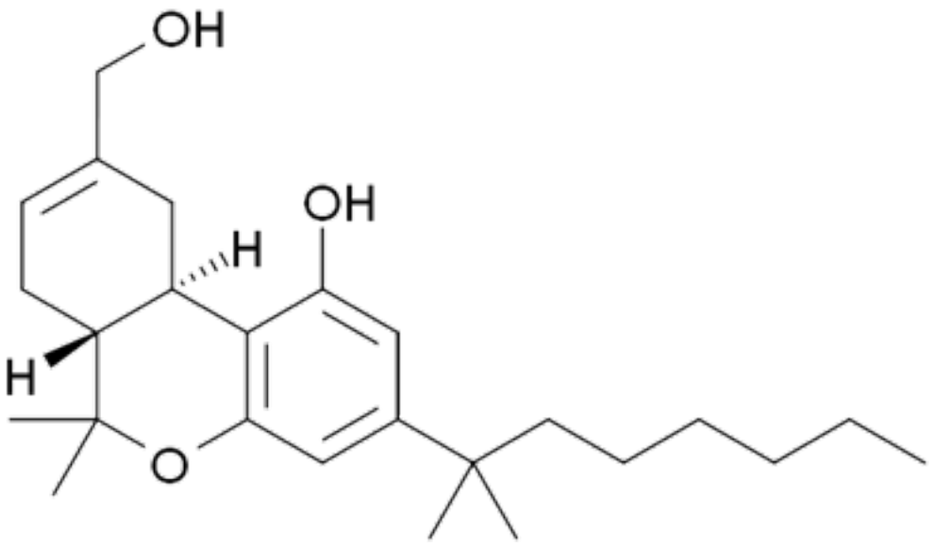
Gas chromatography–mass spectrometry

- Sample extraction : 1mL medium polar or non polar-solvent (methanol, ethanol, acetonitrile, …) + 100 mg of plant material. Sonication and filtration.

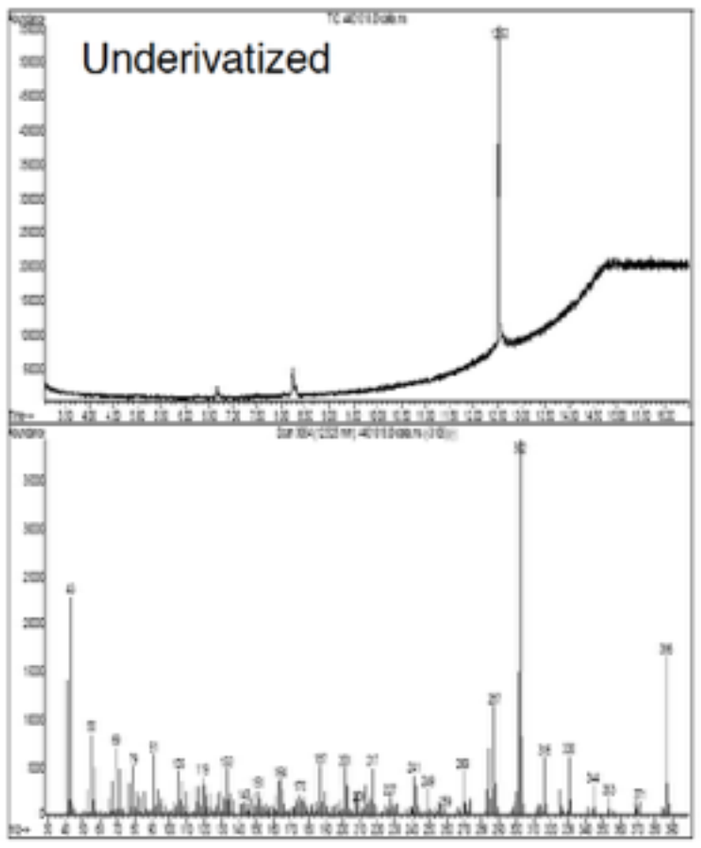
- Derivatization required for trace analysis

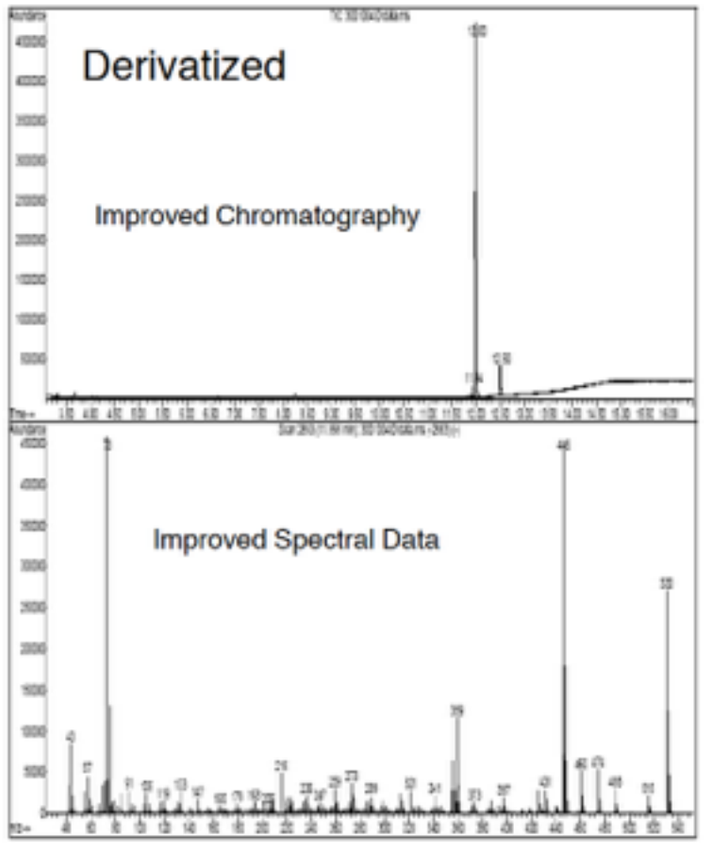
GC-MS

Gas chromatography–mass spectrometry



HU-210





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GC-MS

Gas chromatography–mass spectrometry

Spectral libraries

- NIST Mass Spectral Library (Agilent)
- PMW Mass Spectral Library of Drugs, Poisons, Pesticides, Pollutants (Wiley)
- Forensic Toxicology GC/MS RTL Database (Agilent)
- Mass Spectra of Designer Drugs 2014 (Wiley)
- **SWGDRUG Mass Spectral Library**
- **CSL Cayman Spectral Library**

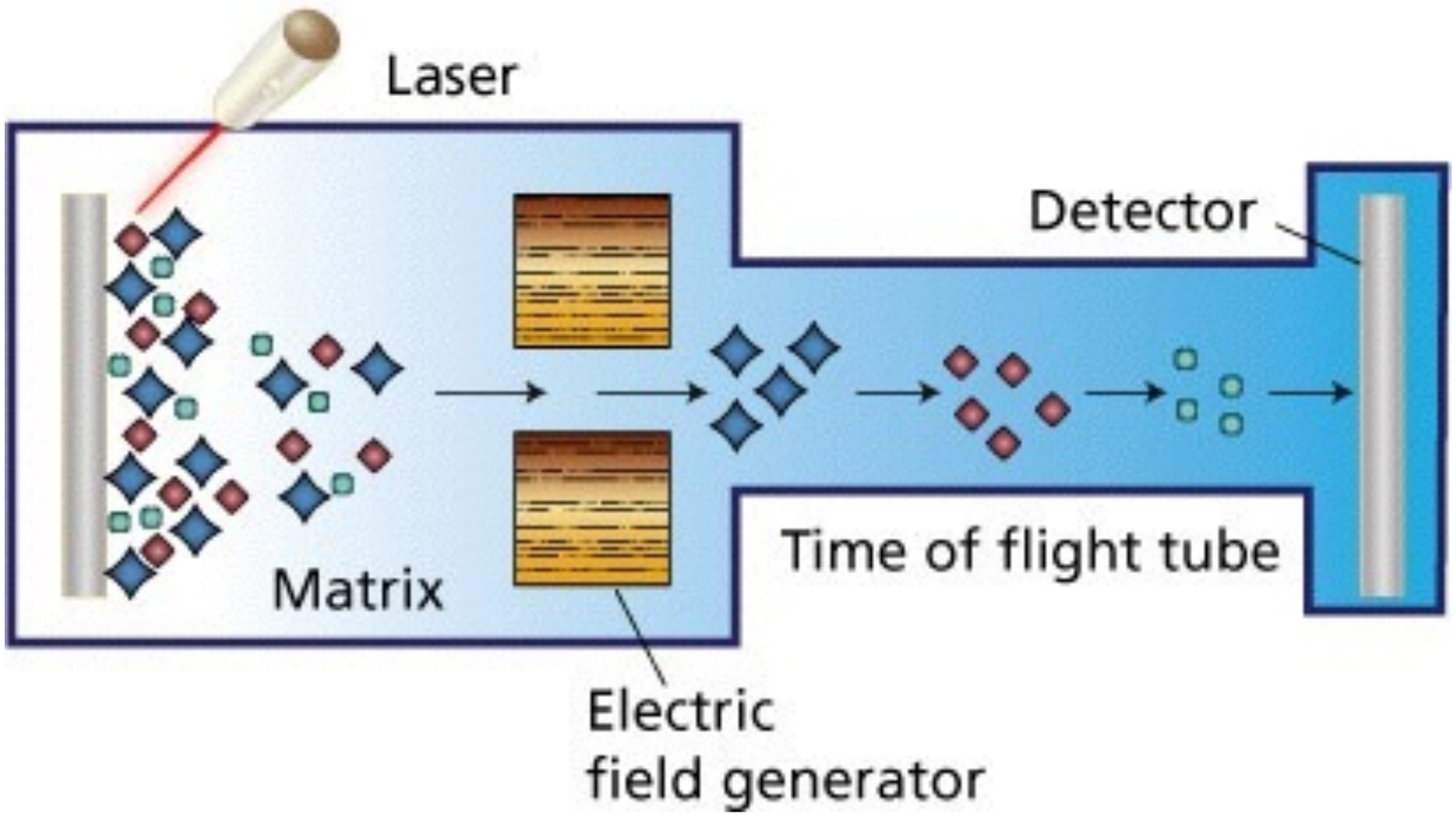
GC-MS

Gas chromatography–mass spectrometry

- Not suitable to analyse regioisomers (requires techniques such as IR, GC-IRD or MS^n)

MALDI-TOF-MS

Matrix-assisted laser desorption/ionization



MALDI-TOF-MS

Matrix-assisted laser desorption/ionization

Research Article

Journal of MASS SPECTROMETRY

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Direct screening of herbal blends for new synthetic cannabinoids by MALDI-TOF MS

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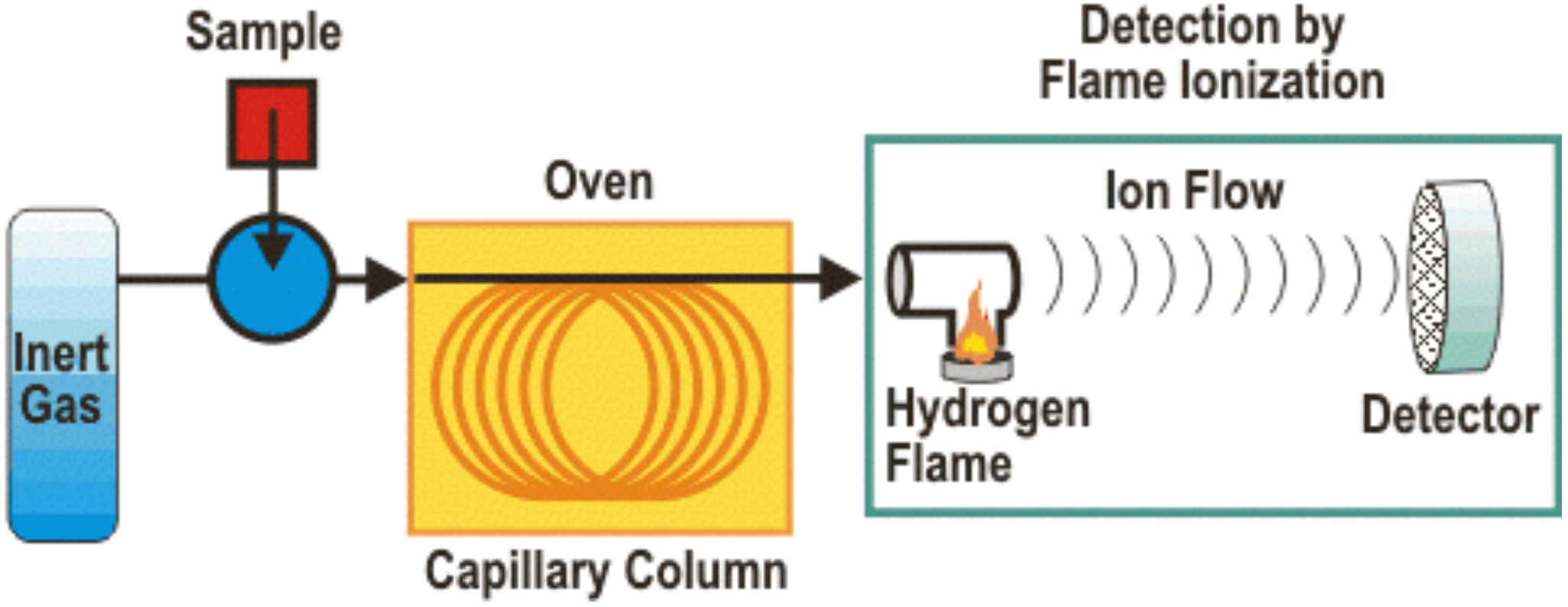
GC-FID

Flame ionization detector



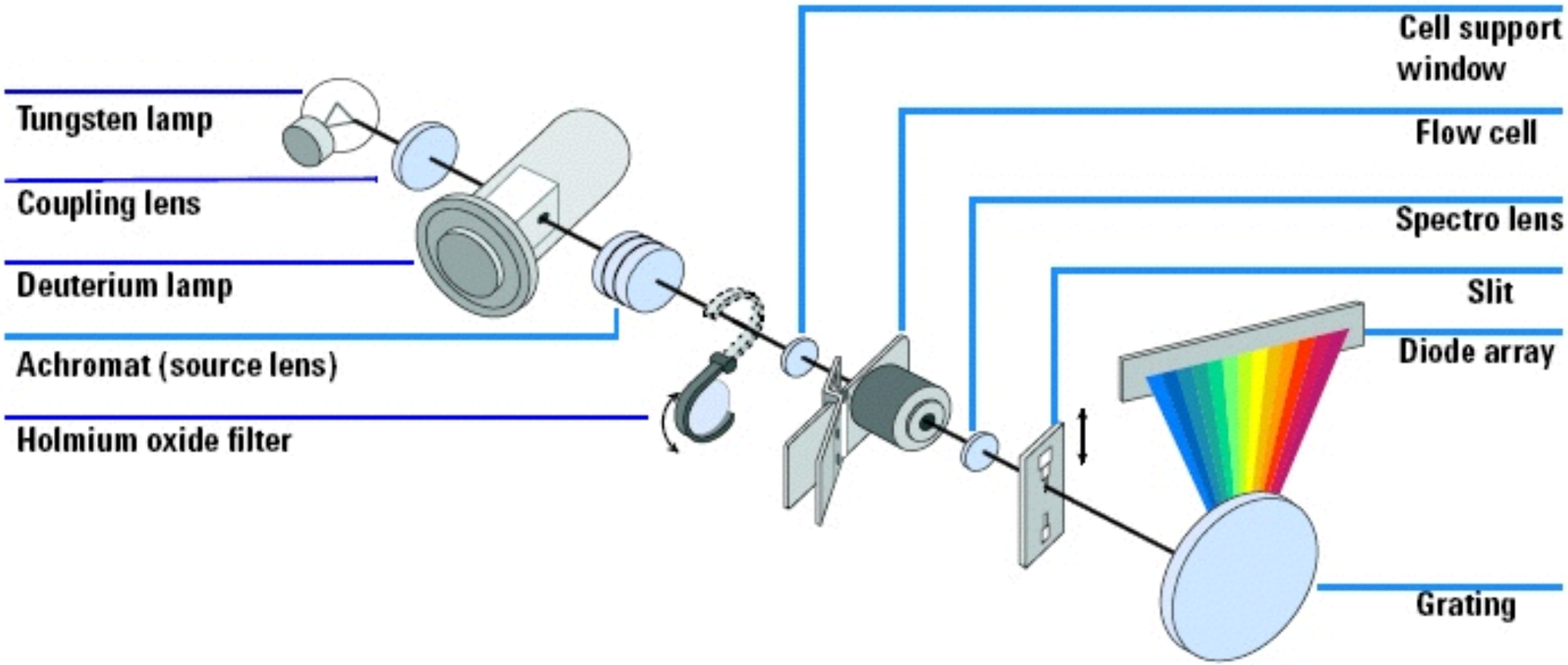
GC-FID

Flame ionization detector

- Suitable for qualitative and quantitative analysis
- For low concentration, use of more sensitive technique (e.g. LC-MS or LC-MS/MS) is recommended

HPLC-PDA

Photodiode Array Detector



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Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

HPLC-PDA

Photodiode Array Detector

- Suitable for qualitative and quantitative analysis
- Identification by RT and UV spectrum

NMR

Nuclear magnetic resonance

- Identification as well as structure elucidation of unknown new synthetic cannabinoids.

- Cost of NMR spectroscopy and the technical expertise required prevent its widespread application in routine analysis.

BIOLOGICAL MATERIAL

BLOOD / SERUM

URINE

ORAL FUID

HAIR

Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
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ELISA

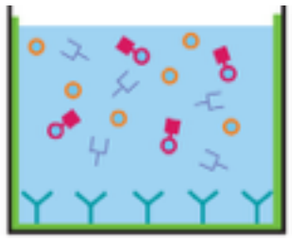
Enzyme-Linked ImmunoSorbent Assay

- Inexpensive, sensitive and rapid screening
- Mass confirmation required

ELISA

Enzyme-Linked ImmunoSorbent Assay

Plates are pre-coated with mouse anti-rabbit IgG and blocked with a proprietary formulation of proteins.



1. Incubate with tracer, antiserum, and either controls or sample.

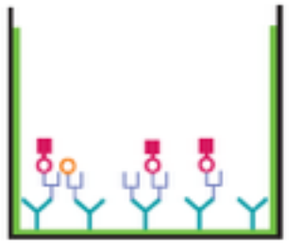
= Mouse Anti-Rabbit IgG

= Blocking proteins

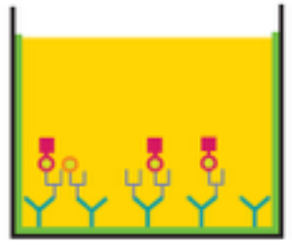
= Acetylcholinesterase linked to JWH Metabolite (Tracer)

= Specific antiserum to JWH Metabolites

= Free JWH Metabolites



2. Wash to remove all unbound reagents.



3. Develop the well with Ellman's Reagent.

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ELISA

Enzyme-Linked ImmunoSorbent Assay

RANDOX TOXICOLOGY

NEOGEN® CORPORATION

IMMUNALYSIS

NMS LABS

Cayman CHEMICAL

Journal of Analytical Toxicology Advance Access published August 14, 2013

Journal of Analytical Toxicology 2013;1–8
doi:10.1093/jat/bkt067

Detection of Synthetic Cannabinoids in Oral Fluid Using ELISA and LC–MS-MS

Warren C. Rodrigues[1], Philip Catbagan[1], Sumandeep Rana[2], Guohong Wang[1] and Christine Moore[1]*

Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Suitable for qualitative and quantitative analysis of low concentration synthetic cannabinoids in complex herbal matrix

- Low LOQ for trace analysis and biological specimens

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Detection mode : MRM
- Ionization mode : ESI+ and ESI-
- Appropriate mass transitions must be selected to avoid interferences between analyses, particularly isomers
- Caution when identified regioisomeric compounds

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

Analyte	*Ionization mode*	*Precursor ion (m/z)*	*Product ions (m/z)*	*Cone voltage (V)*	*Collision energy (eV)*
JWH-019	ESI^+	356.15	154.99	34	25
			126.99		44
JWH-073	ESI^+	328.10	155.12	33	22
			126.85		50
JWH-081	ESI^+	372.10	185.25	33	25
			214.29		25
JWH-122	ESI^+	356.35	169.43	29	25
			214.21		25

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Serum
- Blood
- Oral fluid
- Hair

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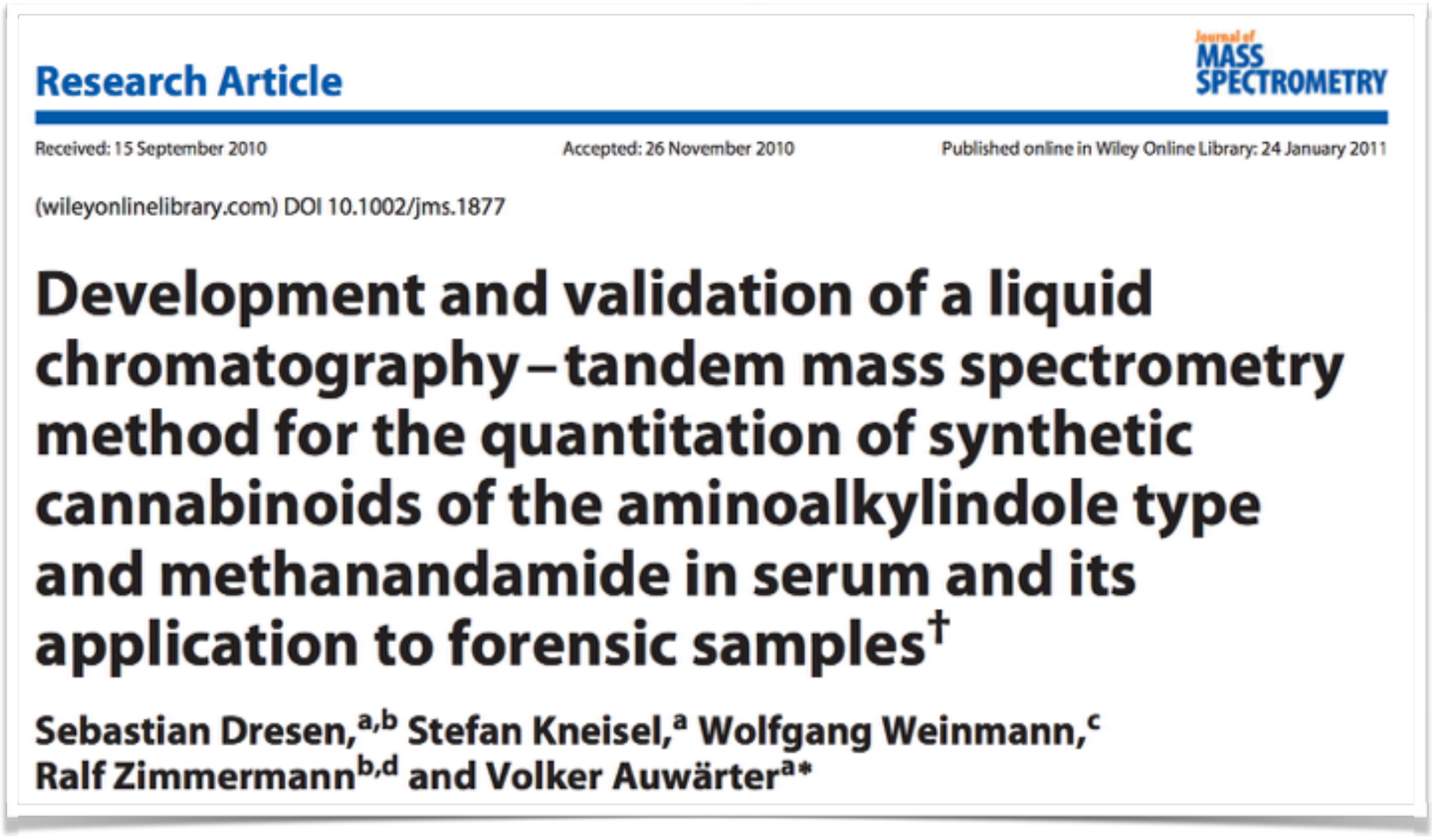
LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Serum



Research Article

Journal of MASS SPECTROMETRY

Received: 15 September 2010 Accepted: 26 November 2010 Published online in Wiley Online Library: 24 January 2011

(wileyonlinelibrary.com) DOI 10.1002/jms.1877

Development and validation of a liquid chromatography–tandem mass spectrometry method for the quantitation of synthetic cannabinoids of the aminoalkylindole type and methanandamide in serum and its application to forensic samples†

Sebastian Dresen,[a,b] Stefan Kneisel,[a] Wolfgang Weinmann,[c] Ralf Zimmermann[b,d] and Volker Auwärter[a]*

Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Serum

1 mL Serum + ISTD

+ Borate buffer pH 9

+ n-hexane/Ethyl acetate 90:10 (v/v)

Mixing

Centrifugation

Evaporation of organic supernatant

Reconstitution with mobile phase

- **Phenyl Hexyl column**
- **Solvant A : Ammonium formate 2mM with 0.1% FA**
- **Solvant B : Methanol**
- **Electrospray ionisation**
- **MRM Mode**
- **LOQ = 0.1 ng/mL**

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Serum

Positive samples	Compound	Concentrations
56	JWH-081	0.11 - 16.9 ng/mL
47	JWH-250	0.14 - 18.1 ng/mL
9	JWH-018	0.30 - 8.17 ng/mL
6	JWH-073	0.23 - 0.6 ng/mL
2	JWH-015	< LOQ (0.1 ng/mL)

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Blood

Journal of Analytical Toxicology Advance Access published August 21, 2013

Journal of Analytical Toxicology 2013;1–5
doi:10.1093/jat/bkt065

Blood Synthetic Cannabinoid Concentrations in Cases of Suspected Impaired Driving

Jillian K. Yeakel[1] and Barry K. Logan[1,2]*

Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Blood

200 µL WB + ISTD
+ Sat. Sodium bicarbonate
+ Sat. NaCl
Vortex
+ n-hexane/Ethyl acetate
99:1 (v/v)
Centrifugation
Evaporation of organic supernatant
Reconstitution with
DI Water/ Methanol 50:50 (v/v)

- **Acquity UPLC HSS T3**
- **Solvant A : Water + 1% FA**
- **Solvant B : Methanol + 1% FA**
- **Electrospray ionisation**
- **MRM Mode**
- **LOQ = 0.1 ng/mL**

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Blood

Case	Toxicology findings (ng/mL)
1	JWH-018: 1.1
2	JWH-018: 0.24
3	JWH-018: 9.9 JWH-250: 2.7
4	JWH-018: pos
5	JWH-018: pos
6	AM2201: 1.4 JWH-081: 0.12 JWH-122: 2.5 JWH-210: 0.10

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Blood

Case	Toxicology findings (ng/mL)
7	JWH-018: 0.1 AM-2201: 0.43
8	AM-2201: 3.1 JWH-250-0.38
9	AM-2201: 0.94
10	AM-2201: 3.6
11	AM2201: 2.8 JWH-081: pos JWH-122: pos JWH-210: pos
12	AM-2201: 4.0 JWH-210: pos

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Oral fluid

Anal Bioanal Chem
DOI 10.1007/s00216-013-6887-0

RESEARCH PAPER

LC/ESI-MS/MS method for quantification of 28 synthetic cannabinoids in neat oral fluid and its application to preliminary studies on their detection windows

Stefan Kneisel · Michael Speck · Bjoern Moosmann · Todd M. Corneillie · Nathaniel G. Butlin · Volker Auwärter

Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Oral fluid

200 µL OF + ISTD

Protein precipitation
with ice-cold acetonitrile

Centrifugation

Evaporation of supernatant

Reconstitution with
mobile phase

- **Phenyl Hexyl column**
- **Solvant A : Ammonium formate 2mM with 0.1% FA**
- **Solvant B : Methanol**

- **Electrospray ionisation**

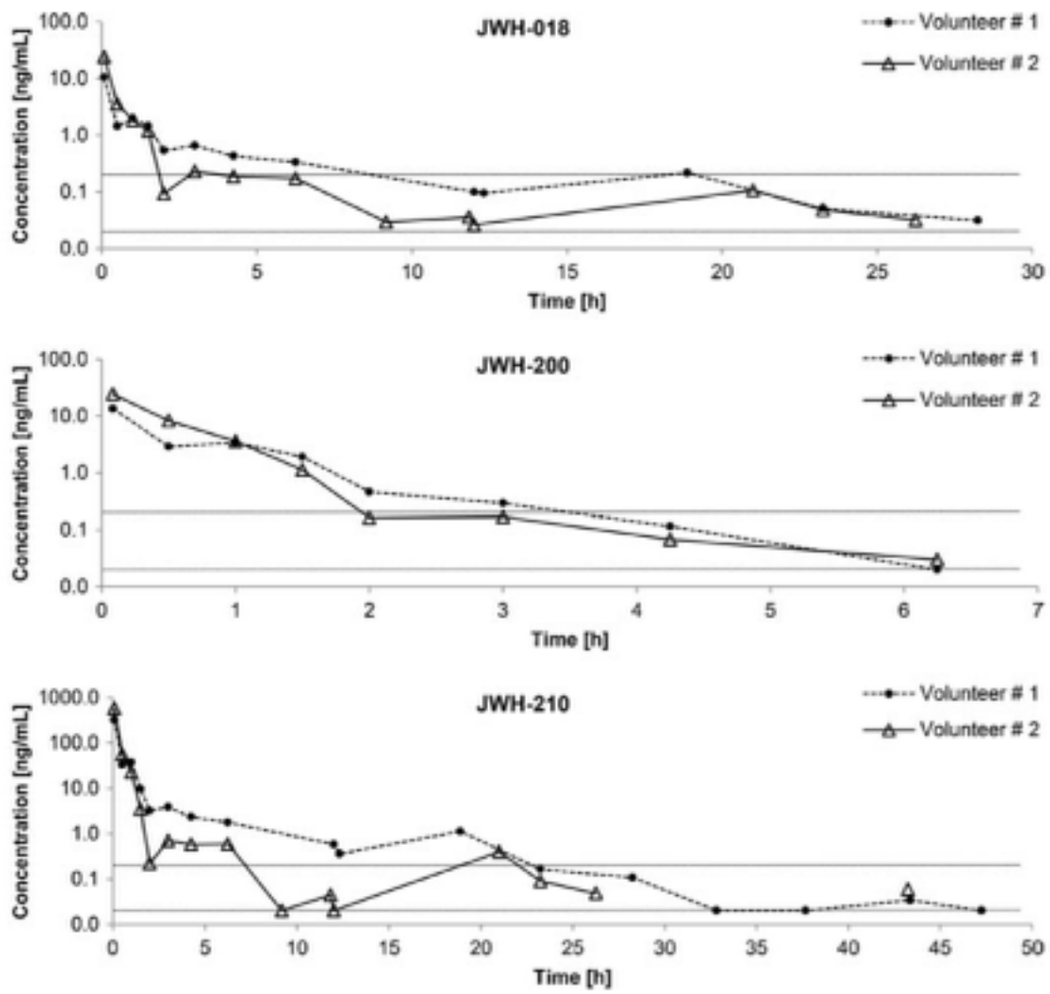
- **MRM Mode**

- **LOQ = 0.1 ng/mL**

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Oral fluid



Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Hair

Research article

Drug Testing and Analysis

Received: 21 June 2013 Revised: 23 August 2013 Accepted: 29 August 2013 Published online in Wiley Online Library: 30 September 2013

(www.drugtestinganalysis.com) DOI 10.1002/dta.1556

Hair analysis as a tool to evaluate the prevalence of synthetic cannabinoids in different populations of drug consumers

A. Salomone,[a]* C. Luciano,[a] D. Di Corcia,[a] E. Gerace[a] and M. Vincenti[a,b]

Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Hair

Decontamination

NaOH 1N 95°C for 10 min

L/L n-hexane/Ethyl acetate
90:10 (v/v)

Evaporation to dryness

Reconstitution with
methanol

- **Acquity BEH C18 column**
- **Solvant A : Ammonium formate 2mM + FA**
- **Solvant B : Acetonitrile + FA**
- **Electrospray ionisation**
- **SRM Mode**
- **LOQ = 0.7 - 4.3 pg/mg**

LC-MS/MS

Liquid chromatography - Tandem mass spectrometry

- Hair

Positive samples	Compound	Concentrations
11	JWH-073	1.6 - 50.5 pg/mg
8	JWH-122	7.4 - 2800 pg/mg
6	JWH-250	
5	JWH-081	
3	JWH-018	
2	JWH-250	
2	JWH-019	
1	AM-1120	

HRMS

High-Resolution-Mass Spectrometry

- Urine

Anal Bioanal Chem (2013) 405:8463–8474
DOI 10.1007/s00216-013-7272-8

RESEARCH PAPER

A high-sensitivity ultra-high performance liquid chromatography/high-resolution time-of-flight mass spectrometry (UHPLC-HR-TOFMS) method for screening synthetic cannabinoids and other drugs of abuse in urine

HRMS

High-Resolution-Mass Spectrometry

- For urine analysis:
  - the main target compound are metabolites: conjugate cleavage step necessary
  - main metabolites are monohydroxylated compounds (for JWHs)

HRMS

High-Resolution-Mass Spectrometry

- Urine

1 mL Urine

Hydrolysis ß-glu 37°C

+ ISTD

+ 0.1 M phosphate buffer (pH 6)

mixed-mode SPE

Acid/Neutral fraction | Basic fraction

Evaporation

Reconstitution with 45% methanol / 0.1 % FA

- **Waters HSS T3**
- **Solvant A : Ammonium acetate 2 mM with 0.1% FA**
- **Solvant B : Methanol**
- **Electrospray ionisation**

HRMS

High-Resolution-Mass Spectrometry

- Accurate mass measurement
- Determine elemental compositions
- Calculation of double bond equivalent
- Mass defect filtering enables non-targeted analysis of related compounds and analogues

HRMS

High-Resolution-Mass Spectrometry

analytical chemistry

Article

pubs.acs.org/ac

Analysis of Synthetic Cannabinoids Using High-Resolution Mass Spectrometry and Mass Defect Filtering: Implications for Nontargeted Screening of Designer Drugs

Megan Grabenauer,* Wojciech L. Krol, Jenny L. Wiley, and Brian F. Thomas

Journée « Cannabinoïdes de Synthèse: aspects toxicologiques »
Vendredi 19 septembre 2014, Palais des Congrès - Futuroscope de Poitiers.

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