

# METHYLMETHCATHINONE (MMC) ISOMER IDENTIFICATION : BRAIN TEASER ILLUSTRATED BY A CASE REPORT

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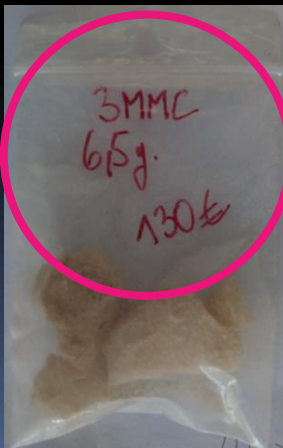
2. Laboratory of Clinical Chemistry, CIRM, University of Liege, Belgium

# Background

- Patient (31-years woman) treated with methylphenidate for withdrawal from addiction to 2-MMC
  - Follow-up: 6 weeks - 6 blood/urine samplings
  - Lab tests to confirm the abstinence
  - Capsules



- 5 unrelated seized samples for identification



# Material & Methods

- **Blood/Urine** (treated or not by  $\beta$ -glucuronidase)
  - Liquid/liquid extraction prior to chromatographic analysis

## General Unknown Screening



### HPLC-DAD Waters™

Alliance 2695 + PDA 2996  
Column: Symmetry C8, 5  $\mu$ m,  
250 X 4,6 mm (Waters)  
Mobile Phase A: 43,5 mM  
Phosphate buffer pH 3,8  
Mobile Phase B: Acetonitrile



### UHPLC-TOF-MS



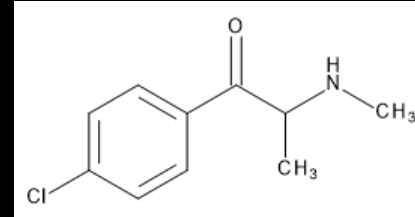
Eksigent LC 100 XL + TripleTOF 4600  
Column: Kinetex 2.6 C18, 100 Å,  
50 x 3.00 mm (Phenomenex)  
Mobile Phase A: 10mM Ammonium  
formate  
Mobile Phase B: ACN/MeOH (50/50)

## Powders

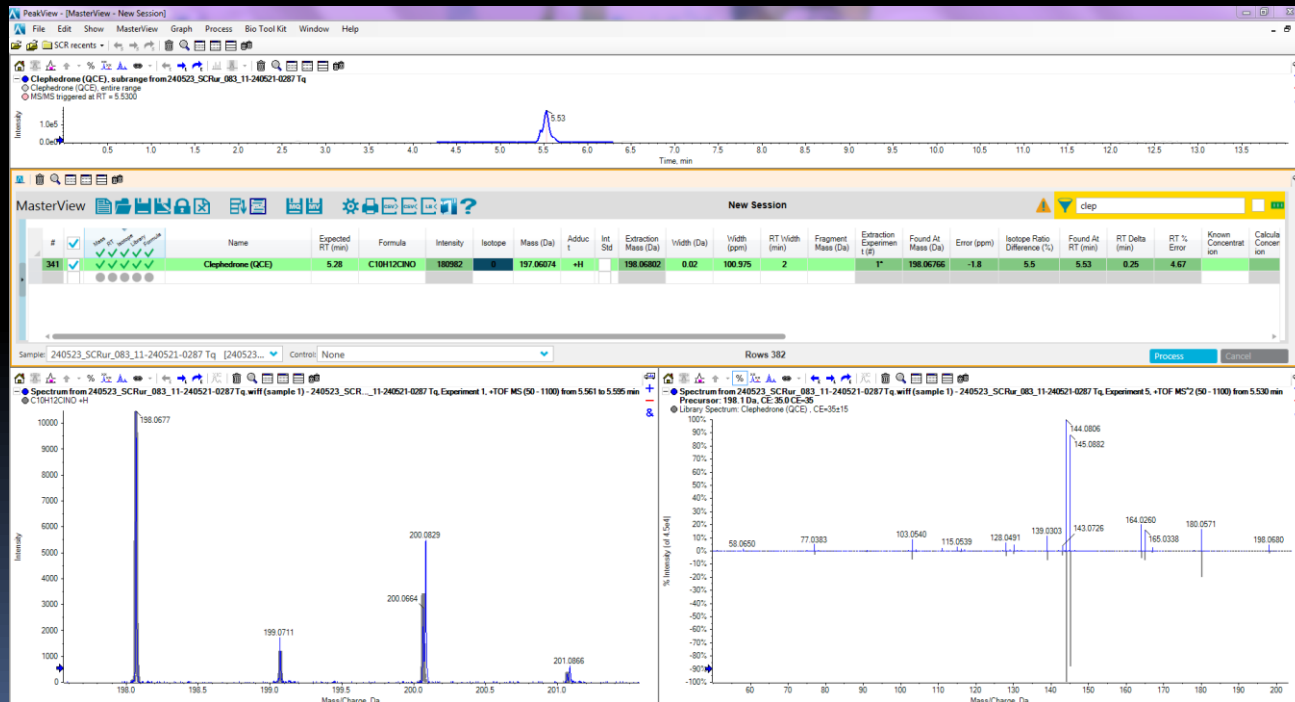
- Dilution in the mobile phase
- Dilution in chloroform  $\rightarrow$  GC-MS-MS (Agilent)
- Dilution in KBr  $\rightarrow$  infrared spectroscopy (Bruker)



# Results and discussion



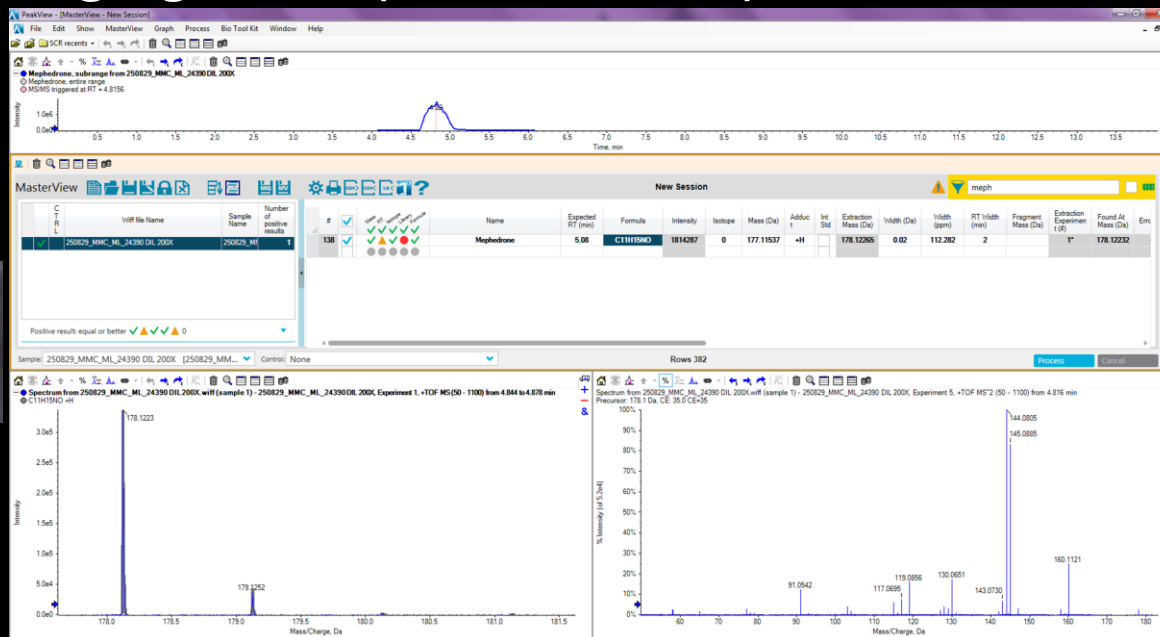
- Patient samples:
  - Methylphenidate, diazepam (nordiazepam, oxazepam), alprazolam, lorazepam, mirtazapine, prothipendyl, pipamperone
  - In the first sample: chloromethcathinone



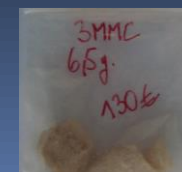
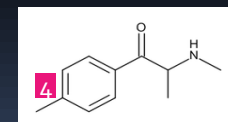
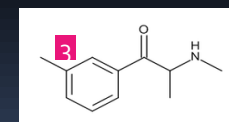
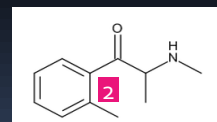
- → request the powder for analysis

# Results and discussion

- Capsule belonging to the patient: methylmetcathinone (MMC)



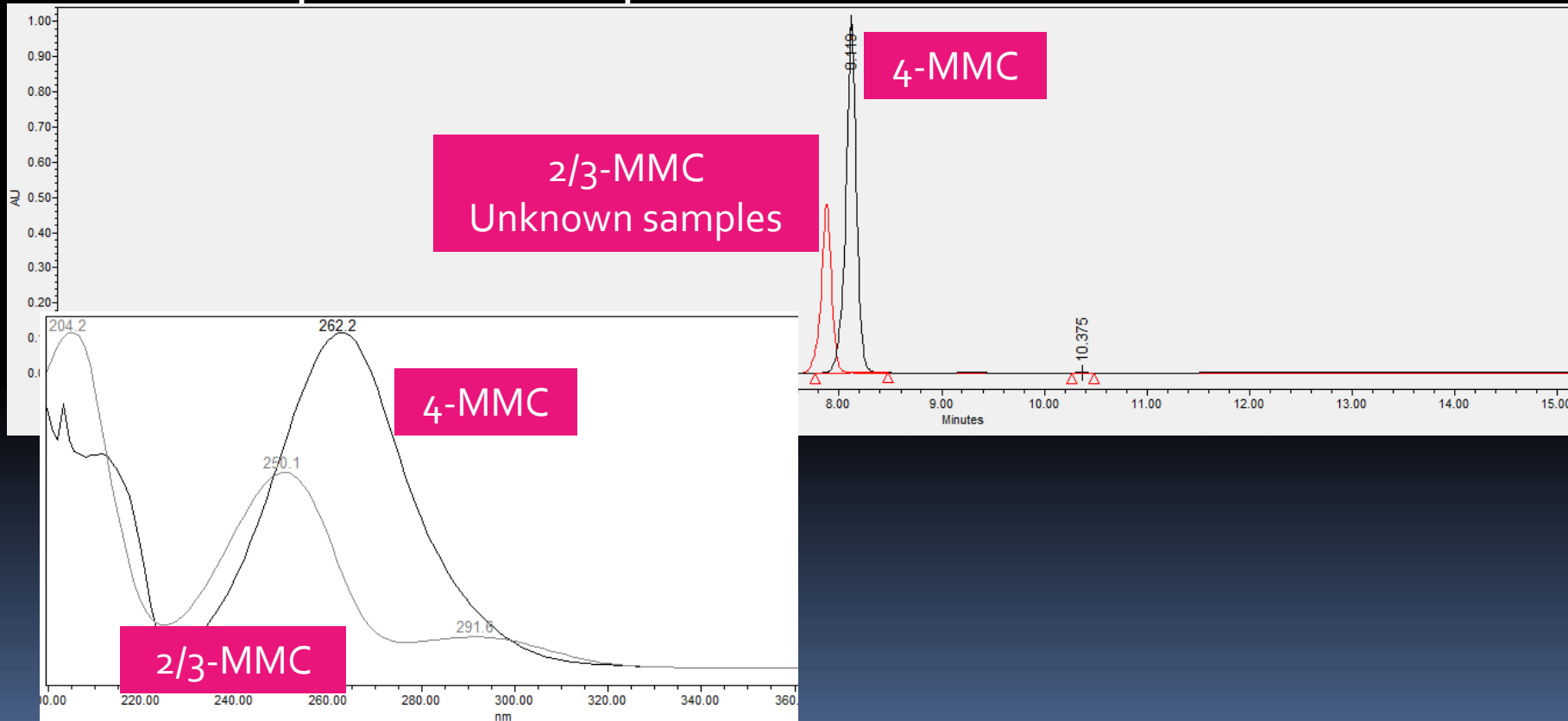
- The compound used before the blood/urine sampling came from a different batch
- 2-, 3- or 4-MMC?
- Is it possible to distinguish between the isomers without reference standards?  
(in the lab, we only had 4-MMC)





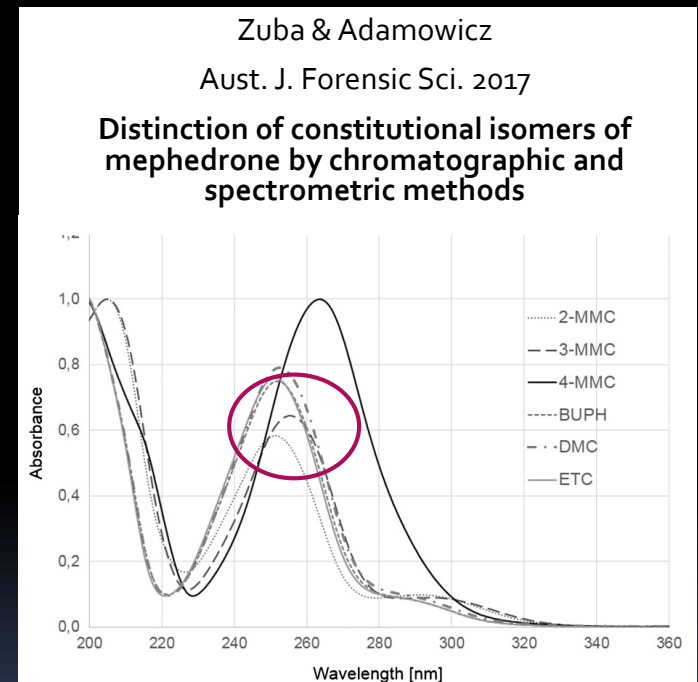
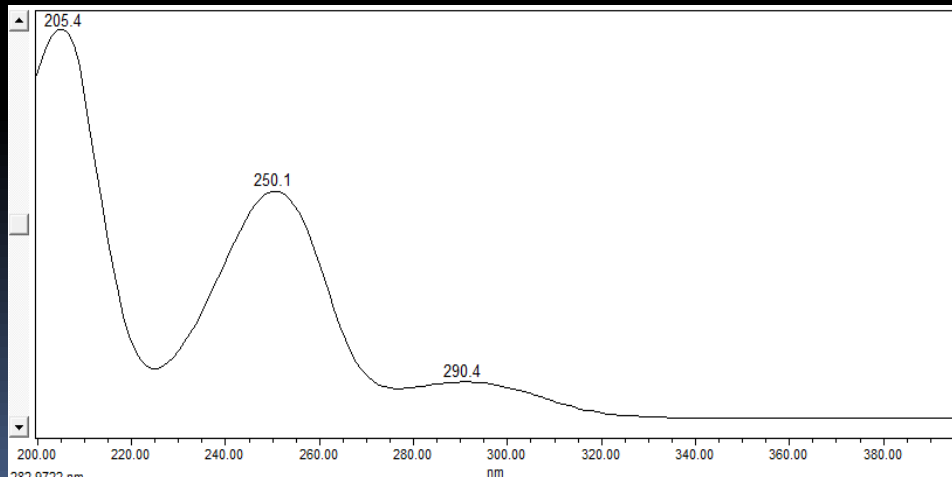
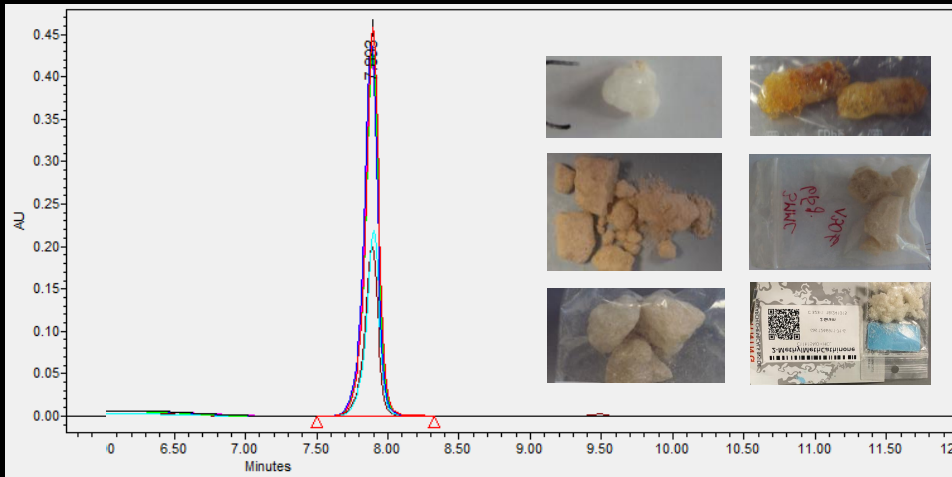
# Results and discussion

**2) HPLC-DAD:** 4-MMC could be ruled out due to its distinct retention time and UV spectrum compared to the powder samples



# Results and discussion

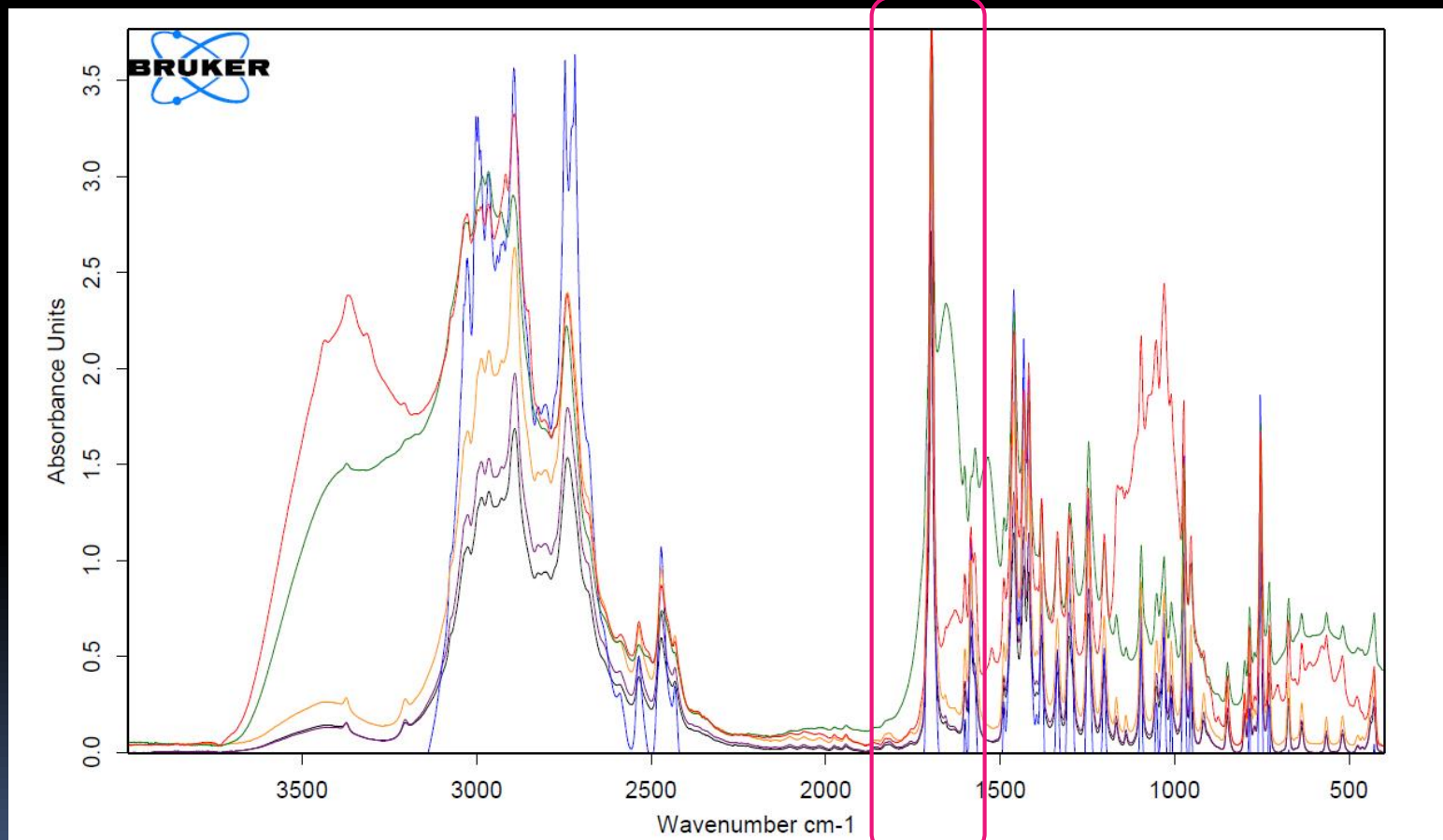
## 2) HPLC-DAD: same retention time and UV spectrum



## 3) GC-MS: same retention time

# Results and discussion

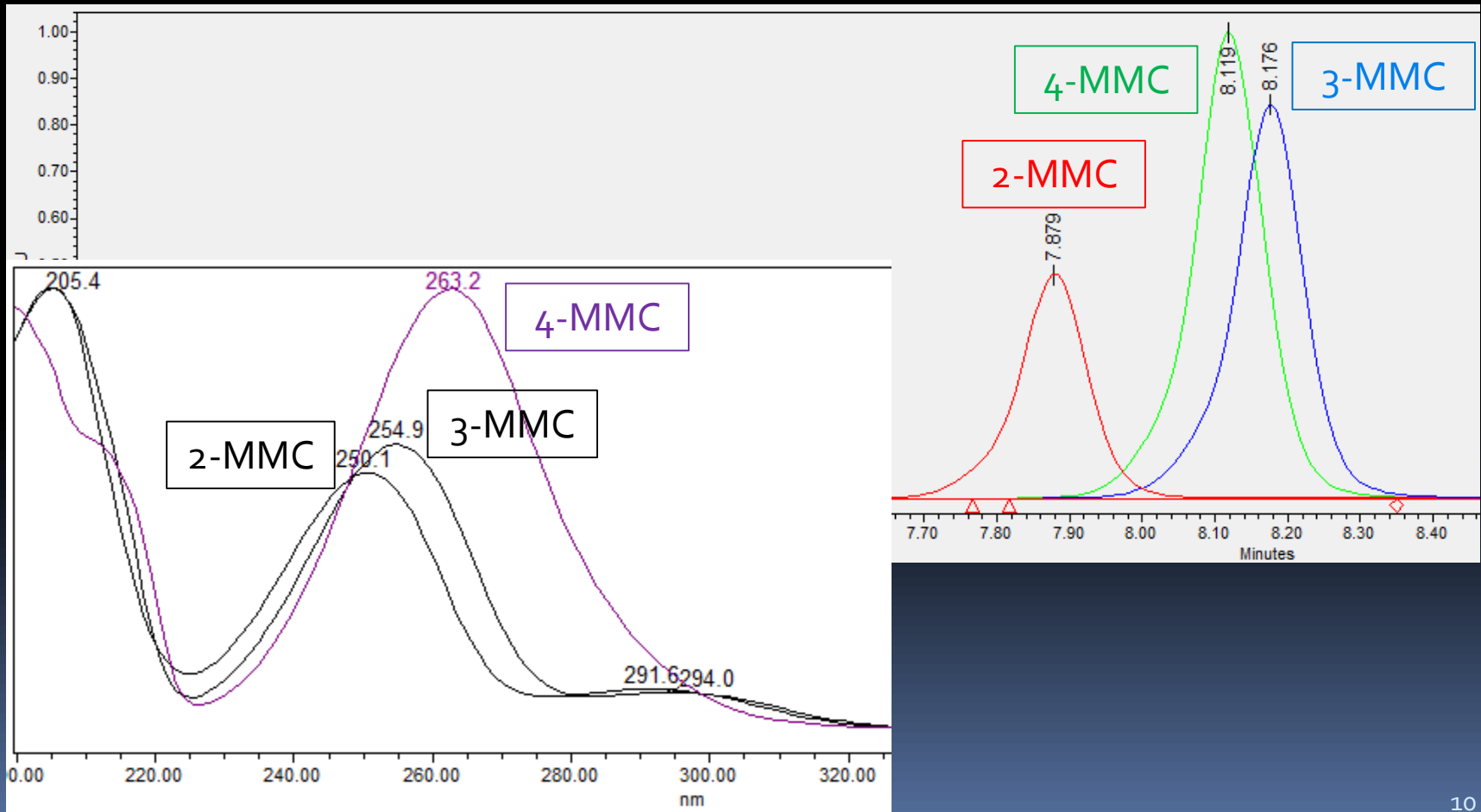
## 4) Infrared spectroscopy



All the samples were confirmed to be 2-MMC

# Results and discussion

After receiving the reference standards



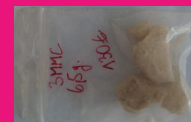
# Results and discussion



39%



41%



85%

## PURITY

Ranging from 39 to 85%  
Significant inter-batch variability!



84%



82%



80%

# Results and discussion

## Cathinones



Increasingly being produced in Europe (France,...)



Ban of 4-MMC, then 3-MMC (2021) in the Netherlands → replaced by 2-MMC, 3-CMC



The substitution of cathinones was also observed in France: 1465 samples sold as 3-MMC (Chenorhokian S. et al., ToxAc 2025, 37)

- 23% = 3-MMC
- 32% = 2-MMC
- 30% = 3-CMC

- Routes of administration: oral ingestion, snorting, injection



Effects:

- Stimulation, euphoria, elevation of mood, improved mental function
- Intensity: 4-MMC > 3-MMC > 2-MMC
- Increase synaptic [ ] of dopamine, norepinephrine and serotonin

# Results and discussion

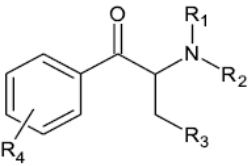
## Cathinones



Distinguishing between the isomers isn't required  
as they are all controlled substances in Belgium

88188

MONITEUR BELGE — 26.09.2017 — BELGISCH STAATSBLAD

2. CATHINONEDERIVATEN: stoffen die derivaten zijn van	2. DÉRIVÉS de la CATHINONE : substances qui sont dérivées de :
 <p><b>Fig. 2. 2-amino-1-phenylpropan-1-one</b></p>	
<p><b>R<sub>1</sub></b> = H, C<sub>n</sub>H<sub>2n+1</sub> (n=1-5), -CH<sub>2</sub>- (inclusief derivaten waarbij het stikstofatoom opgenomen is in een ringstructuur)</p> <p><b>R<sub>2</sub></b> = H, C<sub>n</sub>H<sub>2n+1</sub>, (n=1-5), -CH<sub>2</sub>- of benzyl (alleen indien R<sub>1</sub>=H), (inclusief derivaten waarbij het stikstofatoom opgenomen is in een ringstructuur)</p> <p><b>R<sub>3</sub></b> = H, C<sub>n</sub>H<sub>2n+1</sub> (n=1-5), al dan niet opgenomen in een ringstructuur met de phenylring of de amino-groep</p> <p><b>R<sub>4</sub></b> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, OCH<sub>3</sub>, halogeen, OCH<sub>2</sub>O, phenyl (op eender welke positie van de phenylring zoals afgebeeld in figuur 2). Ook meerdere substituties met deze groepen op de phenylring zijn mogelijk.</p>	<p><b>R<sub>1</sub></b> : H, C<sub>n</sub>H<sub>2n+1</sub> (n=1-5), -CH<sub>2</sub>- (ainsi que les dérivés pour lesquels l'atome d'azote fait partie d'une structure cyclique)</p> <p><b>R<sub>2</sub></b> : H, C<sub>n</sub>H<sub>2n+1</sub> (n=1-5), -CH<sub>2</sub>-, ou benzyl (pour autant que R<sub>1</sub> = H), (ainsi que les dérivés pour lesquels l'atome d'azote fait partie d'une structure cyclique)</p> <p><b>R<sub>3</sub></b> : H, C<sub>n</sub>H<sub>2n+1</sub> (n=1-5), inclus ou non dans une structure cyclique reliée au groupe phényl ou amino.</p> <p><b>R<sub>4</sub></b> : H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, OCH<sub>3</sub>, halogène, OCH<sub>2</sub>O, phényl (quel que soit sa position sur le groupe phényle tel qu'illustré par la figure 2). Ainsi que les produits de polysubstitution de la structure phényle par un ou plusieurs de ces groupes.</p>
<p><b>Uitgezonderd:</b> bupropion</p>	<p><b>A l'exception de :</b> bupropion</p>

# Results and discussion

## Methylphenidate

### Mechanism of action

- Central nervous system stimulant
- Acts by blocking the reuptake of dopamine and norepinephrine

### Indications

- Attention Deficit Hyperactivity Disorder (ADHD)
  - Narcolepsy
- Off label in this case

### Adverse effects

- Nervousness, depression, anxiety, insomnia,...
- Can cause addiction and dependence



The patient discontinued her medical follow-up  
after 2 months

# Conclusion

- Increasing popularity of MMC
- Identification of NPS isomers
  - Legal status differs in some countries
  - Activity can vary between isomers
- The ability to distinguish between isomers requires the use of analytical reference standards and/or additional analytical methods  
(HPLC-DAD still very usefull)
- One NPS can be sold for another and purity can vary greatly

