# Severe intoxication after uptake of alleged ecstasy tablets adulterated with the synthetic cannabinoid ADB-PINACA - a case report

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## Introduction

Consumption of drugs is associated with various potential health risks and even experienced drug users are at risk, especially due to varying contents of active ingredients or the addition of unknown pharmacologically active adulterants. Several intoxication cases and even deaths have been reported due to particularly high contents of active ingredients (e.g. high MDMA concentration in ecstasy pills) or addition of potent analgesics (e.g. fentanyl derivatives to street heroin). The increasing availability and number of often highly potent new psychoactive substances (NPS) on the market - like synthetic cannabinoids and designer opioids - has aggravated this problem. By the end of 2017, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) listed more than 670 NPS with more than half of them still present on the market in 2016. This demonstrates the complexity of the current drug market in Europe and the ongoing challenges for physicians, law enforcement and last but not least, clinical and forensic toxicologists.
We present the case of a 24 and 22 years old couple in need of intensive medical care after the intake of a supposed ecstasy tablet containing unexpected compounds.

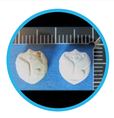
## Case History

Police and paramedics were informed by an emergency call by patient S. that he and his girlfriend are in bad condition after the intake of ecstasy tablets.

Patient S. (♂, 24 years old) was found somnolent but responsive on the couch in his flat and was admitted to ER due to a suspected drug intoxication. He suffered from nausea and vomiting during transport.

Patient L. (♀, 22 years old) was found comatose on the floor after vomiting. She was cyanotic, spastic, tachycardic (up to 170 bpm) with no response to stimuli, requiring immediate intubation.

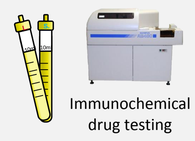
Due to the ecstasy-unlike symptoms, police searched the flat for additional drugs. One and a half tablets with a butterfly motive were the only findings.



**Conditions on Admittance**

Both patients were still under poor general conditions. S. was somnolent but responsive. L. was still comatose, intubated and not responsive to stimuli and admitted to the intensive care unit.

| | Patient S. | Patient L. |
|---|---|---|
| BP [mmHG]: | 130/81 | 160/80 |
| heart rate [bpm]: | 97 | 102 |
| $SpO_2$ [%]: | 95 | 99 |
| Urine Screen: | Amph. positive | Amph. positive |

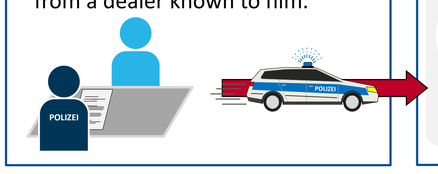


Immunochemical drug testing

S. had a grand mal seizure on day one but was released after two days at good health.

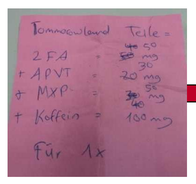
L. also had multiples seizures on day one and no response to direct approach. Hypoxic brain damage was suspected at this time. She could be extubated the day after, and was released after three days without physical impairments.

Both patients were interrogated by the police after being discharged from the hospital and S. provided details about the purchase of six “Tomorrowland” tablets on the day of the incident from a dealer known to him.



**Findings at the house search in the dealers appartment**

Police found large amounts of powders and tablets, including 2 brown tablets with a butterfly logo, 2.1 kg of caffeine powder, tobacco, a tablet press with different logos, a scale, and multiple handwritten notes containing information on NPS and different recipes including so-called “Tomorrowland Teile”.




More than 50 labeled zip bags containing 3 to 10 g of white, white/brown, grey and brown powder, tobacco samples, and blood and urine samples of the two patients were sent in for analysis to the Forensic Science Institute at the State Office of Criminal Investigation.

The dealer was arrested and accused of drug trafficking, possession of narcotics and attempted homicide.

He admitted production of about 300 ecstasy tablets - named “Tomorrowland Teile” - containing 50 mg 2-FA, 50 mg PV-8, and 100 mg caffeine or taurine, each.

To confirm/exclude the initial charge of attempted homicide, the biological specimens of the two patients and aliquots of the questionable ecstasy tablets were sent to the Institute of Forensic Medicine Freiburg to assess their potential health risk.

## Analytical Results

The Forensic Science Institute analyzed serum samples from both patients, taken approximately 3 h (S.) and 2 h (L.) after the intake of the tablets. Both samples were positive for 2-fluoroamphetamine (2-FA), the synthetic hallucinogens diphenidine and methoxphenidine (MXP), the synthetic cathinone α-PVT, as well as the synthetic cannabinoid ADB-PINACA. These results confirmed the initial suspicion of the police and the paramedics that this was not a usual ecstasy intoxication.
In addition, a total of 57 different exhibits - including tablets, powders, tobacco and liquids - found at the dealer’s residence and the tablet found at the patients flat (tablet P.) were analyzed qualitatively using accredited infrared spectroscopy, GC-MS and LC-MS/MS methods. Besides MDMA and isoamyl nitrate, the synthetic cannabinoids ADB-CHMINACA and ADB-PINACA, 12 designer stimulants/hallucinogens (2-FA, 3-fluorophenmetrazine (3-FPM), 3-methylethcathinone (3-MEC), 5-MAPB, 5-MeO-MiPT, α-PVT, clephedrone (4-MEC), diphenidine, MDAI, MDPV, MXP, PV-8) as well as different mixtures of the latter were detected. Three tablets with similar appearance like the “Tomorrowland” tablets found in the patients’ apartment, were of special interest. The analytical findings of all tablets with a butterfly logo are listed on the right.

**Results Serum**

| Patient S. | Patient L. |
|---|---|
| Diphenidine | Diphenidine |
| MXP | MXP |
| 2-FA | 2-FA |
| α-PVT | α-PVT |
| ADB-PINACA | ADB-PINACA |
| Caffeine | Caffeine |
| | *Propofol** |
| | *Midazolam** |

**from emergency treatment*

**Results “Tomorrowland“ Tablets**

| Patients‘ Flat *(320 mg)* | Dealer‘s Appartment (1) 255 mg | (2) 175 mg | (3) 175 mg |
|---|---|---|---|
| Diphenidine | Diphenidine | - | 5-MAPB |
| MXP | MXP | - | - |
| 2-FA | 2-FA | - | - |
| α-PVT | α-PVT | - | α-PVT |
| PV-8 | PV-8 | - | PV-8 |
| ADB-PINACA | ADB-PINACA | - | - |
| Caffeine | Caffeine | Caffeine | Caffeine |

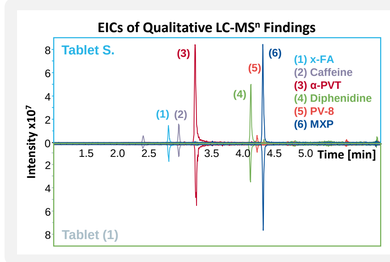
1 mg/mL stock solutions of the previously homogenized samples (4 tablets, 1 powder) were diluted with LC eluent (c = 2.5 µg/mL) and analyzed by LC-$MS^n$ using the Toxtyper workflow.
Two in-house built spectra libraries containing about 1000 drugs, drugs of abuse and NPS including about 180 synthetic cannabinoids,

**Toxtyper**
**LC-ion trap MS**

were used for compound identification. Additionally, a semi-quantitative evaluation of the screening data was used to estimate the ADB-PINACA content of the tablets. A 5-point calibration using D9-ADB-PINACA as internal standard in LC eluent was prepared.

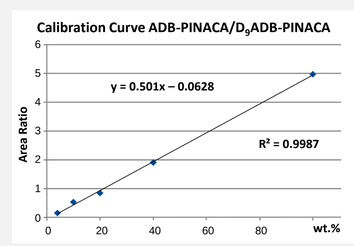
**LC-$MS^n$ Screening Results “Tomorrowland“ Tablets / Powder**

| Patient Tablet P. | Dealer‘s Appartment Tablet (1) | Tablet (2) | Tablet (3) | Powder |
|---|---|---|---|---|
| Diphenidine | Diphenidine | - | 5-MAPB | Diphenidine |
| MXP | MXP | - | - | MXP |
| x-FA | x-FA | - | - | x-FA |
| α-PVT | α-PVT | - | α-PVT | α-PVT |
| PV-8 | PV-8 | - | PV-8 | PV-8 |
| ADB-PINACA | ADB-PINACA | - | - | ADB-PINACA |
| Caffeine | Caffeine | Caffeine | Caffeine | Caffeine |



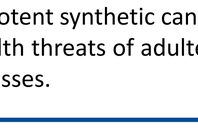

**Semi-Quantitative LC-$MS^n$ Screening ADB-PINACA**

$MS^1$ data of the $[M+H]^+$ ions of ADB-PINACA (m/z 345.2) and D9-ADB-PINACA was used for semi-quantitative evaluation of the screening results.




| Tablet P. | Tablet (1) | Powder |
|---|---|---|
| 7 wt.% | 10 wt.% | 12 wt.% |

Serum samples of the two patients, the 4 tablets, and the powder were analyzed quantitatively for designer drugs (DD) and synthetic cannabinoids (SC) using our accredited routine LC-MS/MS methods. Identification of 152 DD and 104 SC was carried out by retention time and two/three MRM transitions per compound.



**Sciex Qtrap 4000**
**LC-MS/MS**

**Quantitative Results: Serum**

| | Patient S. [ng/mL] | Patient L. [ng/mL] |
|---|---|---|
| Diphenidine | < 1.0 | 4.1 |
| MXP | 10 | 20 |
| 2-FA | 15 | 67 |
| α-PVT | < 1.0 | 1.7 |
| PV-8 | < 1.0 | < 1.0 |
| ADB-PINACA | ≈ 6.2 | ≈ 30 |

**Quantitative Results: Tablets**

| | Tablet P. [wt.%] | Tablet (1) [wt.%] | Tablet (2) [wt.%] | Tablet (3) [wt.%] | Powder [wt.%] |
|---|---|---|---|---|---|
| Diphenidine | 4.0 | 2.8 | - | - | 2.3 |
| MXP | 4.9 | 5.4 | - | - | 4.1 |
| 2-FA | 31 | 47 | - | - | 18 |
| α-PVT | 8.6 | 7.0 | - | 12 | 9.1 |
| PV-8 | < 1.0 | < 1.0 | - | 22 | < 1.0 |
| 5-MAPB | < 1.0 | < 1.0 | - | 22 | < 1.0 |
| ADB-PINACA | 11 | 8 | - | - | 12 |

**Calculated Active Ingredient Content of a Tablet**

Given the wt.% of the different NPS in tablets P. and (1) and assuming a tablet weight similar to the tablet found in the dealer’s apartment (255 mg), the tablets ingested by patients S. and L. had estimated active ingredient contents as shown in the table on the right.

| | Content [mg] |
|---|---|
| Diphenidine | 7 - 10 |
| MXP | 12 - 13 |
| 2-FA | 79 - 119 |
| α-PVT | 17 - 21 |
| PV-8 | *< 2.5* |
| 5-MAPB | *< 2.5* |
| ADB-PINACA | 20 - 28 |

## Conclusion

Qualitatively identical active ingredients were detected in the “Tomorrowland” tablet from the patients’ apartment as well as in a similar tablet with a butterfly logo and powder material found in the safe in the dealer’s apartment. Besides 2-FA, MXP, and α-PVT - ingredients of “Tomorrowland“ tablets according to notes also found in the dealer’s safe - these three samples additionally contained 8 to 12 wt.% of the synthetic cannabinoid ADB-PINACA and trace amounts below 1.0 wt.% of PV-8 and 5-MAPB. The latter might be explained by contamination during storage or handling of the powder materials in the production process of the tablets.

Synthetic cannabinoids are usually consumed by smoking and show completely different effects compared to MDMA or other stimulant drugs. Considering that the seized notes also included a recipe for “killer tobacco” - tobacco mixed with ADB-PINACA - it seems like the addition of ADB-PINACA to this batch of “Tomorrowland” tablets occurred by accident, e.g. by mixing up the multiple zip bags with different powders.

The intake of a tablet with a similar active ingredient content like the tablets found in the two apartments would easily explain the detected serum concentrations and the observed symptoms of the two patients. When smoked, 1 mg of ADB-PINACA clearly shows pharmacological effects. After oral consumption, an extensive first-pass effect would probably reduce the ADB-PINACA bioavailability. Due to saturation of the liver enzymes involved in the phase I metabolism step this might have been of only minor relevance in this case. Therefore, oral intake of 20 to 28 mg ADB-PINACA may possibly lead to severe or even life-threatening side effects. Serum concentrations of diphenidine, MXP, α-PVT, and PV-8 were in the low ng/mL range resulting in only minor, if any, physiological effects. 2-FA serum concentrations reached pharmacologically active concentrations of 15 and 67 ng/mL, respectively. According to the medical records, without quick medical care this severe intoxication could have led to severe brain damage due to respiratory insufficiency or even death, at least for the female victim. Fortunately, both patients were released from hospital without physical impairment.

To our knowledge, this is the first report of an accidental intoxication with the synthetic cannabinoid ADB-PINACA after oral intake. Although the alleged ecstasy tablet contained a mixture of several designer stimulants/hallucinogens, the highly potent synthetic cannabinoid ADP-PINACA was considered to be the main toxic agent in this potentially life-threatening mixed intoxication.
This case exemplifies the possible health threats of adulterated drugs of abuse and shall remind physicians and toxicologists to check for all types of NPS even if the assumed drug preparation or route of administration would initially rule out specific compound classes.