Acute intoxication of two adults after intake of alleged ecstasy tablets containing the synthetic cannabinoid ADB-PINACA

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Introduction

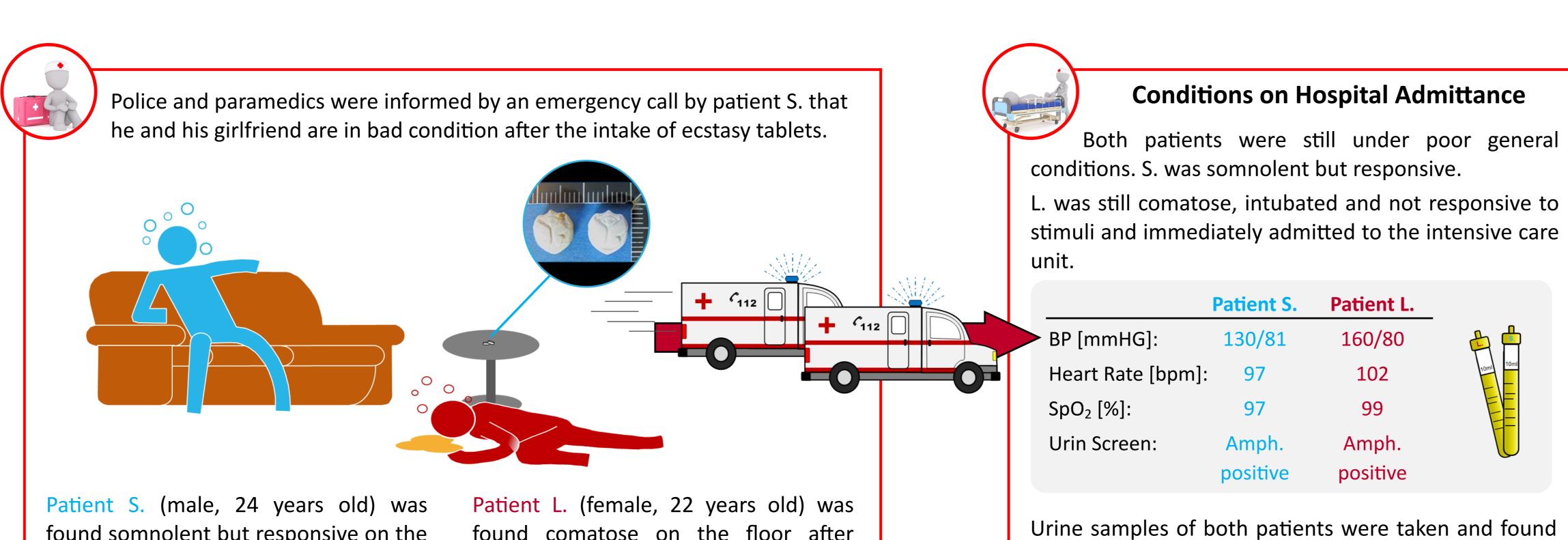
Drug abuse is associated with various potential health risks and even experienced drug users are at risk, especially due to varying content of active ingredients or the addition of unknown pharmacologically active adulterants. The increasing availability and number of often highly potent new psychoactive substances (NPS) on the market - like synthetic cannabinoids and designer opioids - has aggravated this problem. 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 or other drugs of abuse.

By the end of 2017, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) listed more than 670 different NPS with more than half of them still present on the European drug market in 2016. This demonstrates the complexity of the current drug market and the ongoing challenges for physicians, law enforcement and clinical and forensic toxicologists.

We report the case of a couple in need of intensive medical care after the intake of a supposed ecstasy tablet containing unexpected compounds.

approximately 3 h (S.) and 2 h (L.) after the intake of the tablets.

police and the paramedics that this was not a usual ecstasy intoxication.

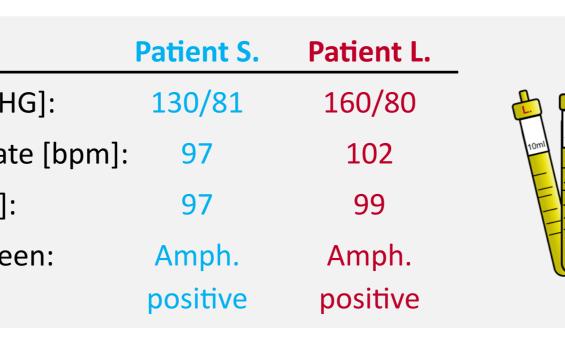


found somnolent but responsive on the couch in his flat and was admitted to ER due to a suspected drug intoxication. He suffered from nausea and vomiting during transport.

found comatose on the floor after vomiting. She was cyanotic, spastic, tachycardic (up to 170 bpm) with no response to stimuli, 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 Hospital Admittance after being discharged from the hospital and S. Both patients were still under poor general conditions. S. was somnolent but responsive. L. was still comatose, intubated and not responsive to



Urine samples of both patients were taken and found to be positive for amphetamine in the routine immunological drug screening.

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.

Case History

Both patients were interrogated by the police provided details about the purchase of six "Tomorrowland" tablets on the day of the incident from a local dealer known to him.



The dealer was arrested and accused of drug 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.

Findings at the House Search in the Dealers Appartment

Conclusions

Qualitatively identical active ingredients were detected in the "Tomorrowland" tablet from the patients' apartment as well as in a

explained by contamination during storage or handling of the powder materials in the production process of the tablets.

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

Synthetic cannabinoids are usually consumed by smoking and show completely different effects compared to MDMA or other

The intake of a tablet with a similar active ingredient content like the tablets found in the two apartments would easily explain the

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

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

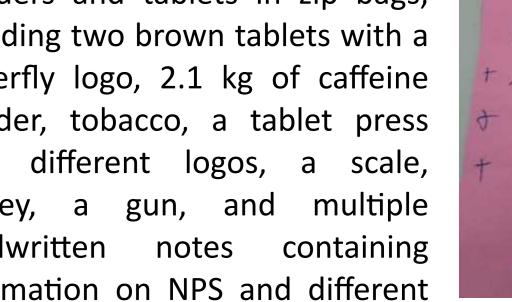
records, without quick medical care this severe intoxication could have led to severe brain damage due to respiratory insufficiency or

Although the alleged ecstasy tablet contained a mixture of several designer stimulants/hallucinogens, the highly potent synthetic

even death, at least for the female victim. Fortunately, both patients were released from hospital without physical impairment.

cannabinoid ADP-PINACA was considered to be the main toxic agent in this potentially life-threatening mixed intoxication.

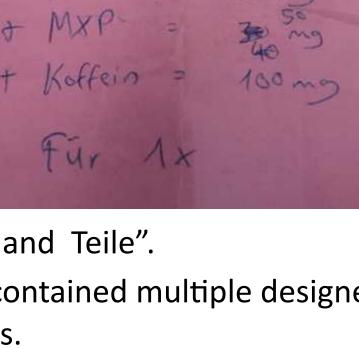
Police found large amounts of powders and tablets in zip bags, including two brown tablets with a butterfly logo, 2.1 kg of caffeine powder, tobacco, a tablet press logos, a scale, notes containing information on NPS and different



recipes including so-called "Tomorrowland Teile".

According to the labeling, the zip bag contained multiple designer stimulants and synthethic cannabinoids

In total, more than 50 different zip bags - each of them containing 3 to 10 g of different white, white/brown, grey and brown powders, tobacco samples - and blood and urine samples of the two patients from the day of hospital admittance were sent in for analysis to the Forensic Science Institute at the State Office of Criminal Investigation.



Zip Bag Content **According to Labeling**

ADB-Pinaca

MDMB-Chminaca

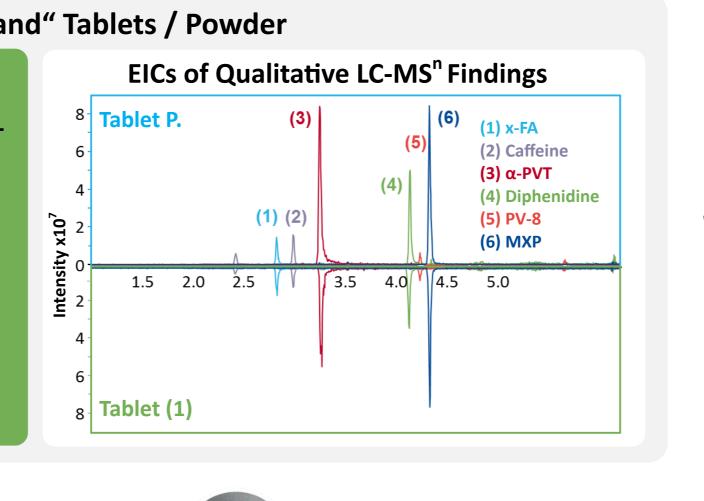
Diphenidine

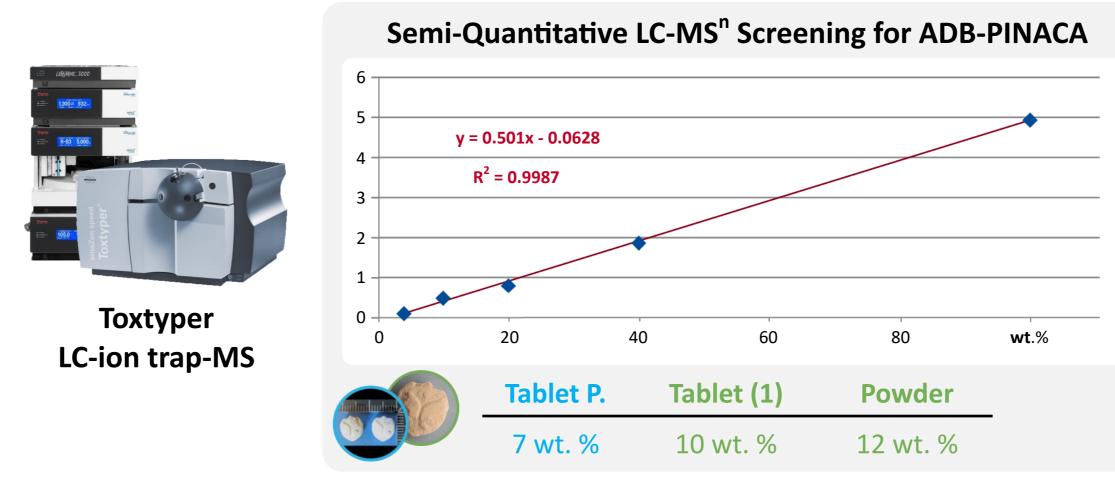
Analytical Results

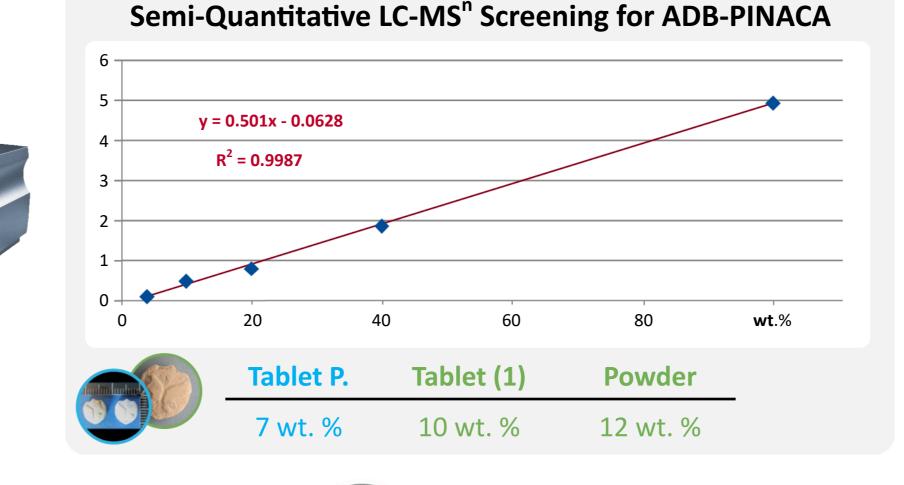
- Methanolic solutions (c = 1 mg/mL) of the previously homogenized samples (4 tablets, 1 powder) were diluted with LC eluent (c = 2.5 μg/mL) and analyzed by LC-MSⁿ using the Toxtyper workflow. Two in-house built spectra libraries containing about 1000 drugs, drugs of abuse and new psychoactive substances including about 180 synthetic cannabinoids, 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 in LC eluent using D9-ADB-PINACA as internal standard was prepared. MS¹ 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.

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

LC-MSⁿ Screening Results "Tomorrowland" Tablets / Powder α-PVT α-PVT PV-8 PV-8 ADB-PINACA ADB-PINACA Caffeine Caffeine







The analytical findings of all tablets with a butterfly logo are listed below.

the patients' apartment, were of special interest.

Results Serum			Results "Tomorrowland" Tablets			
Patient S.	Patient L.		Patients' Flat (320 mg)	Dea (1) 255 mg	ller's Appartn (2) 175 mg	nent (3) 175 mg
Diphenidine MXP	Diphenidine MXP		Diphenidine	Diphenidine	-	5-MAPB
2-FA	2-FA		MXP	MXP	-	-
α-PVT	α-PVT		2-FA	2-FA	-	-
ADB-PINACA	ADB-PINACA		α-PVT	α-PVT	-	α-PVT
Caffeine	Caffeine		PV-8	PV-8	-	PV-8
	Propofol* Midazolam*		ADB-PINACA	ADB-PINACA	-	-
*from emergency treatment		Caffeine	Caffeine	Caffeine	Caffeine	

The Forensic Science Institute analyzed serum samples from both patients, taken

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

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

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

qualitatively using accredited infrared spectroscopy, GC-MS and LC-MS/MS methods.

Serum samples of the two patients, the four tablets, and the powder were analyzed quantitatively for designer drugs (DD) and synthetic cannabinoids (SC) using our 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.

as shown above.

Quantitative Results: Serum Patient S. Patient L. [ng/mL] [ng/mL] PV-8 < 1.0 ADB-PINACA Given the wt.% of the different NPS

Quantitative Results: Tablets [wt.%] [wt.%] [wt.%] [wt.%] 5-MAPB **ADB-PINACA**

Calculated Active Ingredient Content of a Tablet Content [mg] Diphenidine 7 - 10 12 - 13 MXP 79 - 119 17 - 21 α-PVT PV-8 < 2.5 5-MAPB ADB-PINACA 20 **- 28**

To our knowledge, this is the first report of an accidental intoxication with the synthetic cannabinoid ADB-PINACA after oral intake.

<u>Disclosure:</u> None of the authors has financial relationships with a company as defined **<u>Reprint:</u>**

bags with different powders.

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.

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