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The effects of synthetic cannabinoid UR-144 on the human body—A review of 39 cases

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ABSTRACT

UR-144 [(1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone] is a synthetic cannabinoid, which has been detected in many 'legal highs', seized from the global drug market since the beginning of 2012. It has gained popularity as a 'legal' alternative to classic cannabis in countries where it was not controlled. Despite the widespread distribution of this substance, the data on its effects on the human body are scarce. Therefore, this paper describes the results of analysis and observed effects in 39 cases in which UR-144 was determined in blood.

Symptoms were noted from the blood sampling forms filled out by the representative doctor. The determined concentrations of UR-144 were in the range of trace amounts (LOD—0.15 ng/mL; LOQ—0.5 ng/mL) up to 17 ng/mL. The most common observed effects included slurred speech, dilated pupils, sluggish and abnormal pupillary reaction, cheerful behaviour, poor coordination, and staggering. Less frequently observed were: verbosity, narrow pupils, loss of consciousness, pale or reddened facial skin, blackout, euphoria, agitation, hallucinations, hindered communication, shaking hands, seizures, convulsions, somnolence, delayed movements, redness of the conjunctiva, and tachycardia.

The discussed cases show the effects observed after UR-144 use. This study can assist in the recognition of possible effects caused by this substance.

1. Introduction

Recreational use of synthetic cannabinoids has become increasingly popular during the last few years. This is primarily because these compounds produce psychoactive effects similar to cannabis, and often are not controlled. One of the most popular synthetic cannabinoids in recent years has been UR-144 [IUPAC name: (1-pentyl-1*H*-indol-3-yl)-(2,2,3,3-tetramethylcyclopropyl)-methanone]. Alternative abbreviations for this substance include TMCP-018, KM-X1, MN-001 and YX-17. UR-144 was invented in 2006 by Abbott Laboratories [1] and was first reported in herbal incenses seized in June 2012 in Korea [2]. It has rapidly spread all over the world and has been detected in places such as Europe, Japan and the USA [3–5]. Marketing of UR-144 was a response by the black market to by-pass the new drug law. UR-144 was among the most popular synthetic cannabinoids in the past year in Poland, found in herbal blends, resinous samples (with macroscopic appearance similar to that of hashish), and powders. According to the Report of the Chief Sanitary Inspector, UR-144 was the most popular new psychoactive substance (NPS) on the drug market in Poland in the period of 2013–2014. This substance was determined in 41% and 34% of 'legal highs' preparations in 2013 and 2014, respectively [6].

UR-144 is mostly smoked (mixed, e.g., with tobacco or herbs) in order to achieve marijuana-like effects. It can also be taken orally, or vaporised and inhaled. The UR-144 starting doses are reported by users as 0.5–2 mg, and experienced users' doses typically range between 2.5–20 mg [4,7]. User-reported effects typically start 0.5–2 min after smoking, peak after 3–5 min, and end after approximately 1–2 h (but may last approximately 4 h after high doses). Tolerance to UR-144 may develop, leading users to consume larger doses [4,7].

Synthetic cannabinoids are not detected in routine medical screenings for drugs of abuse. Diagnosis is usually based on a medical interview and observation. Despite the widespread distribution of UR-144, the data on its effects on the human body are scarce. There is no specific toxidrome associated with synthetic cannabinoids exposure and diagnosis based on the physical examination can be challenging. Therefore, this paper describes

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the results of analysis and observed effects of 39 cases in which UR-144 was determined in blood. This study can assist in the recognition of possible effects caused by this substance.

2. Material and methods

Blood samples were sent to the Institute of Forensic Research, Krakow, Poland, in 2012–2015, with provisions of investigative bodies (police and prosecutors) to carry out toxicological analysis for the presence of psychoactive substances.

Detection and determination of UR-144 in blood samples were carried out according to previously published screening and targeted LC–MS/MS methods [5,8].

Discussed symptoms come from blood collection forms (filled out by a physician).

3. Results and discussion

3.1. Frequency of detection

UR-144 was first detected in Poland in samples seized in March 2012. It quickly gained popularity, and since July 2015 it has been controlled under the Drug Addiction Counteraction Act (narcotic drug of I-N group). In cases sent to the Institute for toxicological analyses between the periods of 2012–2015, UR-144 was found in blood collected from 39 living individuals. UR-144 was detected in 30 cases in 2015 and in 7 cases in 2014 respectively. This showed a significant increase in frequency compared to single identifications made in 2012 and 2013. It should be noted that this compound has not been found yet in any cases in 2016, which suggests that it has been replaced on the market by other synthetic cannabinoids in 2015, when it was added to the list of controlled substances. The cases within this study which tested positive for UR-144 were mostly related to DUID and traffic accidents, as well as cases involving drugs possession and use. All UR-144 users were men aged between 16 to 42 with an average age of 23.4 and a median of 22.0 years old.

In most cases (26 out of 39), UR-144 was the only substance present. In 13 cases other compounds were also detected (number of identifications in the order of decreasing frequency): tetrahydrocannabinol (THC) and 11-nor-9-carboxy-delta-9-tetrahydrocannabinol (THCCOOH) (6), ethyl alcohol (3), diazepam (3), amphetamine (2), 3′,4′-methylenedioxy-α-pyrrolidinobutyrophenone (MDPBP) (2), and MDMB-CHMICA (2). In individual cases, α-pyrrolidinopentiophenone (α-PVP), pentedrone, nordiazepam and clonazepam were found. Furthermore, THCCOOH alone (without THC) was detected in four cases, but as it is an inactive metabolite and indicates previous use of cannabis, these cases were treated as cases with only UR-144 (as psychoactive substance). The frequent presence of UR-144 along with THC and/or THCCOOH in blood is not surprising, as it may be the result of simultaneous administration of synthetic cannabinoid with marijuana or administration of cannabis herb enhanced by a synthetic compound. The detailed connections between UR-144, other NPS and conventional drugs are presented in Fig. 1.

3.2. Concentrations found

The determined concentrations of UR-144 in all 39 cases were in the range from trace amounts (limit of detection and limit of quantification of the applied method were 0.15 and 0.5 ng/mL, respectively) up to 17 ng/mL (mean concentration 3.3 ng/mL, median 1.6 ng/mL). The concentrations of other substances in blood in 13 cases were as follows: THC—0.5–7.0 ng/mL, THCCOOH—<1–16 ng/mL, diazepam—5–79 ng/mL, amphetamine—10–495 ng/mL, MDPBP—16–42 ng/mL, MDMB-CHMICA—1.8–7.3 ng/mL, α-PVP—26 ng/mL, pentedrone—21 ng/mL, nordiazepam—32 ng/mL, and clonazepam—5 ng/mL. Ethyl alcohol concentrations in breath were in the range of 0.42–0.91 mg/L.

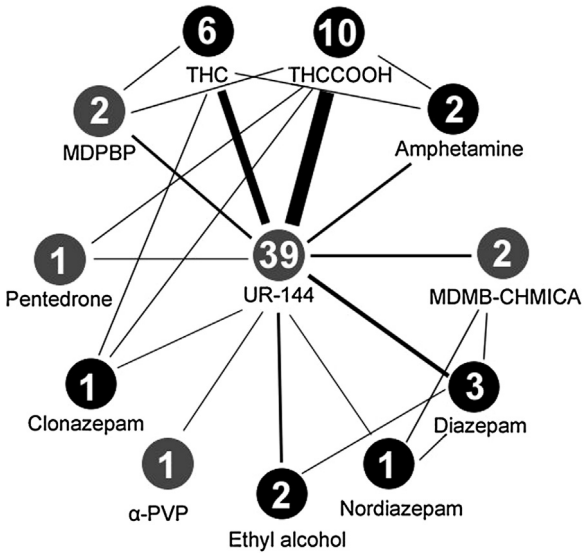

Fig. 1. Connections (simultaneous presence) of UR-144 with other NPS (gray) and conventional drugs (black) in analysed cases. The number of identifications is presented and the thickness of the lines specifies popularity of connections.

3.3. Reported effects

The use of synthetic cannabinoids is a concerning issue. Therefore, the determination of the effects caused by UR-144 is very important. Described symptoms were taken from the blood sampling forms filled out by the respective doctor during sampling. These forms contain the results from a preliminary medical examination and can be useful in assessing whether the tested person is under the influence of alcohol or drugs. The elements of examination of this form include basic observations of the appearance as well as condition of the person examined (among other examination of pupils and their reaction to light, Romberg's test, finger-to-nose test, pulse measurement, evaluation of speech and gait, behaviour and mood, the appearance of facial skin, orientation as to time and place, a test of lifting the objects off the ground). It should be noted, however, that these examinations are not standardised.

The study group consisted of 39 cases, in which four cases showed no symptoms. In a subgroup of individuals who had no symptoms, the determined UR-144 concentrations were in the range of 0.5–5.0 ng/mL (mean 2.0 ng/mL, median 1.3 ng/mL). In the subgroup of individuals with observable symptoms (35 cases), the UR-144 concentrations were in the range <0.5 ng/mL up to 17 ng/mL (mean 3.4 ng/mL, median 1.6 ng/mL). The most valuable seemed to be a group of individuals whose blood contained UR-144 as the only substance, because co-exposure to other drugs can complicate the interpretation of the symptoms since the symptoms may not be solely due to UR-144. Therefore, such a subgroup of individuals with observable symptoms was extracted. In these 25 cases, UR-144 concentrations determined in blood were in the similar range of 0.5–17 ng/mL, however the mean and median were higher (mean 4.1 ng/mL, median 1.9 ng/mL). The concentrations of UR-144 determined in our cases were similar to those previously reported in the literature (0.05–25.9 ng/mL) [9].

The observed effects (Fig. 2 and Table 1) were (in brackets the number of cases in which a specific symptom was observed): slurred (slowed; mumbling) speech (9), dilated pupils (8), sluggish pupillary response to light (8), cheerful behaviour (6), positive