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Case Report

Two fatalities associated with synthetic opioids: AH-7921 and MT-45

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ABSTRACT

In this study, two fatalities associated with the synthetic opioids AH-7921 and MT-45 are reported. Within the last few years, both compounds have emerged on the recreational drug market and are sold as "research chemicals" on the internet. In the first case, a 22-year-old woman was found dead in the bedroom of her apartment by two of her friends. A plastic bag labeled "AH-7921" was found in the apartment and the two friends stated that the deceased had consumed AH-7921 prior to her death. The woman was a known drug addict. In the second case, a 24-year-old man was found dead in his room by his mother. The deceased was sitting on a chair in front of his desk slumped over. Several bags of white powder labeled "MT-45", "Methoxmetamine" and "Methoxphenidine" were found in his room.

Toxicological analyses of femoral blood, heart blood, liver, pericardial fluid, urine, vitreous humor and stomach content of the deceased were performed using liquid chromatography–quadrupole-time-of-flight mass spectrometry (LC–QTOF-MS). Time-of-flight mass spectrometry was carried out on an LC-Triple TOF 5600 system (AB Sciex) with electrospray ionization operated in positive mode. In the first case, additional hair analysis was performed by liquid chromatography–tandem mass spectrometry (LC–MS/MS) and LC–QTOF-MS.

In both cases, the relevant synthetic opioid could be detected in all analyzed samples. The concentration of AH-7921 was determined to be 450 μg/L in femoral blood. MT-45 was present at a concentration of 2900 μg/L in femoral blood. Besides methoxmetamine which could qualitatively be detected in femoral blood, urine and stomach content no methoxphenidine was found. In summary, deaths of the young individuals could be, by exclusion of other causes of death, attributed to the consumption of an overdose of AH-7921 and MT-45, respectively.

1. Introduction

In recent years, new psychoactive substances (NPS) have flooded the recreational drug market. The two largest groups monitored by the EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) are the synthetic cannabinoids and the cathinones [1]. Other than these two groups, there is a broad range of various other compounds such as new benzodiazepines, tryptamines, phenethylamines and opioids. Most recently, synthetic opioids have appeared on the drug market, including fentanyl derivatives and other opioid agonists such as AH-7921 and MT-45 which are described in the present cases. The chemical structures of AH-7921 and MT-45 are given in Fig. 1.

The synthetic opioid AH-7921 (3,4-dichloro-*N*-[(1-dimethylamino)cyclohexylmethyl]benzamide) is a potent agonist on μ-opioid receptors [2]. It is used by opioid addicted users as a substitute (e.g. for heroin), but was also found as one of the active compounds (in combination with two synthetic cannabinoids and α-pyrrolidinobutiophenone) in an illegal herbal-type drug sold over the internet in Japan [3]. AH-7921 was first developed in the 1970s by Allen and Hanburys Ltd. as a potential analgesic drug. The name Doxylam was proposed for this compound, but it was never sold commercially. In December 2014, AH-7921 became a controlled substance in Germany.

MT-45 (IC-6) is a synthetic opioid which was invented as an opioid analgesic medicine in the 1970s by Dainippon Pharmaceutical Co. [4,5]. Chemically, it is a piperazine derivative (1-cyclohexyl-4-(1,2-diphenylethyl)piperazine) which shows a completely different structure compared to most other opioid agonists. Its analgesic activity is comparable to that of morphine [6]. As a "research chemical", it is typically sold on the internet and

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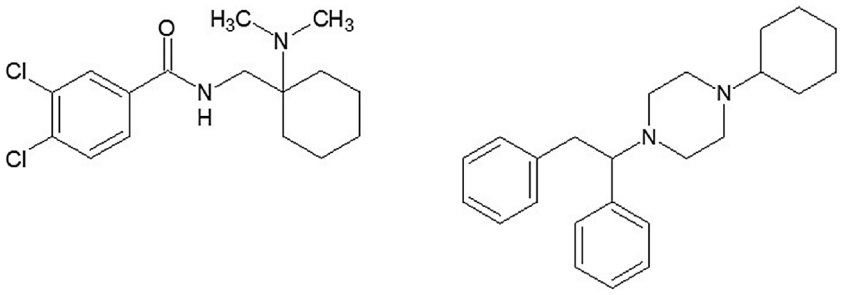

Fig. 1. Structures of AH-7921 (left) and MT-45 (right).

has been identified in chemical and herbal products along with synthetic cannabinoids, cathinones and a phenethylamine derivative [7]. Since May 2015, MT-45 is a controlled substance in Germany.

In this study, two fatalities associated with the synthetic opioids AH-7921 and MT-45 are presented. The quantitative analyses for AH-7921 and MT-45 were performed using liquid chromatography–quadrupole-time-of-flight mass spectrometry (LC–QTOF-MS). Concentrations were determined for femoral blood, heart blood, liver, urine, pericardial fluid, vitreous humor and gastric content. In case of AH-7921, additional hair analysis was performed by LC–MS/MS and LC–QTOF-MS.

2. Case reports

2.1. Case 1—AH-7921

In 2013, a 22-year-old woman was found dead in the bedroom of her apartment by two of her friends. Last signs of life were dated three days prior to the deceased being found. A plastic bag labeled "AH-7921" was found in the apartment (Fig. 2). The two friends indicated that the deceased had consumed AH-7921. Further, the woman was a known drug addict. During autopsy, cerebral edema with moderate to clearly increased intracranial pressure was determined. In addition, signs for an incipient pneumonia in the central lung sections were found. The internal organs were full of blood. Furthermore, no morphological signs of preexisting internal diseases were found.

2.2. Case 2—MT-45

In 2014, a 24-year-old man, with a known history of amphetamine abuse, was found dead in his room by his mother. The deceased was sitting on a chair in front of the desk slumped over. Nearby, an e-cigarette with an unknown liquid was found as well as other paraphernalia suggesting drug abuse including a spoon, a glass and ascorbic acid stored in a container. Furthermore, several bags of white powder labeled "Methoxphenidine", "Methoxmetamine" and "MT-45" were found. Autopsy revealed brain and hemorrhagic pulmonary edema and hyperemia of the internal organs. The urinary bladder contained 450 mL of urine. All other findings were unremarkable.

3. Materials and methods

3.1. Reagents and chemicals

All reagents and solvents were of analytical grade or the highest purity available and obtained from Sigma-Aldrich (Steinheim, Germany), except for β-glucuronidase/arylsulfatase from Helix pomatia (Merck, Darmstadt, Germany), purified water (ELGA LabWater, Celle, Germany) and petroleum ether (Chemsolute, Renningen, Germany). Standard substances were purchased from LGC Standards (Wesel, Germany), while the certified reference standard AH-7921 was obtained from Cayman Chemical. Stock solutions of AH-7921 and MT-45 were prepared at a concentration of 1 mg/mL in methanol. The stock solution of MT-45 was prepared

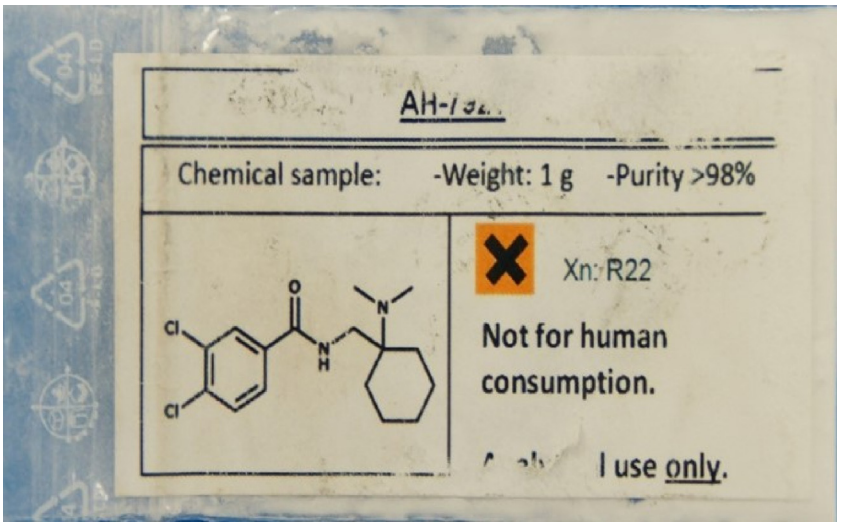

Fig. 2. "Research chemical" found in the apartment of the deceased.