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Prolonged sedation and unconsciousness after intoxication with the novel semisynthetic cannabinoid hexahydrocannabioctyl (HHC-C8): Two case descriptions

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ABSTRACT

Semisynthetic cannabinoids (SSCs) are compounds closely related to the major phytocannabinoids. SSCs have recently appeared as legal alternatives to Δ^9-tetrahydrocannabinol (Δ^9-THC), the primary psychoactive compound in the *Cannabis* plant. Δ^9-THC has been consumed by humans for millennia and has low acute toxicity, but recent evidence indicates elevated toxicity from exposure to some SSCs. The present study describes two case reports with confirmed intoxication with a novel SSC, hexahydrocannabioctyl (HHC-C8). In the first case, a young male was found deeply unconscious and hospitalized. The clinical picture was mostly neurological with recurring seizures and coma. The patient was comatose for two days with a slow gradual improvement over the following two weeks. An HHC-C8 blood concentration of 72 ng/mL was determined in a sample taken at time of admission and the compound was also confirmed at a concentration of 6 % in a cannabis product of the same type and purchased at the same store. In the second case, a female was hospitalized after having slept for 14 hours and found in a minimally responsive state. The patient suffered pronounced somnolence and sedation for 3 days after which she gradually recovered. In a blood sample taken 40 hours after ingestion, HHC-C8 was detected at trace amounts along with two putative metabolites. The ingested product, which the patient had purchased at a web shop, was found to contain 7 % HHC-C8. The two cases demonstrate the toxic potential of widely available and often mislabeled cannabis products, the intake of which can lead to intoxications requiring extensive medical treatment.

1. Introduction

Semisynthetic cannabinoids (SSCs) are a new group of cannabinoids chemically related to phytocannabinoids such as (−)-*trans*-Δ^9-tetrahydrocannabinol (Δ^9-THC, Fig. 1) and cannabidiol (CBD). Although several SSCs, e.g. hexahydrocannabinol (HHC), were initially described by cannabis researchers as early as the 1940s, there has been very limited human exposure to these compounds in the following decades [1]. In recent years, largely due to legislative changes in the US starting in 2018, cannabis hemp rich in non-psychoactive CBD and low in Δ^9-THC has become abundant [2]. CBD can serve as a chemical precursor to other psychoactive cannabinoids, which has led to the recent emergence of SSCs on recreational markets, both in Europe and in the US [2–4].

SSCs contain chemical modifications which include alternative positions of the cyclohexene double bond of Δ^9-THC, saturation of the cyclohexene ring, elongation of the *n*-pentyl side chain, and acetylation of the hydroxyl group of Δ^9-THC. Compounds considered SSCs and which have appeared on recreational markets include Δ^8-tetrahydrocannabinol (Δ^8-THC), HHC, Δ^8-tetrahydrocannabiphorol (Δ^8-THCP), Δ^9-tetrahydrocannabiphorol (Δ^9-THCP), hexahydrocannabiphorol (HHCP), tetrahydrocannabinol-O-acetate (THC-O), hexahydrocannabinol-O-acetate

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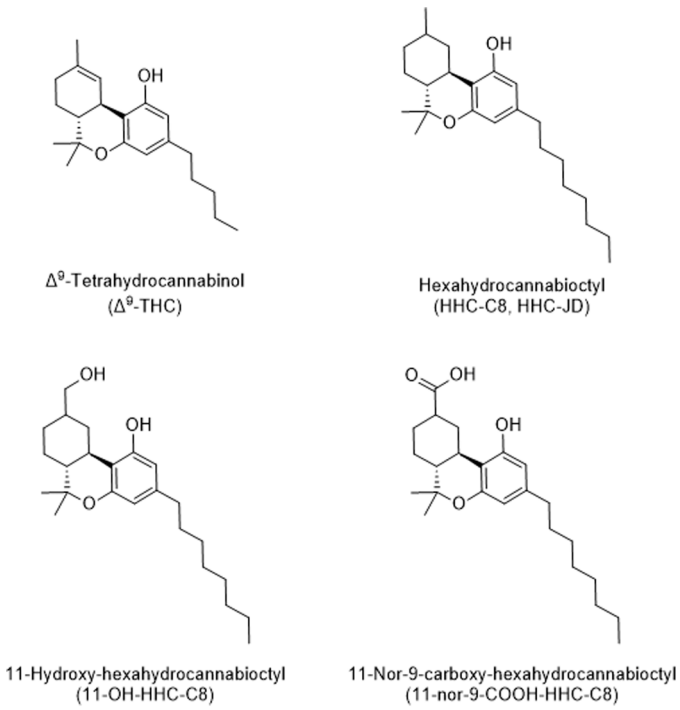

Fig. 1. Chemical structures of Δ^9-tetrahydrocannabinol (Δ^9-THC), hexahydrocannabioctyl (HHC-C8) and two putative metabolites of HHC-C8, 11-hydroxy-hexahydrocannabioctyl and 11-nor-9-carboxy-hexahydrocannabioctyl.

(HHC-O), tetrahydrocannabioctyl (THC-C8, THC-JD) and tetrahydrocannabidiol (H4-CBD) [3,5].

In general, there is a lack of clinical studies investigating the pharmacological activity and toxicity of SSCs. In vitro and animal data indicate cannabinoid receptor 1 (CB1) agonist activity for many of the compounds. In particular, in vitro receptor studies have demonstrated that elongation of the *n*-pentyl side chain to form *n*-hexyl, *n*-heptyl and *n*-octyl homologues enhances the potential for CB1-receptor activation with activity increasing with side chain length [6–9].

For the *n*-heptyl variants, THCP and HHCP, recent case reports have described severe toxicity primarily in the form of neurological symptoms including agitation, seizures and unconsciousness [10–12]. The *n*-octyl homologue of THC, THC-C8, was recently involved in an outbreak of intoxications in Hungary [13]. In the incident, 30 tourists were hospitalized after ingesting gummies later confirmed to contain both the Δ^8- and Δ^9-variants of THC-C8. Reported symptoms were prolonged sedation (up to 3 days), hallucinations, tremors, agitation and confusion.

In the current paper, we report the first detection of a novel SSC, hexahydrocannabioctyl (HHC-C8, HHC-JD), containing an *n*-octyl side chain and with a saturated cyclohexene ring (Fig. 1). The compound was detected in the blood of two patients presenting with serious drug toxicity in the form of prolonged sedation and unconsciousness. In both cases, analytical confirmation of the compound was performed in reportedly ingested cannabis products.

2. Case 1

2.1. Case report

In June of 2024, a young adult Caucasian male was brought to the intensive care unit (ICU) after being found unconscious with froth around his mouth on the floor in his room by his father.

Prior medical history included a suspicion of attention deficit hyperactivity disorder in early childhood, but no formal diagnosis was made. A suspected bilateral tonic-clonic seizure in his mid-teens had led to an epilepsy work-up but with normal findings on cerebral magnetic resonance imaging (MRI) and standard electroencephalography (EEG) the diagnosis was abandoned.

Admission day 1: On the evening before admission, the patient complained of a sore throat and retired to his room after dinner. The patient was found at 5 am the next morning by his father, unconscious, on the floor and with a froth around his mouth. On arrival at the ICU, he presented a Glasgow Coma Scale (GCS) score of 3 with pupils nonresponsive to light, nuchal rigidity, and a temporal temperature of 40.0°C. The patient desaturated to 88 % on pulse oximetry which was corrected to 100 % on 4 L/min nasal oxygen. Initial sinus tachycardia of 130 BPM fell to 100 BPM after IV fluid therapy. The remaining clinical exam was unremarkable. Arterial blood gas showed pH of 7.28, pCO_2 9.7 kPa, normal electrolytes and lactate of 1.2 mmol/L. On arrival the patient had a brief bilateral tonic-clonic seizure successfully treated with 10 mg intravenous midazolam. Due to a repeat bout of seizures and trouble keeping free airways, he was sedated and intubated. A non-contrast computerized tomography (CT)-scan of the head was unremarkable. A lumbar puncture showed < 3 cells/mm^3, normal glucose ratio, and protein. Microscopy of the cerebrospinal fluid showed no signs of microorganisms and a QIAstat meningitis/encephalitis panel also failed to detect any microorganisms. Blood analyses showed unremarkable electrolytes, liver and kidney parameters within normal range, a C-reactive protein (CRP) of 1 mmol/L, and leukocytes of 14x10^9/HPF. On urine toxicology screen (Syva® RapidTest™ d.a.u. 10, Siemens Healthineers, Fig. 2) the patient tested positive for THC. According to the patient's father, he had smoked cannabis just over a week earlier. While in the ICU, the patient's fever subsided. A wake-up trial was done 6 hours after admission with a halt to all sedatives 3 hours prior. EEG showed frequent delta activity with occasional bifrontal, bitemporal and midline sharp waves. On neurological exam, the patient was found without ciliary-, corneal- or vestibulo-ocular reflexes but with intact cough reflex. The patient remained immobile with a GCS of 3 and showed universally brisk tendon reflexes with normal plantar response bilaterally.

On suspicion of status epilepticus, he was loaded with levetiracetam 60 mg/kg. A CT-angiogram, done to rule out basilar artery occlusion, showed no signs of large-vessel occlusion, and a renewed plain head CT

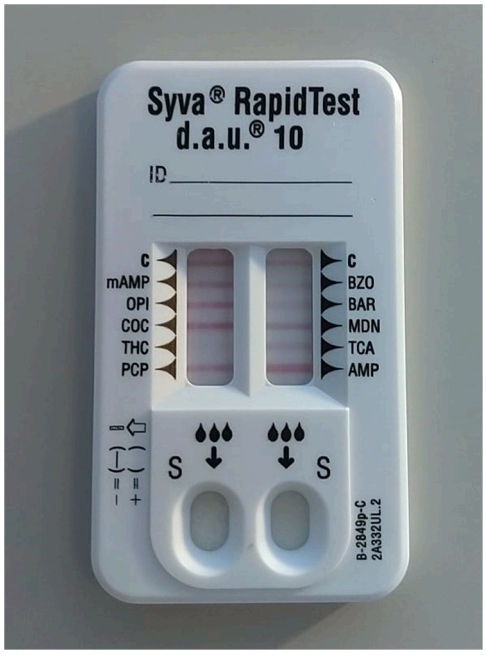

Fig. 2. Urine toxicology screening with the Syva® RapidTest for Case 1. Performed on the day of admission.

remained normal. An MRI-scan without contrast enhancement was normal with no DWI-lesions. Sedation was stopped in the evening and the patient remained at GCS 3. At nighttime, he presented with three minutes of general convulsions with head turning to the right and dilated pupils. The seizure was effectively treated with 5 mg of IV midazolam and restart of propofol sedation.

Admission day 2: Propofol sedation was discontinued, and a new wake-up trial was performed. The patient rose to a GCS of 6 E1V1M4. A continuous EEG showed rhythmic anterior activity of 7–9 Hz with intermittent diffuse 1½-3 Hz activity but with no signs of epileptic activity. All blood tests were within normal range including ammonium. In the afternoon the patient was extubated and transferred to the regular neurological ward. Subsequently he rose to GCS 8 E2V2M4 with no signs of focal neurological pathology and normalization of all vital parameters.

Admission day 3: The patient showed further improvements in consciousness, achieving a GCS of 10 E3V2M5 and began responding to his next-of-kin with a verbal greeting. A third EEG was performed to investigate the patient's continued drowsiness, revealing a continuous encephalopathic pattern, though slightly less pronounced than earlier.

Admission day 4: The patient was more awake and able to speak, although with significant latency, severely impaired attention span and executive dysfunction. Additionally, he displayed several episodes of cognitive arrest. A follow-up EEG showed normalization of the previously observed encephalopathic pattern. The patient was able to walk with a standing walker.

Admission day 6: The patient continued to improve in alertness achieving a GCS of 14 E4V4M6. A Montreal Cognitive Assessment (MoCA) revealed severe cognitive impairment with a score of 7/30. Neurological examination identified an unsteady gait and a tendency to walk into objects though there were no signs of focal motor impairment, sensory deficits or visual field loss. Neuropsychological and occupational therapist assessment identified impaired attention, disorientation, reduced fine motor skills and semantic word retrieval. The patient required extensive guidance to perform even simple activities-of-daily-living (ADL) tasks.

Admission day 7–16: The patient demonstrated slow but steady improvement in cognitive and motor function. Reevaluation by a neuropsychologist revealed mild impairments in attention and working memory along with mild executive dysfunction. Assessment by a speech therapist identified deficits in sentence completion. The patient was discharged to his home on day 17.

At a follow-up visit 2.5 months after discharge, the patient reported feeling sluggish and fatigued for 2–3 weeks following discharge with gradual improvement thereafter eventually returning to his usual state. He had been able to resume his vocational education three weeks prior to the follow-up visit without requiring additional educational support. On a follow-up MoCA test he scored 25/30 displaying difficulties with clock drawing, category fluency, and delayed word recall. Laboratory reports from initial blood samples taken at admission were positive for HHC-C8. Upon further questioning, the patient disclosed that he and a friend had orally consumed a cannabis product labeled "Super Hash" which was purchased at a specific convenience store the day before admission. The ingested amount was not specified. This was considered the likely cause of the initial seizures and prolonged encephalopathic state especially given the gradual spontaneous improvement and extensive paraclinical investigation. Interestingly, his friend reportedly experienced no adverse effects after ingestion.

2.2. Toxicological analysis

Two blood samples were secured from Case 1: At the time of admission to the ICU (Sample A), and one taken on admission day 7 (Sample B). Sample A was stored at 5°C and shipped to the laboratory 6 days after sampling, while Sample B was stored at 5°C for 97 days before being shipped to the laboratory.

A broad toxicological screening with subsequent quantification of relevant drugs was performed on sample A, while cannabinoids were quantified in both sample A and B. Sample A was found positive for the cannabinoid HHC-C8 and two predicted metabolites (see Fig. 1 and Figs. S1–3) as well as HHCP at a very low concentration (Fig. S4). Concentrations of cannabinoids are shown in Table 1. Additional findings in Sample A were lidocaine 0.02 mg/kg, midazolam 0.02 mg/kg, paracetamol 7 mg/kg, methicillin, betamethasone, benzylpenicillin, ceftriaxone and propofol, which were administered as part of the hospital treatment. In sample B, HHC-C8 was no longer detectable, but the sample still contained trace amounts of the two predicted metabolites.

2.3. Cannabis product analysis

The reportedly ingested product was purchased from the same convenience store 85 days after the patient was admitted to the ICU. The product was produced by Sense Organics ApS and labeled "Bubba Kush - Super Hash" and the packaging stated the content to be 15 % CBD and 30 % THC-S. According to the company's website THC-S is a Danish translation of tetrahydrocannabinol acid (THCA), the natural precursor to Δ^9-THC. Both CBD and THCA were not scheduled as narcotics in Denmark at the time of publication. The product was formulated as hashish and contained 2.0 g of material. Photos of the purchased product are shown in Fig. 3.

Qualitative analysis of the cannabis product by gas chromatography-mass spectrometry (GC-MS) revealed the primary components to be HHC-C8 and phytocannabinoids cannabinol (CBN), cannabigerol (CBG) and CBD (Fig. S6). The product did not contain Δ^9-THC or THCA in significant amounts. HHC-C8 was not scheduled as a narcotic in Denmark at the time of purchase. Concentrations determined by quantification with liquid chromatography-mass spectrometry (LC-MS) of cannabinoids are shown in Table 2.

3. Case 2

3.1. Case report

In August of 2024, a Caucasian female in her thirties presented to the Emergency Department (ED) following an extended period of sleep lasting approximately 14 hours, during which she exhibited a somnolent state and responded minimally to verbal stimuli.

Admission day 1: Upon arrival at the ED, a urine toxicology screen which tests for 12 types of drugs was conducted (NanoSticka®, Ferle, Sweden). The only positive result was for THC/Cannabis, with a detection threshold of 50 ng/mL.

At the time of admission, the patient was hemodynamically stable and did not require respiratory support. The GCS was between 11 and 13. The patient showed a brief response to pain stimulation by opening her eyes. The pupils were equally dilated, and she had spontaneous movements of her extremities. To prevent urinary retention, urinary catheterization was performed, and the patient was intravenously supplemented with a solution of isotonic sodium chloride.

Table 1.
Results from quantification of cannabinoids in whole blood of Case 1. Sample A was taken at the time of admission, while sample B was taken a week after admission.

Compound	Blood concentration (ng/mL)	
	Sample A	Sample B
HHC-C8	71	<LLOQ
11-OH-HHC-C8 *	25	0.6
11-nor−9-COOH-HHC-C8 *	6.6	0.6
HHCP	0.5	N.D.

<LLOQ: Below lower limit of quantification. N.D.: Not detected.
*Semi-quantitative results (see Supplementary Material for details).

Fig. 3. Packaging and content of cannabis product from Case 1. The product was marketed as a souvenir and collector's item and as not intended for human consumption.

Table 2
Results from quantification of cannabinoids in the cannabis product from Case 1.

Compound	Concentration (% w/w)
HHC-C8	6 %
HHCP	0.09 %
Δ^9-THC	0.2 %
CBD	1.5 %
CBN	22 %

Laboratory investigations revealed a mild leukocytosis (11.2 $\times 10^9$/L), a modest elevation in alanine aminotransferase at 76 U/L, and a minor increase in myoglobin (168 μg/L). Tests for ethanol, paracetamol and salicylate were negative.

The neurological examination was unremarkable, and in the absence of a comprehensive patient history, a CT scan of the brain was performed to rule out any gross intracranial pathology. The non-contrast CT showed no abnormalities.

Admission day 2: The patient was able to provide incoherent verbal responses in a somnolent state but did not open her eyes to verbal stimuli. The patient's condition remained unchanged for another 24 hours, with only minor signs of increased awareness.

Admission day 3: The patient became more alert with a GCS score of 13–14. She removed the urinary catheter, requested food, and dressed independently. Later that day, the patient was discharged, after having slept in the ED for approximately 55 hours. At the time of discharge, the patient remained in a mildly somnolent state, exhibiting slurred speech, decreased responsiveness, lack of initiative, as well as sleeping intermittently during conversation. At this point, the patient had been asleep for approximately 72 hours including the time before admission but not accounting for any additional sleep after discharge.

The patient's vital parameters were stable during the admission, with a blood pressure fluctuating between 106/62 and 158/103 mmHg from day to day. However, the heart rate progressively decreased from 115 bpm at the time of admission to 64 bpm at discharge. The respiratory rate remained consistent, ranging from 14 to 16 breaths per minute. No fever was recorded.

During the admission, the patient's partner handed over two bags of cannabis products to ED-personnel labelled "Mango Hash" and "Luksus Slasker". The partner had found the bags in their home and had discovered evidence suggesting that the cannabis products were purchased online as "potpourri".

Prior to discharge, the patient reported consuming less than a gram of the product labeled "Mango Hash" orally.

Blood and urine obtained from the patient about 40 hours after consumption, along with the reportedly ingested cannabis product, were analyzed to confirm and trace the origin of the intoxication.

3.2. Toxicological analysis

A blood and urine sample were secured from Case 2. The blood sample was taken the day after admission, approximately 40 hours after the reported ingestion of the cannabis product and shipped to the laboratory the same day. The urine sample was taken the day after admission.

A broad toxicological screening with subsequent quantification of relevant drugs was performed on both the blood and urine sample. The blood sample was found to contain two putative metabolites of HHC-C8 (Fig. 1 and Figs. S2–3) as well as low concentrations of H4-CBD (Fig. S5) and the major metabolite of Δ^9-THC, 11-nor-9-COOH-THC (see Table 3). HHC-C8 and HHCP were detected in blood but were below the lower limit of quantification (LLOQ) of 0.53 ng/mL (Fig. S1 and S4). The deconjugated urine sample confirmed the findings in blood and additionally contained trace amounts of Δ^9-THC. The major hydroxylated metabolite of Δ^9-THC, 11-hydroxy-tetrahydrocannabinol (11-OH-THC), was not detected in either blood or urine. The only other toxicological finding was lidocaine.

3.3. Cannabis product analysis

Two cannabis products were obtained from the patient's partner and the reportedly ingested product was investigated. The product was labeled "Mango Hash" and was produced by NordicWeed. The product was formulated as hashish and contained 5.4 g of material. Photos of the cannabis product are shown in Fig. 4.

Qualitative analysis of the cannabis product by GC-MS revealed the primary components to be HHC-C8, CBN, CBG, CBD (Fig. S7). Concentrations determined by quantification of cannabinoids with LC-MS are shown in Table 4. The product did not contain Δ^9-THC or THCA in significant amounts. HHC-C8 was not scheduled as a narcotic in Denmark at the time of purchase.

4. Discussion

The present paper describes two cases of intoxication with HHC-C8 confirmed by detection in biological samples and cannabis products. At the time of writing there was no scientific literature on HHC-C8, so interpretation of the intoxications was based on knowledge from similar compounds, such as THC-C8, THCP and HHCP, as well as the primary psychoactive phytocannabinoid Δ^9-THC.

The patient in Case 1 presented with more severe symptoms including prolonged unconsciousness and recurring seizures, which required intubation and sedation. HHC-C8 was measured at 71 ng/mL in the blood sample taken at admission with no other detected drugs explaining the clinical symptoms. Intake of HHC-C8 was further supported by the detection of two putative metabolites of the compound. In the reportedly ingested cannabis product, HHC-C8 was determined to be

Table 3
Results from quantification of cannabinoids in whole blood and urine from Case 2. Both samples were taken approximately 40 hours after reported ingestion.

Compound	Blood concentration (ng/mL)	Urine concentration (ng/mL)
HHC-C8	<LLOQ	<LLOQ
11-OH-HHC-C8 *	5.9	1.1
11-nor−9-COOH-HHC-C8 *	11	1.7
HHCP	<LLOQ	N.D.
H4-CBD	0.95	3.8
Δ^9-THC	N.D.	0.7
11-nor−9-COOH-THC	1.8	115

<LLOQ: Below lower limit of quantification. N.D.: Not detected.
*Semi-quantitative results (see Supplementary Material for details).

Fig. 4. Packaging and content of cannabis product from Case 2. The product was marketed as potpourri and collector's item and as not intended for human consumption.

Table 4
Results from quantification of cannabinoids in the cannabis product from Case 2.

Compound	Concentration (% w/w)
HHC-C8	7 %
HHCP	0.1 %
Δ^9-THC	0.16 %
CBD	1.4 %
CBN	23 %

the primary psychoactive component at a concentration of 6 % w/w. It should be noted that the analyzed cannabis product was of the same type and purchased at the same store as the ingested product, but it is unknown whether the two products are from the same batch. The product was reportedly administered orally, at an unknown amount. The only available package size at the convenience store 85 days later was 2 g. An estimated maximal dose of HHC-C8 would be 120 mg, in the case that the patient ingested the entire package content of 2 g. It is however likely that the actual dose was somewhat smaller. In comparison, oral doses of Δ^9-THC are commonly in the range of 5–20 mg, while doses $\geq$ 30 mg are considered high [14].

For the patient in Case 2, the symptoms were less severe and can be described as prolonged somnolence and sedation. Unfortunately, the earliest blood sample available for toxicological analysis was taken approximately 40 hours after reported ingestion. HHC-C8 was detected below the LLOQ but the two putative metabolites, 11-nor-9-COOH-HHC-C8 and 11-OH-HHC-C8, were estimated at 11 and 5.9 ng/mL, respectively. The patient reported to only have ingested Product A. The package was labeled to contain 5.9 g of the product while the remaining content was measured to be 5.4 g. Assuming the stated package amount was correct, an amount of 500 mg product was ingested by the patient resulting in an HHC-C8 dose of 35 mg.

In Case 2, the SSC H4-CBD was also detected in both the blood and urine sample at 0.95 and 3.8 ng/mL, respectively. H4-CBD is a reduced form of the non-psychoactive phytocannabinoid CBD. Although, little is known about the pharmacological effects of H4-CBD, receptor studies have found H4-CBD to lack potential for activation of the CB1-receptor, but instead possess CB2-receptor agonism [6]. Considering that the psychoactive effects of cannabinoids are mediated through the CB1-receptor and that CB2 primarily is expressed in immunological tissues [15], it is unlikely that H4-CBD contributed significantly to the intoxicated state. Interestingly, the source of H4-CBD was not identified as the compound was not detected in the two analyzed cannabis products. It is thus likely that another cannabis product was ingested in the days leading up to the hospitalization.

In Case 2, the major metabolite of Δ^9-THC, 11-nor-9-COOH-THC, was detected at a concentration of 1.8 ng/mL in the blood sample, as well as in urine at 115 ng/mL, while Δ^9-THC itself was detected only in urine at 0.7 ng/mL. This indicates exposure to Δ^9-THC at some point prior to hospitalization. As the detection windows for Δ^9-THC and 11-nor-9-COOH-THC in urine are several days and even as high as weeks for chronic users [16], the exposure was not necessarily recent. Δ^9-THC and its metabolites were not detected in samples from Case 1.

For THC-C8, both the Δ^8- and Δ^9-variants were investigated for CB1-receptor activation by Janssens et al. [6]. They determined efficacy (E_{max}) values of 297 and 156 % relative to Δ^9-THC, for Δ^8- and Δ^9-THC-C8, respectively. They also studied HHCP and found E_{max} values of 231 and 301 % relative to Δ^9-THC, for the 9*R*- and 9*S*-epimers of the drug. Martin et al. investigated Δ^8-THC-C8 and found increased receptor affinities as well as greater potency in terms of ED_{50} in pharmacological assays in mice [9]. Compared to Δ^8-THC, they found Δ^8-THC-C8 to have 5-fold greater receptor affinity and 10- to 20-fold greater potency. The available in vitro data thus indicates a potential for a higher CB1-mediated maximal response and potency of these compounds compared to Δ^9-THC.

Another aspect is pharmacokinetics. A longer side chain length relative to Δ^9-THC leads to increased lipophilicity, which may affect absorption and distribution in various ways. Δ^9-THC itself is a lipophilic compound with a LogP value of 6.97 [17] and is known to accumulate in tissues [16]. This is evident by Δ^9-THC and its metabolites having detection windows in urine of several weeks after repeated intake [16]. This effect may in part contribute to the apparent sustained pharmacological effects of SSCs containing *n*-heptyl and *n*-octyl side chains relative to Δ^9-THC, especially considering two putative metabolites of HHC-C8 were still detectable in the blood 1 week after ingestion of the drug in Case 1 after a presumed single dose.

For Δ^9-THC, serious adverse effects are rare, but there have been case reports describing serious toxicity after consumption of larger amounts or intake of highly concentrated preparations. There have been several studies presenting cannabis intoxications especially accidental ingestion of cannabis edibles in the pediatric population after the decriminalization of cannabis in many parts of the US [18–21]. At least two cases have described coma after ingestion of Δ^9-THC. In 1977, a 19-year-old man was found comatose and with muscular rigidity after smoking a product alleged to contain Δ^9-THC and complete recovery was not achieved until 4 days after admission [22]. In a separate case, a 14 month old child was comatose for more than 48 hours after ingestion of an estimated 2 g hashish [23]. Thus, there are some indications that Δ^9-THC may trigger similar toxic states at high doses in susceptible individuals but considering the wide-spread human consumption of traditional cannabis over several millennia, the prevalence of such severe toxic reactions is low.

Case reports involving HHCP, THCP and THC-C8 indicate prolonged pharmacological effects as well as increased severity of the toxidrome relative to Δ^9-THC [10–12]. The symptomatology in the present cases is comparable with published cases of similar cannabinoids describing symptoms such as seizures, sedation and unconsciousness.

SSCs are currently widely available in many European countries and the products are often, as in the two present cases, mislabeled to contain only natural cannabinoids. This can easily result in the public regarding the products as relatively safe legal highs, while in reality they can contain quite high doses of SSCs leading to severe intoxications that require hospitalization.

Certain SSCs have been criminalized in many European countries. For instance, in Denmark, HHC was the first compound to be banned in May 2023 [24], while HHCP, THCP and H4-CBD were scheduled in January 2024 [25]. In September 2024, a new general legislation was introduced in Denmark banning all cannabinoids with a similar structure to Δ^9-THC but with a variable position or absence of the double bond in the cyclohexene ring and any side chain configuration at the C3 carbon using the dibenzopyran numbering system, thus including THC-C8 and HHC-C8 [26].

5. Conclusion

Two case reports involving intoxications after consumption of the novel SSC, HHC-C8, were described. In Case 1, an oral dose of possibly as high as 120 mg HHC-C8 was ingested which resulted in severe toxicity including recurring seizures and coma. A slow gradual recovery was achieved over more than two weeks. In Case 2, consumption of an oral dose of approximately 35 mg HHC-C8 resulted in pronounced somnolence and sedation with recovery over 72 hours. The case descriptions are consistent with previous reported intoxications with related compounds such as HHCP, THCP and THC-C8. The widespread availability and perceived safety of cannabis products containing SSCs present a challenge for public health.

CRediT authorship contribution statement

Lisa Maria Gemmerli Krogh: Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Nicoline Løkken:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Brian Schou Rasmussen:** Conceptualization, Investigation, Methodology, Writing – review & editing. **Nanna Reiter:** Conceptualization, Investigation, Methodology, Writing – review & editing. **Ragnar Thomsen:** Conceptualization, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. **Tobias Melton Axelsen:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Emilie Lund Laursen:** Conceptualization, Investigation, Methodology, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.toxrep.2025.101912.

Data availability

The data underlying this article cannot be shared publicly for the privacy of individuals reported in the study. Parts of the data may be shared on reasonable request to the corresponding author.

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