First case report of recreational use of diphenyl-2-pyrrolidinemethanol (D2PM)

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INTRODUCTION

Case report

A 21 year old male with no significant past medical history, presented following ingestion of three tablets of 'Head Candy' purchased in a local high street shop. He was a regular user of 'herbal highs'. After ingestion, he felt mildly euphoric for several hours, but as the effects were wearing off he had two 'sniffs' of "poppers" (usually n-butyl nitrite, iso-butyl nitrite or a mixture of the two). Approximately one hour later he became dizzy and developed ischaemic sounding chest discomfort and a feeling of heaviness in the right arm, which lasted for 1 hour. He attended the Emergency Department (ED) approximately 2 hours after the chest discomfort had resolved.

On arrival in the ED, he was agitated with a heart rate of 126 bpm and blood pressure of 213/109 mmHg. He was apyrexial and had unassisted oxygen saturations of 100%. His pupils were dilated but reactive to light; the remainder of his neurological examination was normal. His admission electrocardiogram (ECG) showed a sinus tachycardia, with normal QRS and QTc duration. Biochemical, haematological and arterial blood gas investigations were normal on admission.

He was treated with benzodiazepines for both his agitation and hypertension. His methaemoglobin concentration was measured and found to be normal (0.5%). He was admitted for overnight observation and treated with a total of 20mg of oral diazepam. His symptoms, agitation and hypertension settled with this management and he was discharged asymptomatic the following morning.

Figure 1. Head Candy, BZP Free, Herbal High 'Party Pill' containing Glaucine and D2PM. *TICTAC Communications Ltd*

TOXICOLOGICAL SCREENING

Informed consent was obtained from the patient for toxicological analysis of samples collected on admission; these were sent to the Analytical Unit at St George's, University of London, UK. Routine qualitative analysis of the blood and urine specimens, using full scan electron impact ionisation (EI) gas chromatography–mass spectrometry (GC-MS), after liquid-liquid extraction, identified the presence of diphenylprolinol (diphenyl-2-pyrrolidinemethanol (D2PM)) and glaucine. Blood concentrations were estimated at 0.17mg/L and 0.10mg/L respectively, using single ion monitoring (SIM). No other drugs or alcohol were detected using a broad toxicology screen of both the blood and urine samples.

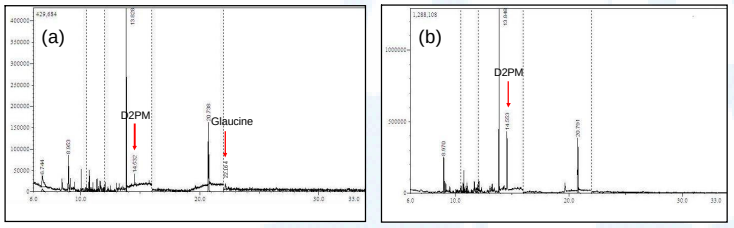

Figure 2. The results of full scan GC-MS analysis of blood (a) and (b) urine.

EXPERIMENTAL

Materials

D2PM (S isomer) was obtained from Sigma-Aldrich (368199) (Poole, Dorset, England). Due to the unavailability of a pure reference standard, glaucine (Glauvent) was obtained in tablet formation (40mg) from Sopharma, Bulgaria. The measured concentration should therefore only be considered an approximation. SKF525A and flurazepam, obtained from Sigma-Aldrich (Poole, Dorset, England), were used as internal standards. Sodium hydroxide (40% solution) and phosphoric acid were also obtained from BDH. HPLC grade methyl-*tert*-butyl-ether (MTBE) was purchased from Rathburn Chemicals Limited (Walkerburn, Scotland).

Sample preparation

The sample and calibrators (100µL) were prepared using liquid-liquid extraction. They were adjusted to an alkaline pH with 1M sodium hydroxide (250µL), after the addition of 100µL of the internal standards SKF525A and flurazepam. The solution was extracted with 4mL MTBE. Following centrifugation the organic layer was transferred to 0.1M phosphoric acid (250µL) and mixed. After phase separation by centrifugation the organic layer was removed to waste.

1M sodium hydroxide (100µL) and MTBE (200µL) were added to the remaining subnatent. The samples were then vortex mixed (30 seconds) and centrifuged. An aliquot of the supernatant was injected onto the GC-MS system.

Gas chromatography-mass spectrometry

GC-MS analysis was performed using a Shimadzu GC-MS-QP2010 with a Shimadzu AOC-20i autosampler. An HP-5 MS (30m x 0.25mm, 0.5µm; 5%-Phenyl)-methylpolysiloxane) analytical column (Agilent, Palo Alto, California), was employed for separation. Helium was used as the carrier gas at a flow rate of 1mL per minute.

The injection volume was 1.0µL and injections were made in splitless mode. The injector was maintained at 225°C and the detector at 200°C. The initial column temperature was set at 150°C and held for 4 minutes. It was then ramped by 30°C/min up to 290°C and held for 9.33 minutes, giving a total run time of 18 minutes. Positive EI mode was used and data were collected using SIM. D2PM and SKF525A and glaucine and flurazepam were quantified monitoring their most abundant ion *m/z*: 70 and 86 and 354 and 86 respectively. Their retention times were 9.43, 10.36, 15.52 and 14.21 minutes.

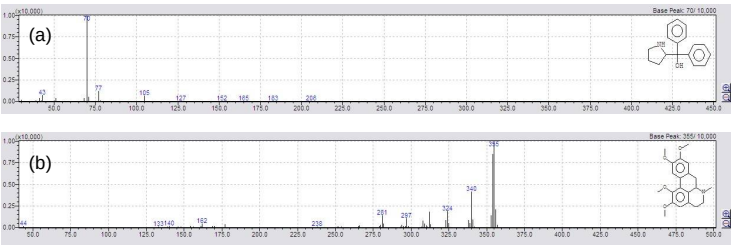

Figure 3. NIST Library ion spectra for (a) D2PM and (b) glaucine.

DISCUSSION

We have described the case of an individual who developed chest pain and sympathomimetic toxicity following ingestion of legally purchased 'Head Candy'. Toxicological analysis demonstrated that he had ingested both D2PM and glaucine. Glaucine has been reported to cause dissociative-type symptoms both with therapeutic and recreational use. Previous reports of glaucine toxicity do not describe sympathomimetic features.

Methods for the syntheses of D2PM are freely available on the internet. It is structurally similar to pipradrol, a drug initially developed to treat obesity, but due to its CNS stimulant properties and abuse potential has largely been removed from the market and controlled under drug legislation since the 1970s. Both isomers of D2PM have been shown to have activity at the cocaine binding site on the dopamine transporter protein.

In a user report of D2PM, published on a recreational drug website, an individual ingested 25mg, followed by a further 20mg 6 hours later. Within 2 hours of ingestion they describe a euphoria similar to that seen with amphetamines, with associated jaw clenching, babbling speach and dilated pupils; the user denied the presence of any 'heart rushes' during D2PM use. There has been a recent media report in the non-medical press of an individual who, following ingestion of 'Neuroblast' purchased from "London Underground" (an internet based website selling legally available recreational drugs), developed 'a surge of adrenaline into my heart', hypertension and difficulty breathing. The newspaper article noted that subsequent toxicological analysis of the pills showed that they contained D2PM (referred to a 'diphenyl prolinol).

Extensive toxicological screening did not demonstrate the presence of any other drugs that could have contributed to our patient's symptoms. Although the patient reported inhaling a small amount of a volatile nitrite prior to developing his symptoms, we do not feel that this was a significant cause of his symptoms as there was no evidence of methaemoglobinaemia.

A more systematic approach to toxicological screening in patients with recreational drug toxicity is required to identify novel or emerging drugs, but also to provide a more systematic means of monitoring trends and providing evidence for legislative authorities.

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