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CASE REPORT

“Synthacaines”: A mosaic of substances for a wide range of effects, from a case

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N-methyl-2-amino-indane

Summary In recent years, a class of new designer drugs commercialized under the generic name of “Synthacaines” have been available both to the surfacweb and the illicit drug market or deep web. We report the case of a 30-year-old man admitted to the psychiatry department for acute anxiety crisis with paranoid experiences associated with dysmorphophobia, who followed one week of intensive use of “synthacaine” he bought on the web. Toxicological analysis of the powder consumed by the patient allowed to identifying a mixture of 4 different drugs: 2-aminoindane, N-methyl-2-amino-indane, methiopropamine and lidocaine.

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Case description

In recent years, a class of new designer drugs commercialized under the generic name of “Synthacaines” have been available to the illicit drug market or deep web. “Synthacaine” is the contraction of 2 words “synthetic” and “cocaine”, its name suggests to the consumer this is

“legal cocaine” developed to mimic the cocaine effect. It is sold both on surface and dark web with a price 3 to 4 lower than cocaine (from “what illegal drug cost on the dark web consulted on qz.com”).

We report the case of a 30-year-old man admitted to the psychiatry department for acute anxiety crisis accompanied by a sense of imminent danger, impending death and an urge to escape. When he arrived, the patient has been complaining of intense fatigue because he didn’t sleep since one week and he had visual hallucinations, like dysmorphophobia responsible for self-harming acts. The patient had

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the sensation that his body changed, seeing, for example, his arm turned to evil animals he had to destroy. Effectively, the patient had voluntarily burned himself on repeated occasion during the last week before his admission.

The patient said he took a new drug named "synthacaine" he bought on the dark web. The patient could not describe precisely the frequency of his consumption; neither the dose, but he always used the nasal passage. This patient had no medical history before this episode. He was a regular and extensive consumer of numerous stimulant drugs like amphetamines, cocaine and large amount of various drugs bought on the dark web. He doesn't have any mental disease, except short and regressive paranoia with cocaine consumption.

Unfortunately, no biologic samples were available to be analysed, but the patient family allowed us to analyse the substance used.

Material and methods

The Fig. 1 represents the batch of "synthacaine" we have analysed. A first black opaque zipped pocket indicate "research used only", "not human consumption, keep away from children and animals" and all the common Hazardous Substances Information System (HSIS) mentions describing a safe content. A second transparent zipped pocket contain a white/beige colour powder, with the following particulars: "synthacaine" and HSIS phrase, different than the black pocket:

- harmful if swallowed (H302);
- harmful if inhaled (H332);
- keep out of reach of children (P102);
- avoid breathing dust (P261).

Because of few scientific data available concerning "synthacaine", various analytics methods were used to identify the active compounds; 1 mg/mL of synthacaine aqueous solutions were used for all the method's investigation. Immunoassays used for urine testing were used as a first screening to clarify the situation. A solution of "synthacaine" was analysed with liquid chromatography technique coupled with tandem mass spectrometry (LC-MS/MS): a 10 mg/L solution was infused and analysed by General Unknown Screening method (GUS method). A 100 mg/L and 1000 mg/L of aqueous solution of synthacaine were infused both in Gas Chromatography with Mass Spectrometry detection (GC-MS) and Ultra Performance liquid chromatography technique coupled with Diode Array Detector.

Results and discussion

The results obtained by immunoassays methods were synthesised in Table 1. Briefly only amphetamine family was positive by immunoassay technic: amphetamine, ecstasy and methamphetamine were detected in the white powder after aqueous dissolution.

Fig. 2 represents the results obtained by chromatography. These methods allow us to specify the nature of the chemical compounds present in the powder: 2-amino-indane

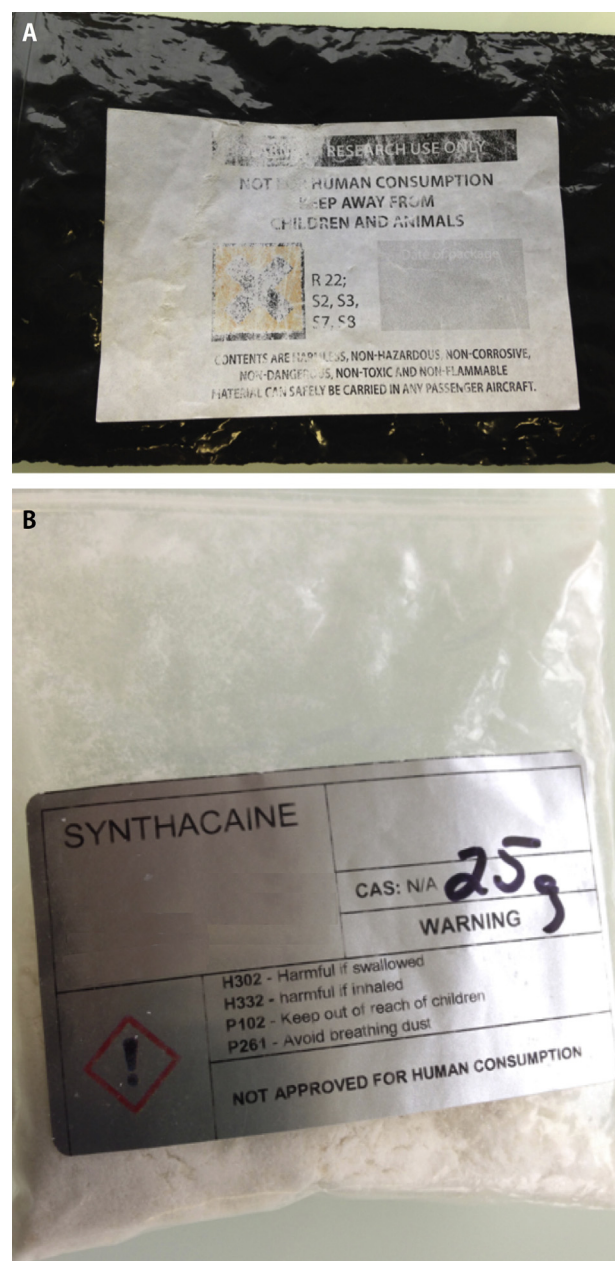


Figure 1. Pictures of the synthacaine analysed, the opaque pocket (A) contained the transparent one with the synthacaine powder (B).

(2AI), N-methyl-2-amino-indane (NM2AI), methiopropamine (MPA) and lidocaine were found with GC-MS, UPLC-DAD and LC-MS/MS methods screening. Chemicals structures of the 4 molecules are represented in Fig. 3.

The real unknown concerning "synthacaine" is the nature of its composition. As we write this column, only 4 publications mentioning the term synthacaine have been identified in Pubmed database [1–4]. The few data available forced us to look for unconventional ways, including the Internet database and consumer's social network.

The composition of "synthacaine" revealed by consumer's forum indicates that synthacaine is known to be a mixture: "...legal substitute of cocaine...", "...dimethocaine-like drug mixture...", "Official name of

Table 1 Immunoassays detection of the drug tested, cut-off, the method used, and results obtained with a 1 mg/L solution of synthacaine.

Drug (target drug)	“Synthacaine” Result	Cut-off (ng/mL)	Method
Cocaine (BEG)	Negative	300	EMIT (Xpand Siemens)
Opioids (morphine)	Negative	300	EMIT (Xpand Siemens)
Benzodiazepin (normetazepam)	Negative	200	EMIT (Xpand Siemens)
Barbiturate (secobarbital)	Negative	200	EMIT (Xpand Siemens)
Cannabis (THC)	Negative	50	EMIT (Xpand Siemens)
Methadone	Negative	300	EMIT (Xpand Siemens)
Amphetamine	Positive	1000	EMIT (Xpand Siemens)
Methamphetamine	Positive	1000	Immunochemistry (Narcocheck)
MDMA	Positive	1000	Immunochemistry (Narcocheck)
Buprenorphine	Negative	10	Immunochemistry (Narcocheck)
Fentanyl	Negative	10	Immunochemistry (Narcocheck)
Tramadol	Negative	10	Immunochemistry (Narcocheck)

BEG: Benzoylcegonine; THC: tetrahydrocannabinol; EMIT: enzyme-multiplied immunoassay technique.

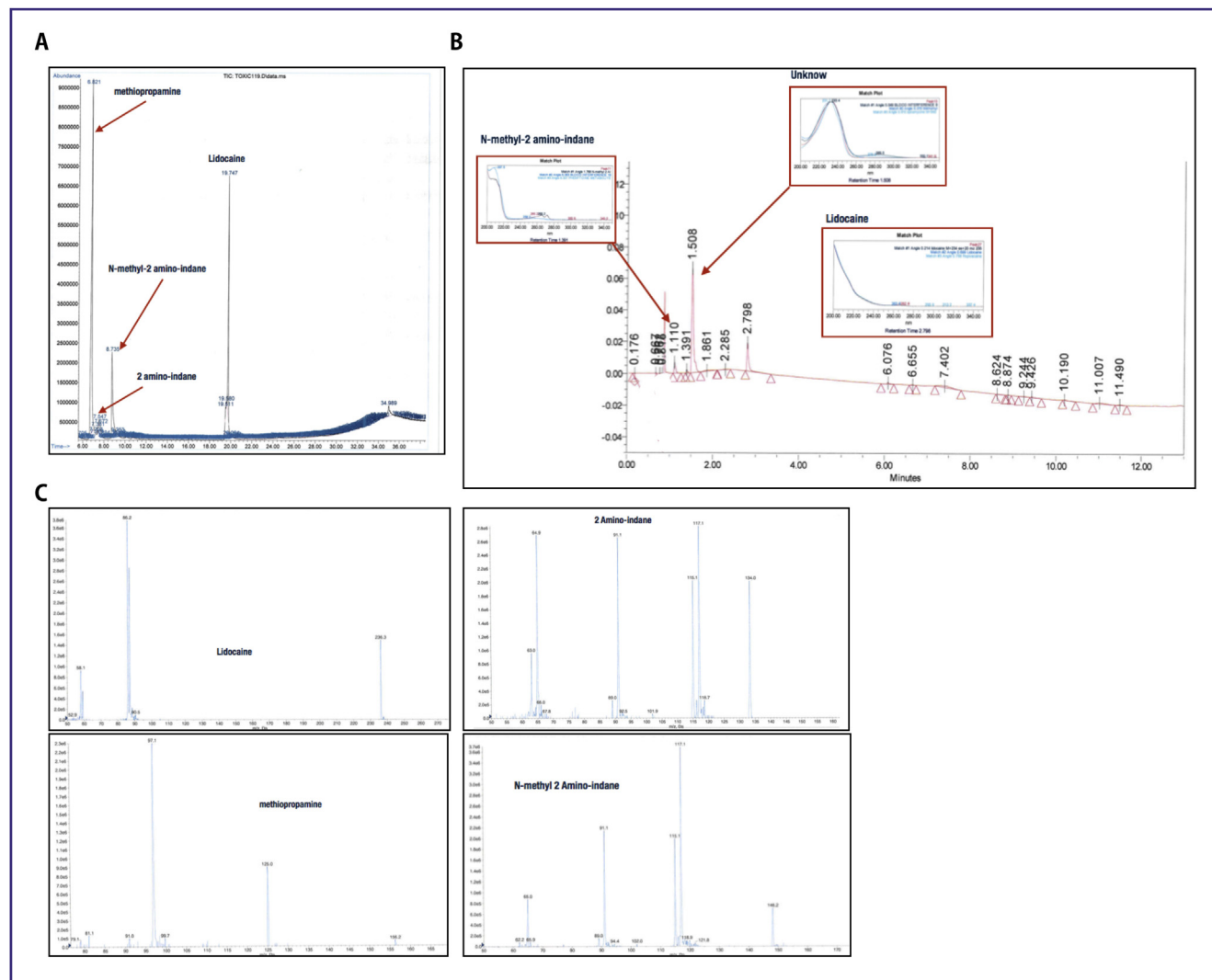


Figure 2. Chromatographic results. A: chromatogram obtained after infusion of aqueous solution in gas chromatography with mass spectrometry detection; B: chromatogram obtained after infusion of aqueous solution in an Ultra Performance liquid chromatography technique coupled with Diode Array Detector; C: chromatogram obtained after infusion of aqueous solution in a high performance liquid chromatography coupled with tandem mass spectrometry.

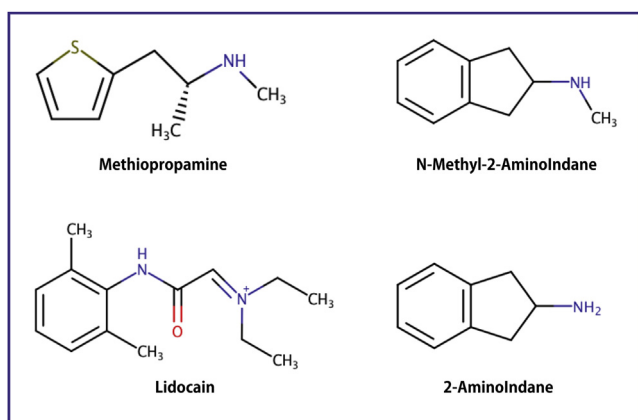


Figure 3. Chemical structures of the four compounds identified in the synthacaine powder analysed.

equal preparation of dimethocain and camfetamine...”, "...secret-recipe...”, “There are all different...”, “...a mixture of methiopropamine/benzocaine or lidocain and sometime 2-aminoindane...”, “...MPA + b-stock of research clinical...” (extracted from psychoactive.fr).

According to the sellers on the surfacweb: “Synthacaine is actually a sophisticated mixture of several chemicals with complimentary chemical properties”, “The recently banned product of MPA has now been replaced with the very popular 3-FPM” ...so instead of dimethocaine and other similar chemicals used by some vendors, we use our own blend of “-caine” (extracted from euechemicals.com).

According to scientific research in 2016, a French team described an acute intoxication with methiopropamine, in 2015; Cumba et al. published identification of a synthacaine’s batch containing a mixture of methiopropamine and 2-aminoindane, whereas in 2014, Lonati et al. published a surprising synthacaine batch containing a synthetic cannabinoids MAM-2201 [2–4]. The specialised Welsh Emerging Drugs and Identification of Novel Substance published via its website the composition of various batch of synthacaine they have analysed; the main compounds that were found were lidocaine, procaine and methiopropamine (extracted from wedinos.org). The main associations were a local anaesthetic (lidocaine or procaine) + methiopropamine occasionally associated with 2-aminoindane [5].

Conclusion

“Synthacaines” are a new marketed class of psychoactive substance, developed to mimic the cocaine effect. “Synthacaines” are sold on specialised website as “legal cocaine” and are available for a price approximately 4 times lower than cocaine. “Synthacaines” are always a combination of substance in which precise molecules compositions varied from seller to other. They usually contain an association of local anaesthetic and amphetamine-like molecules [5]. The effect varies from one consumer to another, but this pharmacologic variability is probably more the consequence of the composition’s difference than a real inter-individual variability. In our case, 3 psychoactive molecules were identified. Considering the MPA, users report similar effects to other stimulants such as MDMA (ecstasy), amphetamine and

cocaine: stimulation, alertness and an increase of energy and focus; with adverse effects reported by users including tachycardia, anxiety, panic attacks, sweating, headaches, nausea, difficulty breathing, vomiting, difficulty urinating and sexual dysfunction. Because of an amphetamine-like core structure, 2AI and NMAI are expected to interact with the norepinephrine, dopamine, and serotonin pathway as with their respective transporters by blocking or releasing monoamines[6,7]. Based on their higher potencies at serotonin transporter than dopamine transporter, 2AI and NM2AI derivative could be more empathogen psychoactivity, than they have potential for abuse and addiction [8,9].

For the aminoindane derivatives, it seems that the drug’s overall behavioural profile would be related to its serotonergic effects, because of their empathogenic and entactogenic effects. MDAI induce serotonin release mainly via serotonin transporter inhibition [9]. Lidocaine is not a NPS but a local anaesthetic. Lidocaine, as other substance like sugar, caffeine, phenacetine, levamisole, is frequently used to cut or adulterate illicit drug [10]. Nevertheless, medical use of lidocaine show that the addition of lidocaine appeared to reduce the discomfort of intranasal unpleasant and painful citrate solution in adult volunteers [11]. Moreover, lidocaine is equally used to enhance or mimic the effects of illicit drugs [10].

The few trip reports available on the consumer forum and self-reported effect available on Wedinos indicate stimulating, significant energy, increased confidence, increased senses, increased stamina, increased libido effect but seem equally to be entactogenic and empathogenic substances (extracted from wedinos.org). Hallucinations caused by the “synthacaine” mixture used by our patient were a rare example of bad trip, one of the first described at this time.

Disclosure of interest

The authors declare that they have no competing interest.

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