

Para-methylthioamphetamine, a new amphetamine designer drug of abuse

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Keywords

Ecstasy

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Abstract

A case study is described of a patient who was intoxicated after the intake of so-called herbal stimulants. A visit to a physician after the intoxication prompted to this investigation and the case was examined for its direct cause. An interview with the patient revealed that the source of the herbal stimulants was a so-called 'S-5 tablet'. Information provided on the packings of the tablet only indicated the presence of natural alkaloids and vitamins. Toxicological analysis however proved that the 'S-5 tablet' contained *para*-methylthioamphetamine (MTA), mainly. MTA is a relative unknown amphetamine designer drug, which has only been studied as a model compound in some structure-activity relationship studies. The fact that MTA appeared in tablets was therefore completely unexpected. Not only the potential abuse of this new amphetamine designer drug is a serious matter of concern, but also the misleading information provided with the tablet.

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In the Netherlands the marketing of herbal stimulants in so-called smart-drug shops is common practice. In principle these herbal stimulants are natural alkaloids which are not scheduled under the national Drug Acts. The sale of these stimulants is therefore legal. The intake of formulations containing these compounds is considered not to be dangerous for the health of a subject. Some of these formulations claim to produce Ecstasy-like effects and are marketed for persons who visit for example 'dance rave', 'techno', or 'acid-house parties'. An example of such a formulation is sold under the name of 'Herbal XTC'. It contains ephedrine and *pseudo*-ephedrine as pharmacological active compounds.

Here we report the case study of a 22 years old male who was intoxicated after the intake of one so-called 'S-5 tablet'. 'S-5 tablets' are sold as a 'smart-drug' formulation, which claims to contain among others herbal stimulants and which after intake should result in a pure Ecstasy feeling. An interview revealed that approximately 1½ h after the intake of one tablet on an 'acid-house party' the victim felt slow and sick. Main symptoms were feeling very warm and oppressed and having palpitations of the heart. After a stay at the First Aid Service of the 'acid-house party', he went home. During a 2 week period he suffered from amnesia and other psychological problems and was not able to perform normal activities. A visit to a physician prompted to this qualitative analytical toxicological investigation.

A 'S-5 tablet' was taken to the laboratory and screening using 2 different immunoassay technologies (Enzyme Multiplied Immunoassay Technique® of Behring Syva and Fluorescence Polarisation Immunoassay of Abbot) indicated the presence of an amphetamine-like compound. GC/MS analysis after trifluoroacetyl derivatisation [1] suggested that the identity corresponded to an unknown amphetamine-like compound and not to one of the classical amphetamines. Careful examination using *N*-trifluoroacetyl-*O*-trimethylsilyl derivatisation [2] finally pointed out that the compound of interest was *para*-methylthioamphetamine (MTA; Figure 1). Synthesis of a reference standard of MTA according to the synthesis of 4-methoxyamphetamine [3] and GC/MS analysis confirmed that MTA was the respective compound present in the 'S-5 tablet'. The purity of the synthesised reference standard was however not sufficient enough to allow correct quantitative examinations. Proton nuclear magnetic resonance spectroscopy and mass spectrometry studies proved that the purity did permit qualitative analysis. Besides MTA, the 'S-5 tablet' also contained caffeine.

Additional 'S-5 tablets' were obtained from the market. Two batches were found in slightly different packings. The provided information on the packings suggested two different compositions (Table 1). In contrast to the declared contents, both batches contained MTA as the main pharmacological compound of which the quantitative analysis is still in progress. The warnings on the packings were not in agreement with the declared contents (Table 1). Therefore, it can be concluded that the declared information is misleading and that the 'S-5 tablet' contains an amphetamine designer drug in an unknown quantity.

The medical and toxicological information regarding MTA is scarce, if available at all. MTA has only been studied a model compound in some structure-activity relationship studies. It has been proven to be a potent selective serotonin releaser, apparently devoid of serotonin neurotoxic effects [4]. MTA can also increase the secretion of several hormones through stimulation of serotonergic neurotransmission [5]. It has never been reported to be abused or clinically used. In other words it is a new amphetamine designer drug of abuse of which possible health risks are unknown.

The appearance of new amphetamine designer drugs is not an unusual phenomenon. However, up to now, the majority of all the known amphetamine designer drugs has been described on beforehand in the 'Ecstasy bible' PIHKAL [3]. New developments

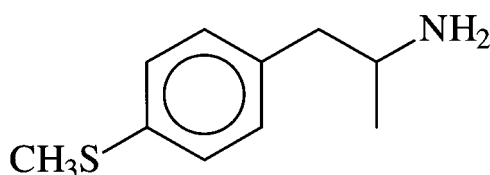


Figure 1
Structure of *para*-methylthioamphetamine (MTA).

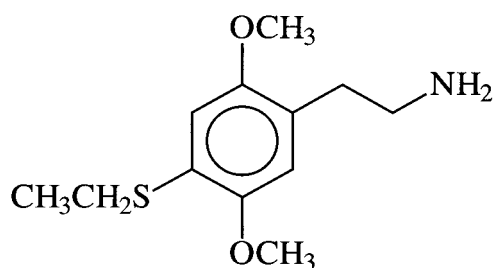
Table 1 Declared information on the packing of 'S-5 tablets'

Batch no.	Ingredients per serving	Warnings on packing
1	104 mg caffeine extract 26 mg Ginko-Bilboa 37 mg Siberian Ginseng vitamin B3, B12 and C	Avoid use if you suffer from glaucoma, renal problems/urinary retention, severe hypertension, coronary renal problems/urinary retention, severe hypertension, coronary heart disease, hyperthyroidism, diabetes, and phenylketonuria or are pregnant/lactating. Do not take stimulants with cardiac medications, monoamine oxidase inhibitor, anti-depressants, narcotics or large quantities of alcohol. Do not take if currently taking medication or suffering illness of any kind.
2	108 mg caffeine 20 mg magnesium stearate 20 mg Avicell 80 mg lactose yohimbe hydrochloride (traces) amino acids	Do not take if: pregnant/lactating or having diabetes, high/low hypertension, depression, psychosis, heart and/or lung complaints. Do not combine it with excessive alcohol consumption, state of mind and/or consciousness changing and/or stimulating drugs.

were in that respect relatively easy to follow and to predict. MTA is in spite of that not described in PIHKAL and the finding of MTA was therefore completely unexpected. The creativity of producers of illicit drugs appears to be more and more difficult to predict and that should be of an increasing concern, especially if the provided information is misleading.

P.S.

After the submission of the manuscript two additional batches of 'S-5 tablets' appeared on the Dutch market. The declared information on the packing of the 3rd batch was almost identical compared to that of the 2nd batch, except that the declared ingredients also mentioned the presence of 20 mg of a synthetic mixture of herbs. The actual ingredient however, was not MTA anymore, but proved to be 4-ethylthio-2,5-dimethoxyphenethylamine (2C-T-2; Figure 2). 2C-T-2 is a compound, of which the use may result in some hallucinogenic effects [3]. In that respect it is probably a different compound than MTA. The 4th batch was sold without any information on the packing and contained MTA again.

**Figure 2**

Structure of

4-ethylthio-2,5-dimethoxyphenethylamine (2C-T-2).

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