

Two cases of confirmed ingestion of the novel designer compounds: 4-methylmethcathinone (Mephedrone) and 3-fluoromethcathinone

¹Analytical Unit and ²TICTAC Communications Ltd, St George's, University of London, UK;
³Guy's & St Thomas' Poisons Unit, London, UK; ⁴Kingston University, Surrey, UK.

Susannah Davies¹, Malgorzata Puchnarewicz¹, Jennifer Button¹, Paul I Dargan³, David M Wood³, Roland Archer³,
John Ramsey², Terry Lee¹ and David W Holt¹

Introduction

Cathinone (Cath) is a pharmacologically active alkaloid (stimulant) extracted from the leaves of the Khat plant (*Catha edulis*)¹. Cath and methcathinone (MC) are controlled under the UK Misuse of Drugs Act (Class C and B respectively). However, derivatives such as ethcathinone (EC), 4-methylmethcathinone (4-MMC or mephedrone) and 3-fluoromethcathinone (3-FMC), which are not controlled under current law, have been produced and marketed to satisfy the drug dance scene culture. The dose, effects and safety of these products have not been evaluated, and are only known from user's discussion forums on drug chat room websites^{2,3}.

Case 2, a 22 year old male, presented after oral ingestion of 200mg of mephedrone and subcutaneous injection of 3.8g of mephedrone. On arrival in the ED he was agitated with 7mm dilated pupils, heart rate 105 per minute and BP 177/111mmHg; these features settled within 6 hours of presentation. Serum and urine from both cases were sent for analysis at St George's - University of London.



Figure 2: Example of powder labelled as and containing 4-MMC found in a drug amnesty bin. Products similar to this can be purchased from Internet websites.

Methods

A screening method was developed for ten methcathinone related compounds (Cath, MC, EC, 4-MMC, 2-FMC, 3-FMC, 4-FMC dimethylcathinone (DMC), 4-methoxymethylaminobutyron (4-MAB) and 4-methoxymethcathinone (4-MoxyMC)). Derivatives of Cath and MC were synthesised in-house as secondary standards by Kingston University. 500µL of urine or serum were extracted by liquid-liquid extraction and screened using gas chromatography with mass-spectrometric detection. Chromatographic separation of all derivatives was achieved over a 12min run. The principle fragment ion for 4-MMC and 3-FMC was *m/z* 58. Confirmation of methcathinone derivatives was performed by acetylation with acetic anhydride. Liquid chromatography with tandem mass spectrometric detection was used to confirm and quantitate 4-MMC and 3-FMC in urine and serum. Quantitative and confirmatory multiple reaction monitoring (MRM)

transitions for 4-MMC and 3-FMC were *m/z*: 178.2/160.1, 145.1, 119.2 and 182.2/164.0, 149.0, 123.0 respectively. Amphetamine D₁₁ was used as an internal standard. An additional compound was seen associated with the standard and urine sample containing 3-FMC. Preliminary investigation by NMR, MS and IR identified 3-fluoroisomethcathinone, a by-product of the synthesis of 3-FMC. Further investigation is required to establish its activity.

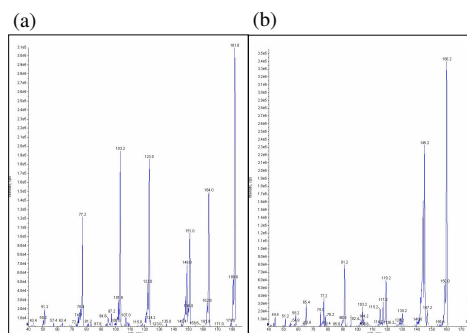


Figure 3: LC/MS/MS parent and product ion scans of (a) 3-FMC and (b) 4-MMC.

Results

Routine toxicological screening showed case 1 to be positive in urine for GBL, cyclizine (administered in ED) and 3-FMC. No drugs were found in the serum. Case 2 was positive for 4-MMC in urine and serum (0.15mg/L), with no other drugs found. No therapeutic or toxic reference ranges are available for 4-MMC and 3-FMC. The cathinone derivatives are not available to purchase as certified reference standards, so quantitative results should be used only as a guide.

References

[1] Manghi, R.A. *et al.* J Psychoactive Drugs. 2009 Mar;41(1):1-10. [2] <http://www.bluelight.ru> Accessed 17Aug09. [3] <http://www.erowid.org> Accessed 17Aug09.

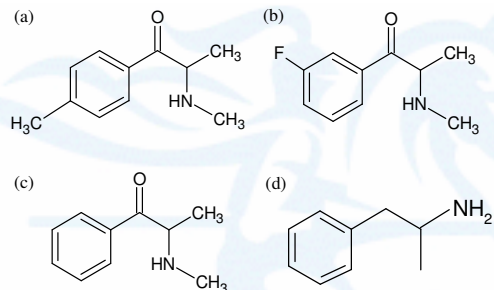


Figure 1: Chemical structures of (a) 4-MMC and (b) 3-FMC, both uncontrolled in the UK. Compared to (c) MC and (d) Amphetamine, currently controlled in the UK.

Cases

Two cases were admitted to an inner-city hospital Emergency Department (ED) on separate days within a 2 week period. Case 1, a 30 year old male, presented with drowsiness (GCS 6/15), respiratory rate 20 per minute, heart rate 47 per minute and BP 140/80mmHg. He was alert and orientated within 2 hours of presentation. He subsequently gave a history of ingestion of 1g of mephedrone, GBL, "neo-doves" and "neo-blues".

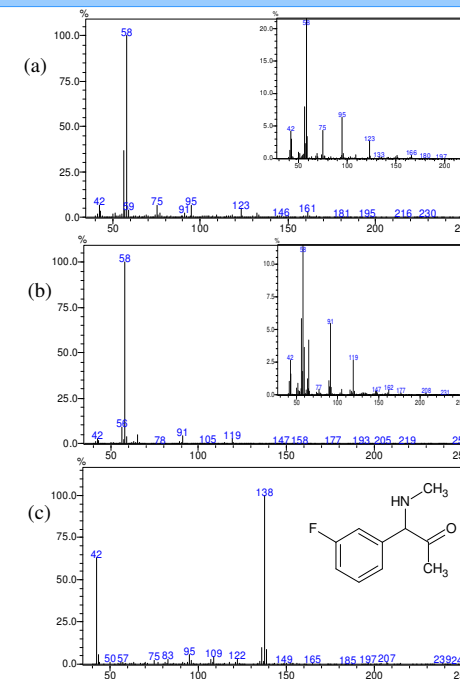


Figure 4: GCMS mass spectra of (a) 3-FMC, (b) 4-MMC and (c) 3-FisoMC, showing the structure of the by-product found with 3-FMC.

Conclusions

The clinical features seen in case 1 were consistent with GBL toxicity, and the 3-FMC was consistent with the history. Case 2 is the first known case of toxicity from lone use of mephedrone. Clinicians and analytical toxicologists should be aware of the potential for use of these compounds in patients presenting with signs of sympathomimetic toxicity.