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Short Communication Open Access

Observations on Methamphetamine Enantiomers

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Abstract

Methamphetamine is a commonly used illegal drug and the use of the d form of methamphetamine (MAMP) can have serious implications for a patient's treatment [1-3]. Thus, correct identification of d methamphetamine is critical when releasing methamphetamine results although most reported positives are the result of illicit use, a small but significant number of MAMP positive findings can be from the use of medications that either contain or can be metabolized to MAMP. Neither common immunoassay screens nor routine mass spectral confirmatory methods can distinguish between the two forms of the drug because both forms have the same elemental composition and only differ in their orientation at the drug's asymmetric carbon [4-7]. Chromatographic chiral analysis which is a separation technique based upon the asymmetric carbon is used to resolve the drug into its enantiomeric forms. Historically, the test to differentiate the enantiomers has been time consuming requiring derivatization of the MAMP and a separate analytical system. The advent of newer chiral columns eliminates the need for derivatization and makes the analytical process simpler to automate [8,9].

Federal workplace drug testing programs have established a threshold of 20% d-MAMP to distinguish between the legal and illegal use. The purpose of this study was to characterize positive MAMP results in the population of our test patients using both the derivatized and non-derivatized analytical procedures. The test population consisted of specimens collected from pain clinics and rehabilitation facilities.

Of the 252,800 specimens tested between 3/28/16 and 2/3/17, we observed 11,264 specimens above our lower limit of quantitation of 50 ng/ml for methamphetamine. The average MAMP concentration was 32,530 ng/mL, while the median concentration was 27,882 ng/mL. There were 198 specimens in with 20% to 60% of the d enantiomer while 142 specimens contained greater than 99% of the l isomer. The average concentration of the d isomer value was 2074 ng/mL. The median concentration of the l isomer specimens was 166 ng/mL. However, 5 of these specimens contained MAMP concentrations greater than 20,000 ng/mL.

Both methods of isomer analysis gave similar results with the d isomer measured to being 99% or greater in purity.

Keywords: Methamphetamine; D and l enantiomers; Drug concentrations

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The finding of d MAMP on a urine drug test may have severe consequences for the patient that go beyond health concerns, including potential dismissal from a physician's practice, discharge from a rehabilitation facility, as well as loss of employment and loss of reputation [3]. Laboratories that differentiate the enantiomeric forms of the drug are limited in their choice of methods. Results for a chiral analysis are expressed as the percentage of the d-enantiomer relative to the total amount of MAMP present.

For the derivatization method 1-fluoro-2-4-dinitrophenyl-5-L-alanine amide (FDAA) also called Marfey's reagent was used [9,10]. FDAA derivatives of D-amino acids exhibit strong intramolecular bonding, which reduces their polarity relative to the corresponding L-amino acid derivatives. Consequently, the D-derivatives are selectively retained on reverse phase columns and elute later than corresponding L-derivatives. The methamphetamine in the test specimen is isolated using a Cerex PSCX solid phase extraction columns followed by derivatization using Markey's reagent. For the non-derivatized separation a Phenomenex LUX 3u 140 × 4.6 mm column using an elution buffer of 5 mM ammonium Bicarbonate pH 11.

Of the 11,264 specimens found positive for MAMP only 198 contained significant amounts of l MAMP. In general, these concentrations were low with median concentrations of 166 ng/mL (Table 1).

	Lux column		Marfey	
Sample ID	**%L**	**%D**	**%L**	**%D**
177	0	100	0.1	99.9
46	0	100	0.1	99.9
571	0	100	7.6	92.4
577	0	100	0.5	99.5
821	0	100	0.3	99.7
96	0	100	0.1	99.9

276	0	100	0.1	99.9
288	0	100	0.4	99.6
296	0	100	0.1	99.9
540	0	100	0.1	99.9
849	0	100	0.1	99.9
970	0	100	0.1	99.9
2	0	100	0.1	99.9
279	91	9	96.9	3.1
304	0	100	0.2	99.8
317	0	100	0.2	99.8
325	0	100	0.1	99.9
327	0	100	0.1	99.9
464	0	100	0.1	99.9
628	0	100	0.2	99.8
682	0	100	0.1	99.9
715	0	100	0.1	99.9
956	0	100	0.1	99.9
114	0	100	0.1	99.9
373	0	100	0.1	99.9
540	0	100	0.1	99.9
674	0	100	0.2	99.8
681	0	100	0.7	99.3
682	0	100	0.1	99.9
803	0	100	0.2	99.8
97	0	100	0.2	99.8
105	0	100	0.6	99.4
174	0	100	0.1	99.9
219	0	100	0.1	99.9

Table 1: Comparison of the LUX column versus Marfey method.

The majority of d-MAMP positive specimens contained high concentrations of this enantiomer. However, concentration cannot be the sole criteria to separate the use of illicit MAMP from the legal form. We observed 5 cases with very high l MAMP. As this cannot be ascribed to inhalation, we attribute these observations to spiking of the urine to mask the presence of the d enantiomer.

The finding that about 1% of MAMP positives specimens are not due to use of the illegal form should make health care workers cautious in classifying patients as meth users. To aid in the differentiation most of this true l methamphetamine findings have low urine concentrations. Chiral analysis is a well-established method that can resolve most cases, and laboratories should provide this test upon request. An accurate interpretation should include medication review and the use of the other interpretive tools.

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