

Department of Clinical Laboratory Sciences

Graduate Masters Theses

Metabolic Profile Of The Drug Famprofazone. Brandy Greenhill, MS. November, 2002.

ABSTRACT

There are several drugs that lead to the production of methamphetamine and/or amphetamine in the body which are subsequently excreted in the urine. The presence of these drugs raises concerns when interpreting positive amphetamine drug testing results. Analyses of the concentrations of the amphetamines and their enantiomeric profile in urine may assist in determining whether their presence is the result of the administration of one of these licit precursor drugs or from the illicit use of methamphetamine. One of the drugs which may give rise to this interpretation problem is famprofazone (Gewodin®, Geislich), an analgesic not available in the United States, but available in European Countries. Following Institutional Review Board approval, two Gewodin tablets (50 mg of famprofazone) were administered orally to five volunteers with no history of amphetamine, methamphetamine, or famprofazone use. The subject population consisted of three females and two males in general good health ranging in age from 29 to 42. Following drug administration, urine samples were collected *ad libitum* for up to seven days and pH, specific gravity, and creatinine values were determined to assess the potential variations in the measured concentrations of methamphetamine and amphetamine. To determine the concentrations of methamphetamine and amphetamine, samples were analyzed using an alkaline liquid-liquid extraction followed by derivatization with N-trifluoroacetyl-*l*-propryl-chloride. Quantitation and enantiomer analysis were then accomplished using gas chromatography/mass spectrometry (GC/MS). Peak concentrations for methamphetamine ranged from 614 to 7,361 ng/ml and 148 to 2,271 ng/ml for amphetamine. Concentrations of both compounds peaked between 3 and 14 hours post-dose. Amphetamine and methamphetamine could be detected 121 hrs and 143 hrs post—dose, respectively, at a limit of detection (LOD) of 5 ng/ml. Using a cutoff of 500 ng/ml of methamphetamine all subjects had at least one positive sample. Using health and Human Services guidelines for defining a positive result, ≥ 500 ng/ml methamphetamine and ≥ 200 ng/ml amphetamine, only four out of five subjects had positive samples over the entire collection period. The percent conversion of famprofazone to methamphetamine ranged from 4% to 15% and 2 to 4% to amphetamine. The amount of amphetamine excreted in urine started at 20% of the methamphetamine concentration in all subjects and increased to as much as 55% in some subjects. Analysis revealed that both *d*- and *l*-enantiomers of methamphetamine and amphetamine were present as a result of famprofazone metabolism. *l*-Methamphetamine (70%) predominated from the first sample collected and remained at a higher percentage than *d*- and *l*-isomers remained relatively close at 55-45% in the earlier samples with *l*-amphetamine increasing to 65-75% toward the end of the collection period. The interpretation of positive urine drug test results is a critical part of forensic

drug testing due to the potential repercussions to an individual. The contribution from another metabolic pathway to the production of amphetamine alone helps differentiate famprofazone administration from illicit methamphetamine use. The detection of both enantiomers differentiates famprofazone use from the most commonly abused form of methamphetamine and all medicinal methamphetamine available in the U.S. which is either d-methamphetamine or l-methamphetamine (Vick's inhaler). Finally, the uniqueness of the initial methamphetamine enantiomer excretion of 70% l/30% d can be used to differentiate famprofazone from illicit methamphetamine usage, which initially is 50/50. The data collected in the study may be applied by forensic toxicologists and MRO's in an effort to differentiate licit famprofazone use from illicit methamphetamine use.