J Forensic Sci, Jan. 1979, Vol. 24, No. 1

CASE REPORT

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Fatal Intoxication from 3,4-Methylenedioxyamphetamine

3,4-Methylenedioxyamphetamine (MDA) is a potent central nervous system (CNS) stimulant chemically and pharmacologically related to amphetamine and mescaline [*1-3*] (Fig. 1). The phenylisopropylamine portion of the molecule gives MDA marked sympathomimetic activity similar to amphetamine demonstrated by peripheral vasoconstriction, tachycardia, pupillary dilation, and effects on other smooth muscles. The CNS stimulatory effects of MDA also mimic those of amphetamine, and at high doses convulsions, hyperthermia, and behavioral changes may occur [*4*]. The 3,4-methyleneoxy group on the phenyl portion of the molecule gives MDA psychopharmacological properties similar to those of mescaline. At an apparent threshold dose of 80 mg, MDA causes marked perceptional distortions that begin approximately 60 min after oral ingestion and last up to 8 h [*5*]. Subjective effects include intensification of feelings, a facilitation of self-insight, and an overwhelming desire to communicate and relate to other people [*6*]. At high doses, hallucinations may appear.

The drug was first synthesized in 1910 by Mannich and Jacobsin [*7*], but the first pharmacological studies demonstrating MDA's stimulatory properties were not conducted until 1939 [*8*]. It was patented in 1940 as an antitussive [*9*], in 1960 as an ataractic [*10*], and in 1961 as an anorexigenic [*11*]; however, the drug has never been commercially available on the licit American pharmaceutical market. Widespread abuse of MDA began in the late 1960s and by April of 1970, the "Berkeley Barb" described MDA "as the new love drug which had been getting rave reviews in the Diggers' Chamber of Commerce" [*12*]. During the next two years MDA became a popular recreational drug in many areas of the United States. In California two fatalities were attributed to its use [*13*]. During this 1970 to 1972 period, many MDA deaths were reported in Canada [*13,14*]. Deaths from MDA still occasionally occur in Canada;[2] however, since 1973 the drug appears to have lost its popularity in the United States and deaths from MDA are extremely rare. This communication concerns one of two fatalities attributed to MDA that recently occurred in the greater St. Louis metropolitan area.

Presented at the 30th Annual Meeting of the American Academy of Forensic Sciences, St. Louis, Mo., 24 Feb. 1978. Received for publication 8 May 1978; accepted for publication 29 June 1978.

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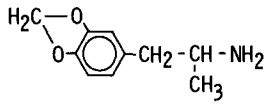
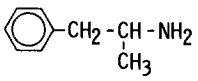
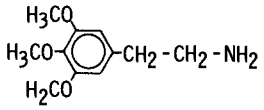


3, 4, - Methylenedioxyamphetamine



Amphetamine



Mescaline

FIG. 1—*Chemical structures of 3,4-methylenedioxyamphetamine, amphetamine, and mescaline.*

Case History

The decedent, a 24-year-old white male, arrived at a party in the early evening. At 7:30 p.m. and again at 8:30 p.m. he ingested one Quāālude® tablet containing 300 mg of methaqualone. Approximately 15 min later he ingested 0.5 g of a white powder believed to contain a mixture of lysergic acid diethylamide (LSD), morphine, and amphetamine. The powder was wrapped in a tissue and formed into a small ball which was swallowed. At 11:00 p.m. he ingested an additional 700 mg of the powder. One hour later, he complained to his hostess that he "felt high and needed to calm his body down." He then lay down to rest. The decedent was reported to be sweating profusely and speaking irrationally at this time. He was described as "one dripping rag." Between 1:00 and 2:00 a.m. he began thrashing about violently and appeared totally incoherent. It was reported that his hands were continuously busy and he appeared to be picking at things. During this time he was attended to by several of the guests. At approximately 2:00 a.m. the decedent's eyes rolled back and he swallowed his tongue. Guests at the party pulled his tongue back, initiated mouth to mouth resuscitation, and swabbed his head and neck with cold towels. The decedent's condition appeared to improve; he looked at the guests and appeared to be "aware," but he made no effort to communicate. He then fell into a deep sleep and began snoring. It was believed by those present that the decedent was recovering; however, at 2:30 a.m. he was found completely unresponsive. An ambulance was summoned. On arrival at an area hospital, the decedent displayed fixed and dilated pupils and a straight-line electrocardiogram. Resuscitation attempts proved unsuccessful and the decedent was pronounced dead at 4:00 a.m.

Autopsy Finding

The decedent was a 24-year-old white male, 187 cm (6 ft, 1½ in.) tall, weighing approximately 77 kg (170 lb). Examination of the external surface of the body revealed no marks of trauma. The autopsy failed to reveal any gross abnormalities other than visceral congestion and features of anoxia. Epicardial, subendocardial, gastric, and subpleural petechiae were present. Only blood and urine specimens were sent for toxicologic analysis.

Toxicology Finding

Given the case history of ingestion of methaqualone and a mixture of LSD, morphine, and amphetamine, a portion of urine was initially screened for these compounds. The ingestion of methaqualone was substantiated by the hydroxymethyl, 3-hydroxyphenyl, and 4-hydroxyphenyl methaqualone metabolites in the urine. Analysis was by the thin-layer chromatographic (TLC) procedure of Goudie and Burnett [*15*]. Further analysis of the urine failed to demonstrate the presence of amphetamine or morphine. No attempt was made to analyze for LSD. A ninhydrin-positive spot was observed running slightly higher than amphetamine in the Davidow et al [*16*] TLC developing system. The spot was eluted from the plate by the method of Freimuth [*17*] and its ultraviolet spectrum in 0.5*N* sulfuric acid was recorded (Fig. 2). The compound possessed ultraviolet maximums at 285 and 234 nm, indicating MDA. The identification of the compound as MDA was confirmed by gas chromatography-mass spectrometry (GC-MS). A portion of the urine extract was analyzed in a Hewlett-Packard 5942 GC-MS equipped with a 1.5-m (5-ft) glass column coated with 3% OV-101 and 0.2% Carbowax on 20-mesh Chromosorb. The resultant electron impact spectra of MDA from the decedent's urine is presented in Fig. 3. A comparison of the ion mass and mass abundance of a pure MDA standard and the MDA in the decedent's urine extract are presented in Table 1.

The quantitation of both MDA and methaqualone in blood was performed by using ultraviolet spectrophotometry. The MDA was determined by the method of Cimbura [*13*] and the methaqualone by the method of Bailey and Jatlow [*18*]. Methaqualone and MDA were separated in the initial blood extract by the procedure outlined in Fig. 4. After the toxicologic analysis was completed, a sample of the powder ingested by the decedent was made available to the laboratory. It contained MDA, but not LSD, amphetamine, or morphine. The results of all analyses are presented in Table 2.

Summary

The symptoms of MDA intoxication exhibited by the decedent prior to death closely mimic those of acute amphetamine poisoning: profuse sweating, violent and irrational

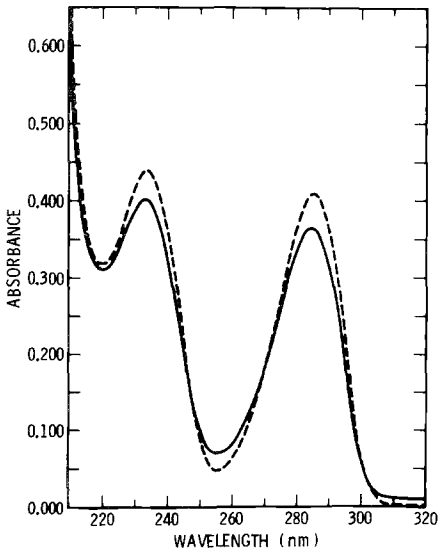


FIG. 2—*Ultraviolet spectra in 0.5*N *sulfuric acid of 15 μg/ml of standard MDA* (solid line) *and spot eluted from TLC* (broken line).

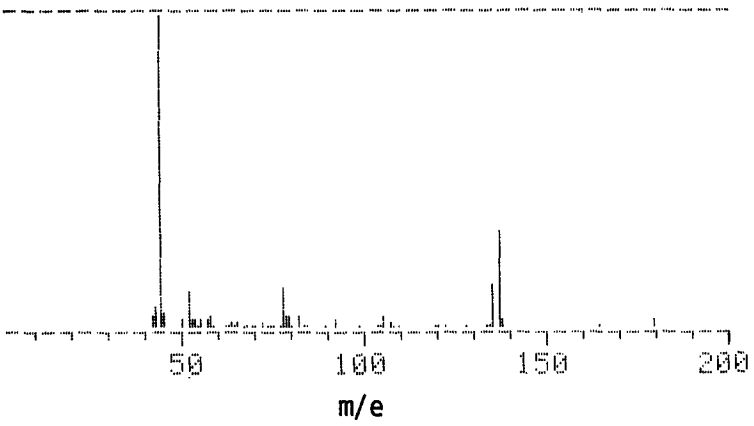


FIG. 3—*Electron impact spectra of MDA extracted from the decedent's urine.*

TABLE 1—*Ion mass and mass abundance of MDA standard and MDA extracted from decedent's urine.*

Ion Mass, *m/e*	Ion Abundance of MDA Standard	Ion Abundance of Urine Compound[a]
44	100.0	100.0
51	12.7	12.1
77	16.4	12.5
78	6.4	4.5
79	4.6	4.4
105	4.3	3.6
135	13.1	13.6
136	35.6	31.0
179	5.2	3.1

[a]Similarity index, 0.9957; molecular weight, 179.2.

behavior, and stereotypically compulsive behavior. Therefore, if amphetamines are not detected in specimens from a person displaying classic symptoms of amphetamine poisoning, hallucinogenic amphetamine derivatives may be considered.

In the case described, a divided dose of 850 mg of MDA ingested within 2 h and 15 min was sufficient to cause the death of a 24-year-old male, 4 h after the final dose. While the methaqualone may have contributed to the demise of the decedent, the authors think that the MDA itself was sufficient to cause death.

Results of limited recovery studies of MDA extraction from blood and elution from TLC plates supported the observations of Cimbura [*13*]. Approximately 85% of MDA is extracted by the method described and its elution from TLC plates is quantitative.

This case points out once again the dangers of false advertising in the illicit market. The decedent, himself a dealer in the illicit drug market, and all present at the party believed the ingested white powder to be a mixture of *m*orphine, LS*D*, and *a*mphetamine, hence MDA. They were totally unfamiliar with 3,4-methylenedioxyamphetamine, MDA.

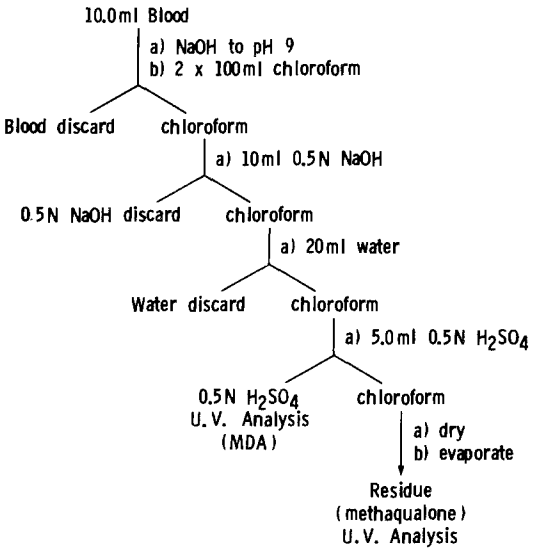


FIG. 4—*Extraction procedure for separating MDA and methaqualone from blood.*

TABLE 2—*Results of toxicologic analysis.*

Sample	MDA	Methaqualone
Blood	10 mg/litre	2 mg/litre
Urine	168 mg/litre	present
Powder	75%	...

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