CASE REPORT

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A Dextromoramide-Related Fatality

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ABSTRACT: A 38-year-old man was found in his car suffering from a heart attack. Serum analysis by capillary gas chromatography and mass spectrometry confirmed the presence of dextromoramide (Palfium®), methadone, and lidocaine. The serum concentrations at admission to the hospital were: 1.9 μg/mL of dextromoramide, 0.4 μg/mL of methadone, and 0.4 μg/mL of lidocaine. A serum alcohol analysis performed using headspace gas chromatography was negative.

KEYWORDS: toxicology, dextromoramide, chromatographic analysis, metabolite

Dextromoramide (Fig. 1) was discovered in 1956 by Dr. Janssen. Subcutaneously, it is approximately 10 times more potent than methadone, 25 times more potent than morphine, and 50 times more potent than pethidine [*1*]. Quantitative analyses of dextromoramide have involved oxidative methods followed by spectrophotometric and high performance liquid chromatographic techniques [*2,3*]. Presented here is a case involving dextromoramide (a drug which was removed from the United States in the 1960s) [*3*] using capillary gas chromatographic techniques.

Case History

After receiving an anonymous phone call, police found a 38-year-old white male in his car suffering from a heart attack. He was taken to the hospital and remained on life support for several months before his death. A search of his apartment revealed a white powder (which proved to be dextromoramide by gas chromatography/mass spectrometry [GC/MS]) and vials of chemical precursors. Subsequent investigation revealed that he was synthesizing the drug.

Toxicological Analysis

Standards and Reagents

Dextromoramide tartrate was supplied by Janssen Pharmaceutica, Piscataway, New Jersey. Methadone was available through Eli Lilly & Co. as the hydrogen chloride (HCl)

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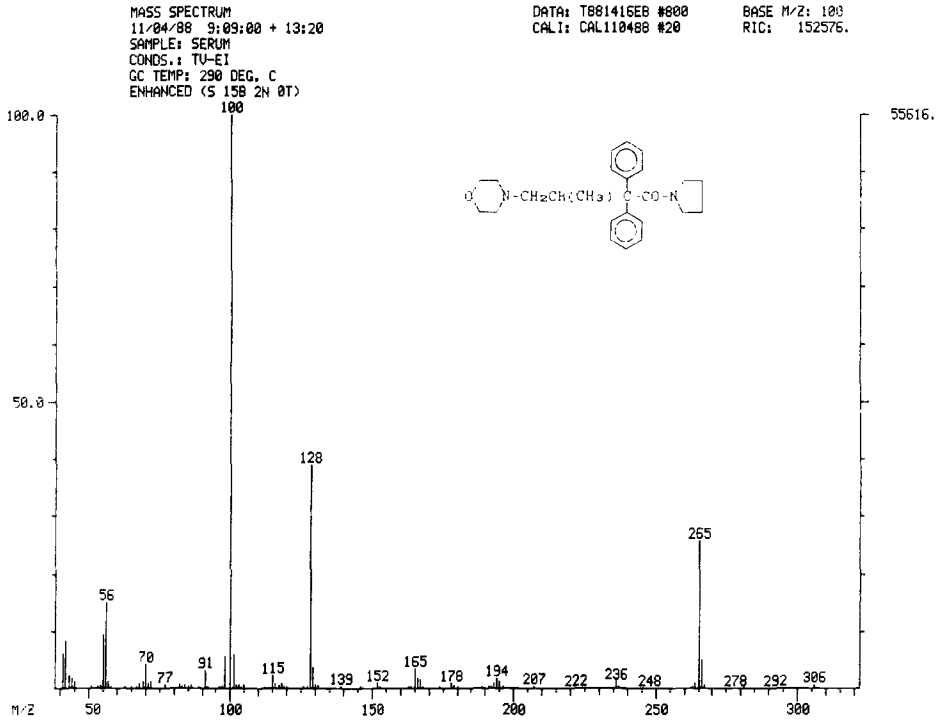

FIG. 1—*Electron impact mass spectrum of dextromoramide.*

salt, while lidocaine and the internal standard prazepam were purchased from USPC. All solvents used were nanopure grade purchased from Krackeler Scientific, Inc., Albany, New York.

Extraction Procedure

To a 16 by 150 mm screwtop vial, 10 mL of *n*-butylchloride is added along with 1 mL of 8-μg/mL prazepam, 1.0 mL of pH 9.4 ammonium buffer, and 2.0 mL of sample. The contents are mixed and centrifuged at 2000 rpm for 5 min. The organic layer is transferred to a clean 16 by 150 screwtop vial and mixed with 5 mL of fresh 1.0*N* HCl. The sample is again centrifuged at 2000 rpm for 5 min after which the organic layer is discarded. The aqueous layer is then transferred to a 60-mL separatory funnel containing 20 mL of chloroform ($CHCl_3$) and 5 mL of pH 9.4 ammonium buffer. After mixing, the organic layer is filtered through Whatman #1 filter paper into a 50-mL beaker and taken to near dryness on a hot plate. The final millilitre is transferred to a 10- by 75-mL test tube and taken to dryness under nitrogen. The sample is reconstituted with 50 μL of ethylacetate for GC analysis.

Capillary Gas Chromatography

Drug screening was performed on a Hewlett Packard 5890 gas chromatograph equipped with a 7673A autoinjector and dual nitrogen phosphorus (NP) detectors. A J&W DB-5 capillary column measuring 15 m by 0.32 mm with a 0.25-μm film thickness was used. Linear velocity was set at 47 cm/s at 250° using helium for the carrier gas. Helium makeup,

air, and hydrogen were set at 30, 80, and 2 mL/min, respectively. The NP collector was operated at 25 pA, measured at 90°. The operating conditions are shown in Table 1. All injections were 2 μL made in the splitless mode.

Gas Chromatography/Mass Spectrometry

Mass spectrometric confirmation was performed on a Finnigan-MAT 4500 instrument operated in the electron impact (EI) mode at 70 eV. The instrument was equipped with a J&W DB-5 capillary column measuring 15 m by 0.25-mm and having a 0.25-μm film thickness. The conditions are shown in Table 2. Samples were evaporated to dryness and reconstituted with 10 μL of methanol. Two microlitres were injected into the instrument which was operated in a splitless mode.

Results

Qualitative analysis of the serum and stomach contents revealed dextromoramide, methadone, lidocaine, and dextromoramide metabolites. Quantitative results for the serum are shown in Table 3. Chromatographic results of the serum are summarized in Fig. 2.

Discussion

Previously described procedures used for the quantitative analysis of dextromoramide in body fluids involved chemical oxidation followed by spectroscopic methods of detection [2,3]. A disadvantage of this approach is the potential interference by dextromoramide metabolites or any compound which contains the diphenyl-methyl moiety, such as methadone. Presented here is a qualitative and quantitative approach to the determination of dextromoramide in serum using capillary gas chromatography.

This method is specific for dextromoramide, distinguishing it from its metabolites and permitting simultaneous quantitation of methadone. However, since previously published

TABLE 1—*Gas chromatographic conditions.*

Injector temperature:	200°C
Initial temperature:	90°C
Initial time:	0.0 min
Rate:	10°C/min
Final temperature:	280°C
Final time:	6.0 min
Detector temperature:	300°C

TABLE 2—*GC/MS conditions.*

Initial temperature:	60°C
Initial time:	1.0 min
Rate:	20°C/min
Final temperature:	300°C
Final time:	7.0 min
Ion source:	150°C
Manifold:	100°C
EM volts:	−1600
Emission current:	−0.28

TABLE 3—*Summary of toxicological analysis.*

Drug	Serum Concentration
Dextromoramide, μg/mL	1.9
Methadone, μg/mL	0.4
Lidocaine, μg/mL	0.4
Ethanol, mg/dL	0.0

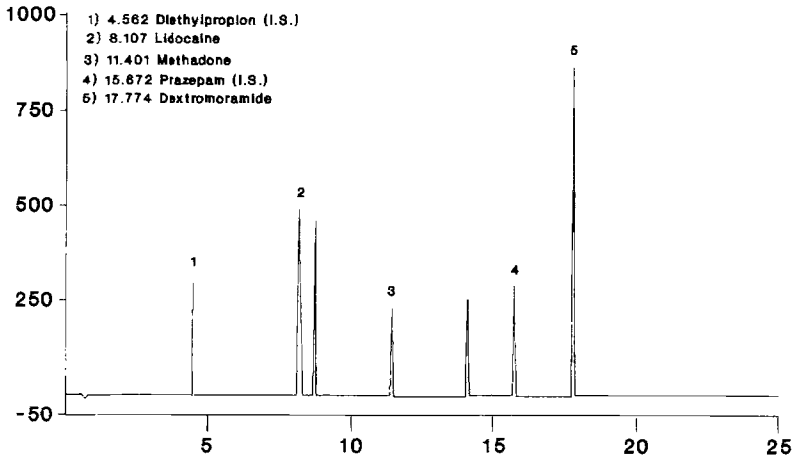

FIG. 2—*Gas chromatograph of serum extract.*

data include the metabolites in measurements of therapeutic serum concentrations, a direct comparison of the parent drug's involvement in the death described here is somewhat difficult.

Table 4 illustrates serum concentrations in four patients receiving a single therapeutic dose of dextromoramide [*3*]. Note that the serum concentrations represent the parent drug plus metabolites. This author also mentioned that one of the metabolites (2'-hydroxy dextromoramide) is thought to be present in an equivalent concentration to the parent drug.

Confirmation of dextromoramide by GC/MS also revealed the following metabolites: a phenol obtained by parahydroxylation of a benzene ring (Fig. 3), a *N,N*-didesalkylation product (Fig. 4), and the 2'-hydroxy dextromoramide product (Fig. 5). If the postulated equivalent concentration of this last mentioned metabolite is assumed, then the 1.9-μg/mL dextromoramide might be doubled to 3.8 μg/mL producing a serum concentration higher than 75% of the above-illustrated therapeutic concentrations.

The effective concentration of dextromoramide is likely to be even higher if the contribution of the other metabolites is assumed. This combined with 0.4 μg/mL of methadone could have produced a respiratory arrest resulting in heart failure and subsequent death of this individual.

Conclusion

In conclusion, presented here is a rapid and sensitive method for the simultaneous quantitative determination of dextromoramide and methadone without interference from

TABLE 4—*Urine and serum concentrations[a] of dextromoramide found over a 48-h period following the ingestion of a single therapeutic dose [3].*

	Patient 1		Patient 2		Patient 3		Patient 4	
Time, h	Urine Conc.	Serum Conc.	Urine Conc.	Serum Conc.	Urine Conc.	Serum Conc.	Urine Conc.	Serum Conc.
1	13.5	21.0	14.5	17.0	14.5	21.5	14.0	30.5
2	14.0	23.0	7.9	18.5	10.0	17.5	14.9	35.5
3	14.5	28.5	15.1	20.0	12.4	28.5	13.5	54.0
4	14.9	29.5	9.5	24.0	10.0	19.8	17.0	45.5
5	20.0	29.0	20.0	5.0	17.2	18.3	13.5	26.0
6	8.5	24.5	6.5	5.0	10.0	21.0	12.9	24.4
7	4.1	22.8	11.0	8.0	15.2	14.5	12.0	23.0
8	5.0	21.0		8.5	9.0	14.0	10.0	24.0
24	6.5	18.5	10.0	7.4	5.2	9.9	5.0	13.0
48	8.0	18.0	9.0	4.0	4.1	1.9	4.0	12.4

[a]Urine concentrations and serum concentrations are in micrograms per 10 mL of urine or serum.

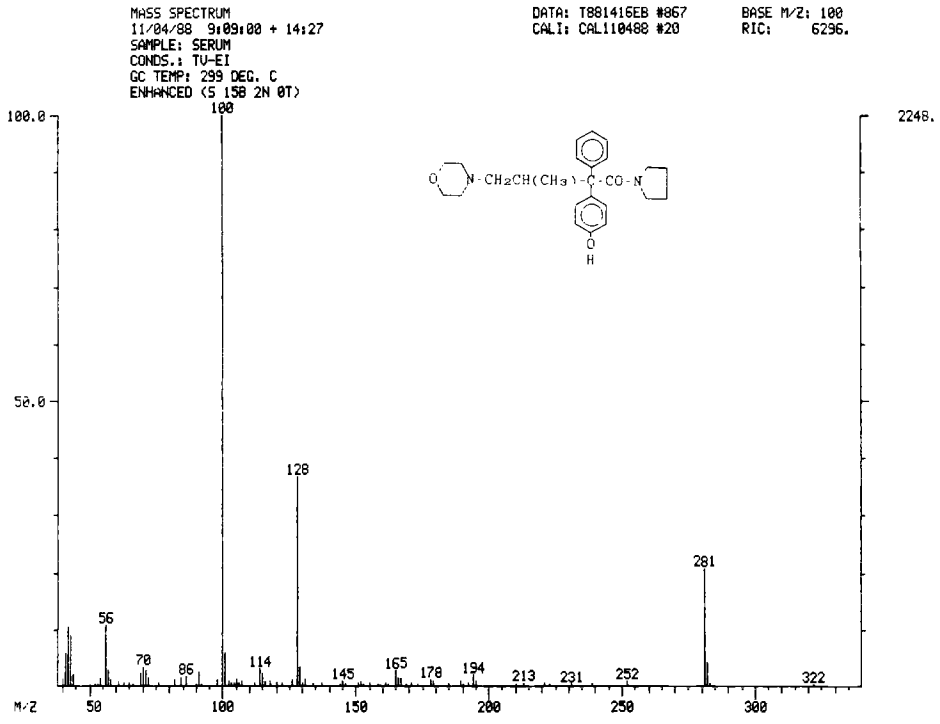

FIG. 3—*Electron impact mass spectrum of paraphenolic dextromoramide.*

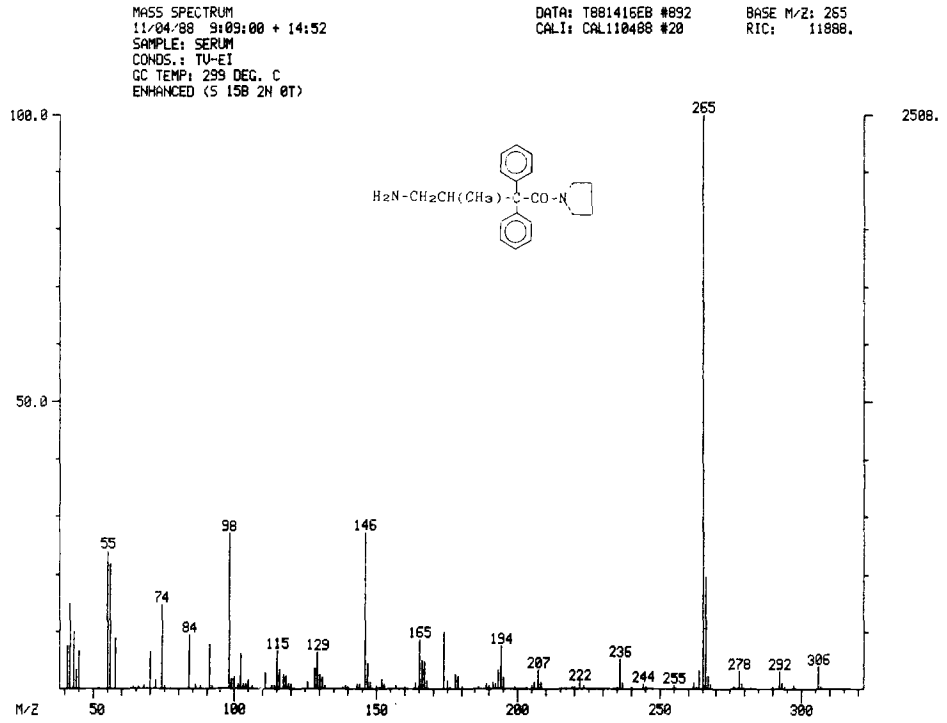

FIG. 4—*Electron impact mass spectrum of* N,N-*didesalkyl dextromoramide.*

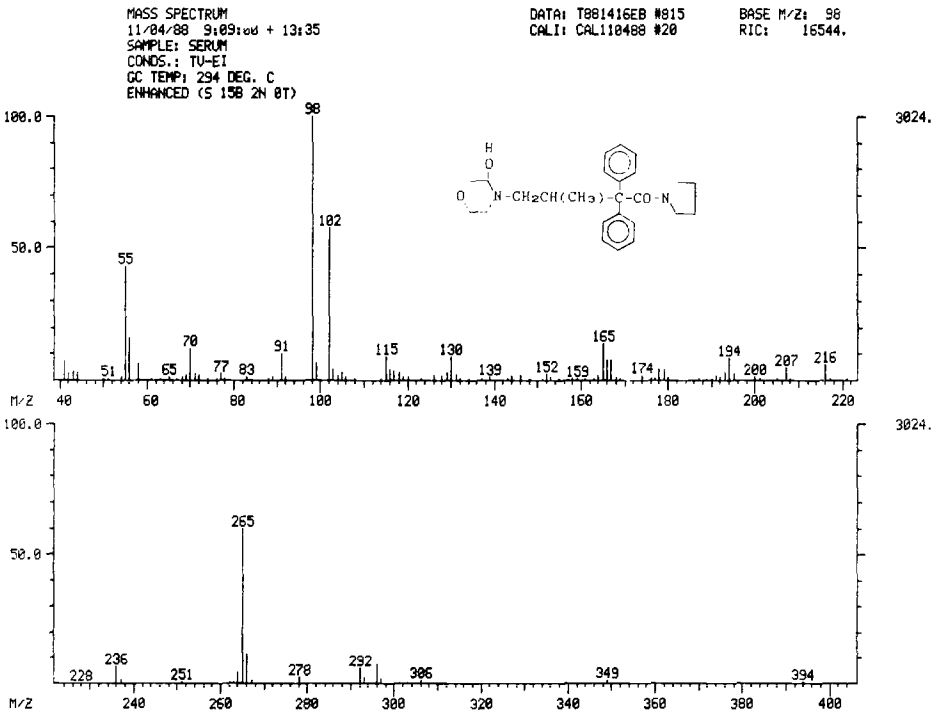

FIG. 5—*Electron impact mass spectrum of 2'hydroxy dextromoramide.*

any of the metabolites associated with these drugs. Also presented are the serum concentrations in what appears to be a dextromoramide-related fatality.

Acknowledgments

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References

[1] Janssen, P. A. J., "Potent, New Analgesics, Tailor-Made for Different Purposes," Acta Anaesthesiologica Scandinavica, Vol. 26, 1982, pp. 262–268.

[2] Caddy, B. and Idowu, R., "Oxidative Determination of Dextromoramide (Palfium) in Body Fluids," *Analyst*, Vol. 104, April 1979, pp. 328–333.

[3] Caddy, B., Idowu, R., Tilstone, W. J., and Thompson, N.C., "Analysis and Disposition of Dextromoramide in Body Fluids," in *Forensic Toxicology: Proceedings of the European Meeting of the International Association of Forensic Toxicologists*, Croom Helm, London, 1980, pp. 126–139.

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