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Drugs and Driving: A Systematic Analytical Approach

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ABSTRACT: To collect useful epidemiological data about drug involvement in highway safety, it is essential that sensitive and specific analytical procedures be used to establish the presence of and to determine the concentrations of drugs and metabolites in samples collected from drivers. This paper describes a comprehensive and systematic screening procedure requiring 6 mL of blood, which has been used for the analysis of samples collected from injured and fatally injured drivers. The procedure uses radioimmunoassay, gas chromatography with selective detectors, and high performance liquid chromatography. Drugs and metabolites presumptively identified are then confirmed primarily using gas chromatography—chemical ionization mass spectrometry.

KEYWORDS: toxicology, screening procedures, traffic safety, epidemiology

The involvement of ethanol and other drugs in driving and highway safety has stimulated considerable toxicological interest in recent years. Most early research and epidemiological studies involved ethanol alone, and its relationship to the impairment of driving skills; this work has been extensively reviewed by Jones and Joscelyn [*1*]. The increasing use and abuse of drugs in addition to ethanol has raised the question of their ability to impair driving performance. A number of recent conferences and literature reviews have helped to place this problem in perspective [*2,3*]. It has become clear that epidemiological studies are essential to accurately determine the role of drugs in highway safety. Workshops organized by National Highway Traffic Safety Administration (NHSTA) [*4*] have identified probable drugs of interest. Before epidemiological studies can be performed it is, however, necessary to develop an analytical screening procedure that will detect these drugs and their pharmacologically active metabolites at subtherapeutic, therapeutic, and toxic concentrations. Nichols [*5*] and Waller [*6*] have previously noted that perhaps the most limiting aspect of epidemiological studies to date is the availability of suitable analytical procedures. It is also necessary to determine blood concentrations of drugs and metabolites if valid interpretation of epidemiological data with regard to drug and cause-effect relationships is to be made.

Previous analytical schemes to screen drugs and driving samples have required urine or blood and urine [*7-9*]. Although drug identifications from urine samples are readily performed, it has proven to be a more difficult sample to obtain from drivers than blood [*10*]; also, drug concentrations in urine are of little interpretative value. Therefore, to obtain data

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concerning drug use among driving populations, a comprehensive drug screening and quantitation scheme requiring as little as 6 mL of blood has been developed. Limiting the volume of blood collected is important especially in cases of traumatic injury or shock.

Radioimmunoassay (RIA) is used to detect the common drugs of abuse, including cocaine and its major metabolite (benzoylecgonine), barbiturates, phencyclidine (PCP), opiate narcotics, and Δ^9-tetrahydrocannabinol (Δ^9-THC). Gas chromatography (GC) with selective detectors is used to screen for the benzodiazepines, tricyclic antidepressants, antihistamines, and other basic drugs. The anticonvulsants and nonbarbiturate sedative-hypnotics are detected by high performance liquid chromatography (HPLC) and thin-layer chromatography (TLC). All presumptive positive results are confirmed and quantitated by other analytical techniques, particularly gas chromatography-chemical ionization mass spectrometry (GC-CIMS).

Samples

For studies involving fatally injured drivers, samples should be collected in glass containers containing sodium fluoride and potassium oxalate with Teflon®-lined screw caps. Samples from either injured drivers or drivers suspected of being under the influence of drugs should be collected in an evacuated blood drawing tube containing the same preservative and after mixing, transferred to a glass container with a Teflon-lined screw cap.

Materials

Chemicals used in preparing buffer solutions, including sodium borate, sodium dihydrogen phosphate, sodium hydroxide, potassium hydroxide, ammonium hydroxide, concentrated sulfuric, and hydrochloric acids, were analytical reagent grade, purchased from Mallincrodt, Inc. A variety of solvents, including toluene, heptane, isoamyl alcohol, hexane, acetone, isopropanol, *n*-propanol, furfural, and ethyl acetate, were also obtained from Mallincrodt, Inc. Chloroform, *n*-butyl chloride, acetonitrile, and methanol were purchased from Burdick and Jackson Laboratories. Absolute ethanol for standard preparation was obtained from U.S. Industrial Chemical Co.

Instrumentation

A variety of gas liquid chromatographs were used during the course of these studies. A Finnigan 9500 gas chromatograph equipped with flame ionization detectors was used for the determination of volatiles. Hewlett-Packard gas chromatographs (Model 5730A) equipped with either nitrogen phosphorous or electron capture detectors were used to detect basic drugs, benzodiazepines, ethchlorvynol, and trichlorethanol. HPLC analyses were performed on a Varian liquid chromatograph (Model 5020) equipped with either a Varichrom variable wavelength ultraviolet (UV) detector or a Varian UV-5 filter spectrophotometer. A Beckman gamma counter was used for the RIA analyses.

GC-MS analysis, in either the chemical ionization (GC-CIMS) or electron impact (GC-EIMS) mode, were performed on a Finnigan 3200 GC-MS. For the GC-CIMS work, the instrument was interfaced with an Incos data system.

Screening

An outline of the procedure is shown in Fig. 1. The application of each of the analytical techniques used will be discussed separately. For all screening procedures blood samples to which drugs and metabolites had been added were analyzed concurrently.

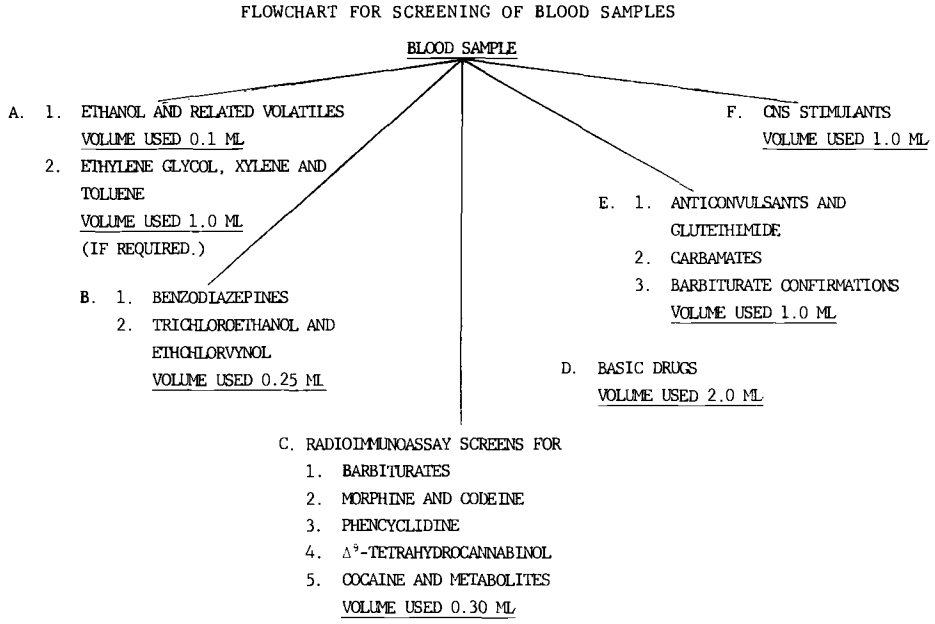

FIG. 1—*Specimen use.*

Radioimmunoassay

Commercially available kits (Abuscreen®, Roche Diagnostics), were used to detect barbiturates, opiate narcotics, cocaine and benzoylecgonine, and phencyclidine (PCP). Although a similar procedure is available for the detection of amphetamine, it was not used because of the cross-reactivity with endogenous β-phenylethylamine.

Preliminary screening for Δ^9-THC was performed using two RIA methods developed under contract to the National Institute on Drug Abuse. One procedure used a tritiated tracer [*11*] and the other an I^{125}-labelled tracer [*12*]. Both of these assays are reported to be specific for Δ^9-THC and to have the sensitivity required to detect Δ^9-THC in blood or plasma samples after the smoking of marijuana. Presently, the procedure using the I^{125}-tracer is used exclusively. The method requires 100 μL of blood.

Gas Chromatography

Several different gas chromatographic procedures were used. Table 1 lists the types of columns and chromatographic conditions employed for these analyses. Silanized glass columns were used for all assays.

Ethanol and related volatiles, ethylene glycol, and aromatic hydrocarbons were screened using GC with flame ionization detection (GC-FID).

GC with electron capture detection (GC-ECD) is extremely useful for halogen containing compounds. Several workers, including Peat and Kopjak [*13*] and Rutherford [*14*] have used this technique to separate and detect the benzodiazepines. For this study, the procedure of Peat and Kopjak [*13*] was modified; 0.25 mL of blood is buffered with an equal volume of saturated sodium borate (pH 9.0) and extracted with 0.25 mL of a mixed solvent (toluene:heptane:isoamyl alcohol, 76:20:4). An aliquot of the organic phase is then injected directly onto the column. A second aliquot is used for the detection of ethchlorvynol and trichloroethanol.

TABLE 1—*Gas chromatographic conditions used for screening analyses.*

Compounds	Column	Packing	Detector	Oven Temperature, °C	Comments	Ref
Ethanol and related volatiles	2 m by 2 mm id	0.2% Carbowax 1500 M[a]	FID	90 isothermal	*n*-propanol (0.2%) used as internal standard	*19*
Ethylene glycol	2 m by 2 mm id	Tenax® 60–80[b]	FID	140 isothermal	propylene glycol (0.1%) used as internal standard	...
Toluene, xylene, and benzene	2 m by 2 mm id	Tenax 60–80[b]	FID	140 to 190 at 10° per minute	headspace	*20*
Benzodiazepines	1.2 m by 2 mm id	3% OV-17 on Gas Chrom Q 100–120[b] or 3% SP-2250 on Supelcoport 80–100[a]	ECD	3% OV-17 at 240, isothermal. 3% SP-2250 at 255 isothermal	modified extraction procedure used (see text)	*13*
Ethchlorvynol-trichloroethanol	0.6 m by 2 mm id	10% SP-1000 on Gas Chrom Q 100–120	ECD	100	...	...
Basic drugs (except amphetamines)	2 m by 2 mm id	3% OV-17 on Gas Chrom Q 100–120 & 3% OV-1 on Gas Chrom Q 100–120[b]	NPD	130 for 2 min, program at 8°/min to 270° and hold for 8 min	Modified extraction procedure used	*15*
Amphetamine, methamphetamine, and phentermine	0.6 m by 2 mm id	8% Carbowax 20*M* 5% potassium hydroxide on Gas Chrom Q 100–120	NPD	100 to 145 at 10° per minute	*N*-propyl-amphetamine (0.2 μg) used as internal standard	...

[a]Supelco, Inc., Bellefonte, PA.
[b]Applied Sciences, Inc., State College, PA.

The nitrogen phosphorous detector (NPD) is ideally suited for the detection and quantitation of basic drugs and their metabolites. Pierce et al [*15*] used GC-NPD to screen postmortem blood samples for these compounds. To obtain the required sensitivity (0.1 μg/mL) and chromatograms that were relatively free of interfering peaks, it was necessary to modify this procedure. Figure 2 outlines the extraction steps used. A similar extraction procedure was used for the amphetamines. Figure 3 details this procedure.

High Performance Liquid Chromatography

Several liquid chromatographic procedures have been published for the analysis of anticonvulsants and barbiturates, including those of Adams et al [*16*], Kabra et al [*17*], and Soldin [*18*]. A reverse phase system, based on these procedures, was used for the detection of the commonly prescribed anticonvulsants (phenobarbital, primidone, phenytoin, and carbamazepine), barbiturates, and nonbarbiturate sedative hypnotics (for example, glutethimide and methyprylon). To 1.0 mL of blood is added 0.5 mL of 0.3*M* sodium dihydrogen phosphate (pH 4.5), 12 μg of 5-ethyl-5-p-tolylbarbituric acid (internal standard), and 10 mL of chloroform. The organic layer is removed after extraction and centrifugation, evaporated to dryness and reconstituted in 100 μL of the HPLC eluent. An aliquot is then injected. The HPLC conditions used are as follows: column: 25-cm by 4.6-mm Lichrosorb RP-8 (E. Merck,

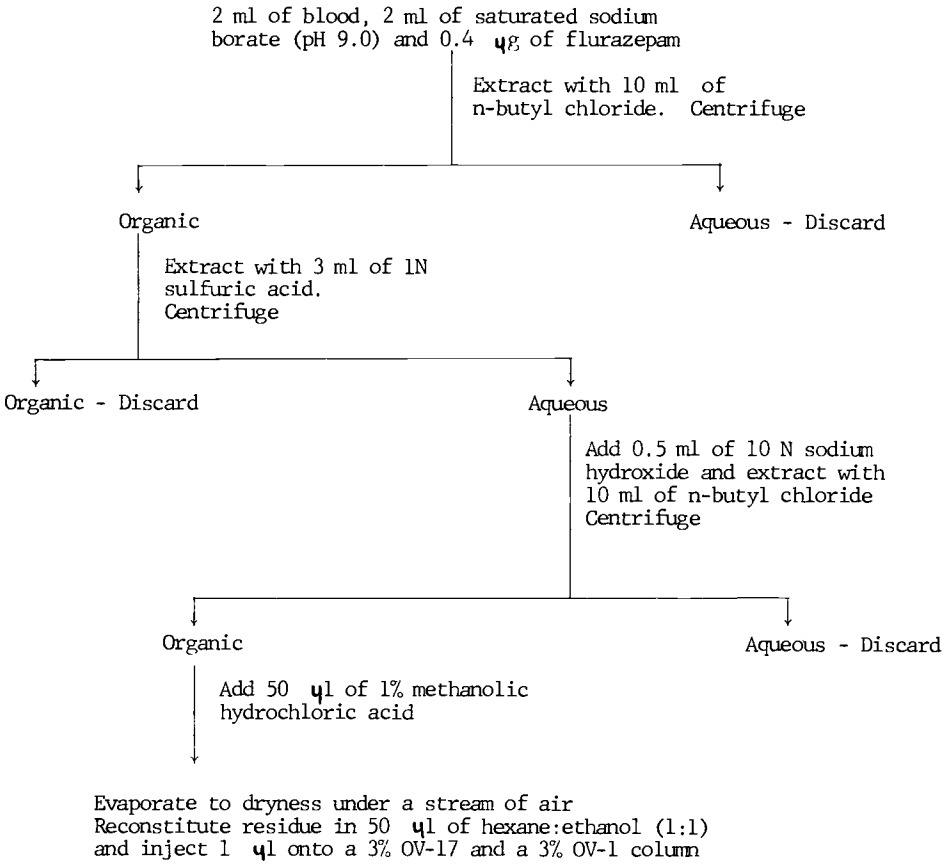

FIG. 2—*Extraction procedure for basic drugs and metabolites.*

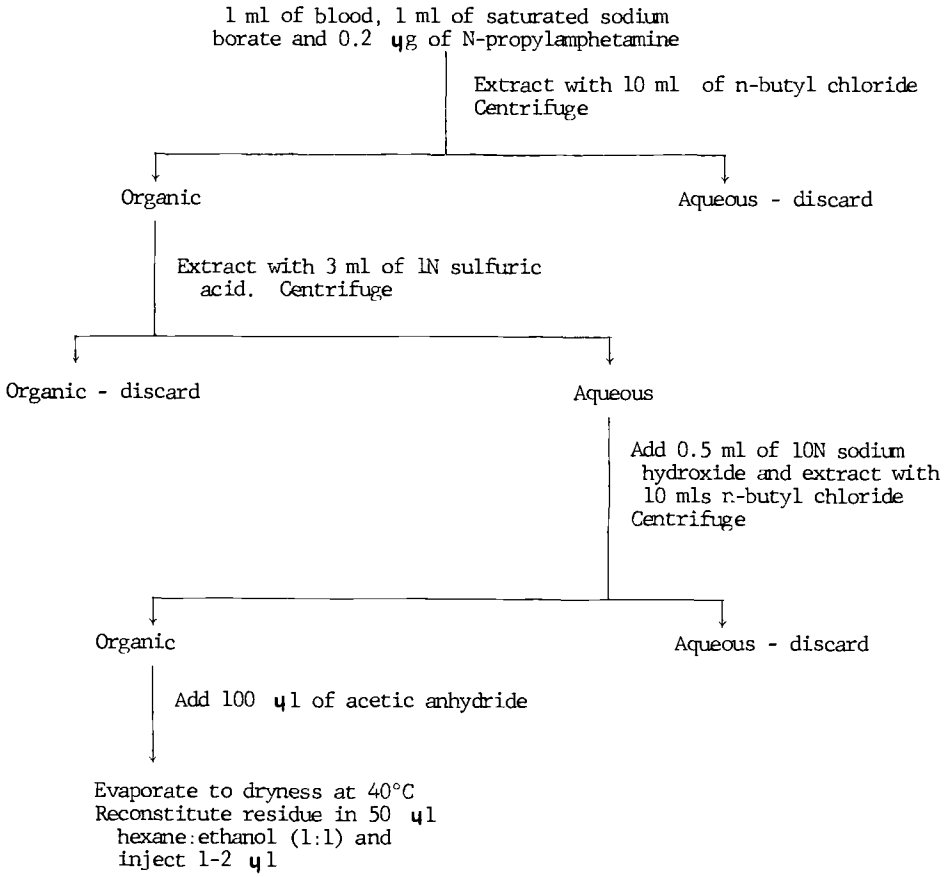

FIG. 3—*Extraction procedure for the amphetamine.*

Darmstadt, Germany), eluent: 28% acetonitrile in water, flow rate: 2.0 mL per minute, detector wavelength: 200 nm.

Thin-Layer Chromatography

The residue from the HPLC screen is redissolved in methanol (20 µL) and screened for carbamates using precoated silica sheets (Silica Gel 60 F_{254}, E. Merck, Darmstadt, Germany), and an eluent of ethyl acetate:methanol:ammonia (85:15:5) [*21*]. The carbamates were detected by spraying with furfural:ethanol (9:1) followed by exposure to hydrogen chloride fumes.

Confirmation of Screening Results

Although several analytical procedures were used for confirmation of presumptive positive findings, GC-CIMS was essential for the identification of basic drugs and those drugs of abuse detected by the RIA procedures. As indicated in Table 1, a two-column gas chromatographic system was used to detect a wide variety of basic drugs at a sensitivity limit of 0.1 µg/mL. Preliminary identification of drugs and metabolites was made by comparing retention times relative to flurazepam to those published by Pierce et al [*15*]. The residue from

this initial screen was then examined by GC-CIMS using a column packed with 3% OV-17 on Gas Chrom Q and a temperature program similar to that used for the NPD screen. A 2-s scan between 100 and 450 *m/z* was used for data acquisition. The use of methane as carrier gas and ammonia as reagent gas, has been shown to produce intense protonated molecular ions for a wide range of basic drugs [*22*]. These gases were therefore used for the confirmations. Using this procedure, a positive identification of compounds detected by the NPD screen could be made by comparison with known CIMS spectra.

It was also necessary to use GC-CIMS to confirm positive findings from the RIA screens for cocaine and benzoylecgonine, PCP, opiate narcotics, Δ^9-THC, and to identify amphetamine or its derivatives detected by GC-NPD. The GC-CIMS procedures used for cocaine and benzoylecgonine, PCP, the opiate narcotics, and the amphetamines have been reviewed by Foltz et al [*22*]; all use ammonia as reagent gas and deuterated internal standards for quantitation. Two GC-CIMS procedures have been used for the confirmation and quantitation of Δ^9-THC. The method presently used involves extraction of Δ^9-THC, methylation, and the formation of the trifluoroacyl derivatives. Capillary column GC and negative ion monitoring are then used to detect Δ^9-THC [*23*].

It was unnecessary to use GC-CIMS to confirm other positive screening results; these could be confirmed using alternative chromatographic procedures or GC-EIMS. Confirmations by GC-EIMS are tabulated in Table 2. All of these confirmations used helium as carrier gas and an electron voltage of 70 eV.

Benzodiazepines were initially identified using GC-ECD. They are also detected by GC-NPD, therefore this technique was used as a confirmation of presumptive positives. Chlordiazepoxide and its metabolites were confirmed and quantitated by the HPLC procedure of Peat et al [*24*].

Barbiturates identified by RIA can be confirmed in the HPLC screen for anticonvulsants and by GC of the methylated derivatives on a 3% OV-17 column using flame ionization detection. The latter procedure was also used to confirm the anticonvulsant drugs. Preferably, the barbiturates are confirmed using GC-NPD on a 2% SP-2110/1% SP-2510-DA on Supelcoport 100-200 column packing without derivatization. Carbamazepine, however, was confirmed using identical HPLC conditions to those employed for screening with the exception that the detector wavelength was set at 280 nm.

Quantitation of Drugs and Metabolites

All drugs and metabolites detected were quantitated using suitable internal standards. The methods used are tabulated in Table 3. Deuterated analogs were used for all the GC-CIMS procedures.

Discussion

Although the analytical procedures described here for screening, identification, and quantitation of drugs and metabolites are generally available to forensic toxicologists, their use to systematically analyze a limited volume of blood has not been previously described.

TABLE 2—*Confirmations performed by GC-EIMS.*

Drug	Column Packing
Volatiles (except ethanol and related volatiles)	Tenax
Trichloroethanol and ethchlorynol	10% SP-1000 on Gas Chrom Q 80-100
Glutethimide and the carbamates	3% OV-17 on Gas Chrom Q 80-100

TABLE 3—*Methods used for quantitation of drugs and metabolites.*

Drug	Internal Standard	Method	Comments	Ref
Ethanol and related volatiles	*n*-propanol	GC-FID	see Table 1	...
Ethylene glycol	propylene glycol	GC-FID	see Table 1	...
Toluene, xylene, and benzene	alternate compound, that is, benzene if toluene is detected	GC-FID	see Table 1	...
Benzodiazepines (except chlordiazepoxide)	flurazepam	GC-ECD	see Table 1—single stage extraction procedure used	...
Chlordiazepoxide	diazepam	HPLC	norchlordiazepoxide, demoxepam, and nordiazepam quantitated simultaneously	*24*
Ethchlorvynol and trichloroethanol	alternate compound, that is, TCE for ethchlorvynol	GC-ECD	see Table 1—single extraction procedure used	...
Basic Drugs (except PCP, opiate narcotics, cocaine, amphetamines, and tricyclic antidepressants)	alternate base, that is, mepivicaine for lidocaine	GC-NPD	choice of internal standard depends upon drug to be quantitated	*25*
PCP, opiate narcotics, amphetamines, cocaine, and benzoylecgonine	deuterated analogs	GC-CIMS	...	*22*
Tricyclic antidepressants	deuterated analogs	GC-CIMS	single stage extraction procedure used	*26*
Δ^9-THC	deuterated analogs	GC-CIMS	positive or negative ion detection used	*22,23*
Barbiturates	alternate barbiturate	GC-NPD	column packing: 2% SP-2110/1% SP-2510-DA Supelcoport 100-120	...
Anticonvulsants, and glutethimide	5-ethyl-5-p-tolyl-barbituric acid	HPLC-UV	see text for conditions	...
Carbamates	diphenhydramine	GC-FID	column packing: 3% OV-17 on Gas Chrom Q	...

In developing this approach, certain problems were encountered in attempting to satisfy sensitivity requirements necessary to detect subtherapeutic concentrations of drugs in blood samples. Although Pierce et al [*15*] developed a GC-NPD procedure for screening basic drugs and their metabolites in postmortem samples, it did not meet the sensitivity requirements and in addition, interfering peaks were often encountered. To overcome these drawbacks, the sample volume was increased to 2 mL and a back extraction procedure used (see Fig. 2). Figure 4*a* shows a GC-NPD chromatogram of a sample following extraction by the method of Pierce et al [*15*]; peaks (numbered 1 to 4) might interfere with the identification of more volatile drugs and metabolites, for example the antihistamines. When the same sample is analyzed using the modified extraction procedure a "cleaner" chromatogram is obtained (Fig. 4*b*). Flurazepam was added to the sample before extraction as a marker. The original reference compound used by Pierce et al [*15*] was prazepam. Unfortunately, this benzodiazepine was poorly recovered by the modified extraction scheme. Flurazepam was chosen as the internal standard because the samples have previously been screened for benzodiazepines; it is also rapidly metabolized to *N*-desalkyl flurazepam and therefore not detected after normal therapy.

Developing a suitable screening procedure for amphetamines was also difficult. Various workers [*27–29*] have described procedures for detection of these drugs in urine or large volumes of blood, but sensitivity limits are in the μg/mL range. Initial attempts to obtain ng/mL sensitivity by GLC using either acyl or trifluoracyl derivatives were unsuccessful because interfering peaks were often encountered on the commonly used silicone phases.

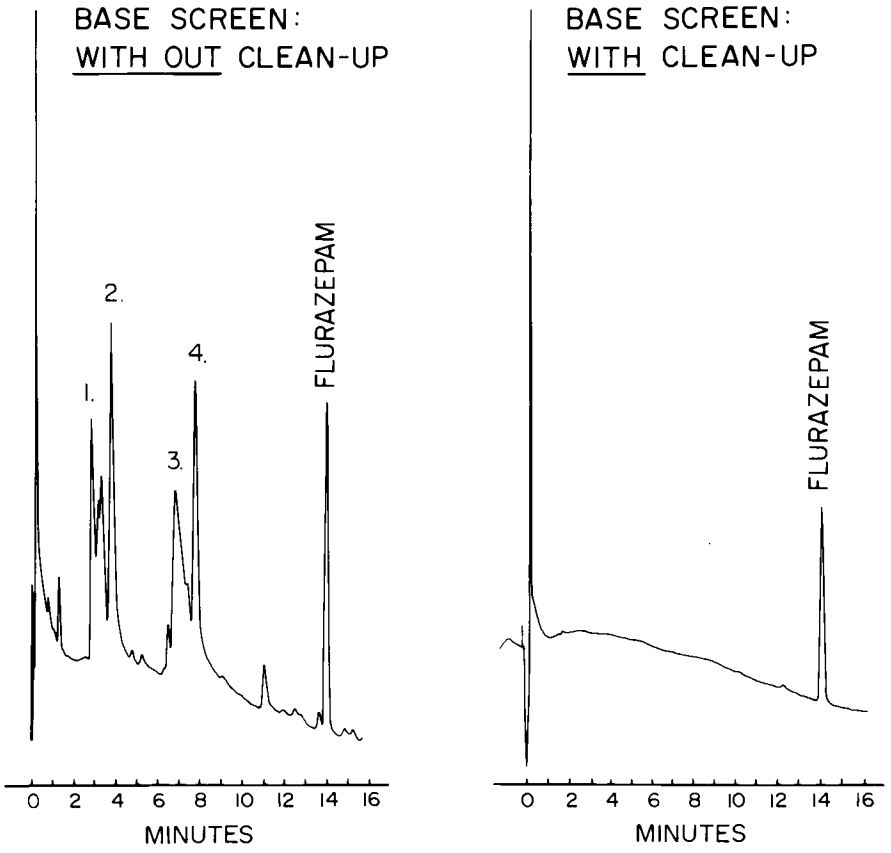

FIG. 4—*GC-NPD tracing of a sample containing methaqualone before* (a) *and after back extraction* (b).

The use of a mixed phase GC packing, potassium hydroxide with either Apiezon L or Carbowax 20*M* has also been described [*27*]. Following the evaluation of different Carbowax 20*M* potassium hydroxide packings, optimum resolution of amphetamine, methamphetamine, phentermine, β-phenylethylamine, and *N*-propyl amphetamine was obtained on an 8% Carbowax 20*M* and 5% potassium hydroxide on Gas Chrom Q 100-120 mesh packing. Table 4 lists the retention times of these amines relative to *N*-proplyamphetamine which was used as the internal standard.

The identification of Δ^9-THC in blood is one of the most challenging toxicological analyses. However, previous drugs and driving studies have shown that Δ^9-THC and metabolites are the most commonly encountered substances [*9*] after ethanol.[2] Two recently developed RIA procedures for blood, one using a tritiated and the other an iodinated tracer are reportedly specific for Δ^9-THC in blood or serum [*11,12*]. However, as with other screening methods, it is imperative that presumptive positives be confirmed. The confirmation technique must be capable of detecting and quantitating Δ^9-THC at concentrations below 0.01 μg/mL, since recent reports indicate that blood concentrations fall below this level 3 h after smoking [*30*]. To date, GC-CIMS has proven the most effective means of both confirming and quantitating Δ^9-THC. Although packed column chromatography and positive ion detection have been shown to be suitable for analysis of Δ^9-THC in serum at concentrations

[2]A. J. McBay and A. P. Mason, personal communication, 1982.

TABLE 4—*Relative retention time (to N-propylamphetamine) of some amines on an 8% Carbowax 20M-5% potassium hydroxide packing.*

Drug	Relative Retention Time
Phentermine	0.83
Methamphetamine	0.91
N-propylamphetamine	1.0
Amphetamine	1.26
B-phenylethylamine	1.85

above 0.001 μg/mL [*22*], a recently developed capillary chromatography-negative ion detection procedure [*23*] is more suitable for the analysis of blood samples in the low ng/mL concentration range. This latter procedure is the one presently being used.

Conclusion

The analytical screening approach described was designed to satisfy two important criteria (a) analysis of small volumes of samples (Fig. 1 summarizes sample use) and (b) the detection and quantitation of a wide variety of drugs, as described in the NHSTA workshop at subtherapeutic concentrations. These criteria can only be met through the use of sensitive analytical procedures. To obtain this sensitivity, screening procedures such as RIA, GC-NPD, and GC-ECD have been used, followed by GC-CIMS for the confirmation and quantitation of presumptive positives. Only these techniques can offer the accuracy as well as the precision needed by the forensic toxicologists. These sensitivity requirements are needed to assure detection of drugs in multiple use situations and to identify drugs that may cause impairment when used therapeutically.

Acknowledgments

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References

[*1*] Jones, R. K. and Joscelyn, K. B., "Alcohol and Highway Safety 1978: A review of the State of Knowledge," U.S. Department of Transportation, National Highway Safety Administration, Washington, DC, 1978, p. 207.

[*2*] Willette, R. E., Ed., *Drugs and Driving*, Research Monograph, No. 11, National Institute on Drug Abuse, Rockville, MD, 1977, p. 137.

[*3*] Joscelyn, K. B., Donelson, A. C., Jones, R. K., McNain, J. W., and Ruschman, P. A., "Drugs and Highway Safety 1980," U.S. Department of Transportation, National Highway Traffic Safety Administration, Washington, DC, 1980, p. 250.

[*4*] Joscelyn, K. B. and Donelson, A. C., "Drug Research Methodology Vol. IV, Epidemeology in Drugs and Highway Safety: The Study of Drug Use among Drivers and its Role in Traffic Crashes," U.S. Department of Transportation, National Highway Traffic Safety Administration, Washington, DC, 1980, p. 73.

[*5*] Nichols, G. L., "Drug Use and Highway Safety, A Review of the Literature," Final Report, Technical Report DOT-H5-800-580, National Highway Traffic Safety Administration, Washington, DC, 1975.

[6] Waller, J. A., "Drugs and Highway Crashes," *Journal of the American Medical Association*, Vol. 215, March 1975, pp. 1477-1482.

[7] Robinson, T. A., "The Incidence of Drugs in the Impaired Driving Specimens in Northern Ireland," *Journal of Forensic Science Society*, Vol. 19, Oct. 1979, pp. 237-244.

[8] Garriott, J. C., DiMaio, V. J. M., Zumwate, R. E., and Petty, C. S., "Incidence of Drugs and Alcohol in Fatally Injured Motor Vehicle Drivers," *Journal of Forensic Sciences*, Vol. 22, No. 2, April 1977, pp. 383-389.

[9] Cimbura, G., Lucas, D. M., Bennett, R. C., Warren, R. A., and Simpson, H. M., "Incidence and Toxicological Aspects of Drugs Detected in 484 Fatally Injured Drivers and Pedestrians in Ontario," *Journal of Forensic Sciences*, Vol. 27, No. 4, Oct. 1982, pp. 855-867.

[10] Joscelyn, K. B., Jones, R. K., Maichel, R., and Donelson, A., "Drugs and Driving: Information Need and Research Requirements," Report DOT-HS-804-774, U.S. Department of Transportation, National Highway Safety Administration, Washington, DC, 1979.

[11] Gross, S. J., Soares, J. R., and Wong, S. L., "Marijuana Metabolites Measured by a Radioimmunoassay Technique," *Nature*, Vol. 252, Dec. 1974, p. 581.

[12] Cook, C. E., Setzman, H. H., Schindler, V. H., Tallent, C. R., Chin, K. M., and Pitt, C. G., "Radioimmunoassay for Cannabinoids, Cannabinoid Assays in Biological Fluids," R. L. Hawks, Ed., Research Monograph No. 42, National Institute on Drug Abuse, Rockville, MD, 1982, pp. 19-32.

[13] Peat, M. A. and Kopjak, L., "The Screening and Quantitation of Diazepam, Flurazepam, Chlordiazepoxide, and Their Metabolites by Electron-Capture Gas Chromatography and High Pressure Liquid Chromatography," *Journal of Forensic Sciences*, Vol. 24, No. 1, Jan. 1979, pp. 46-54.

[14] Rutherford, D. M., "Rapid Micro-Method for the Measurement of Diazepam and Desmethyldiazepam in Blood and Plasma by Gas Liquid Chromatography," *Journal of Chromatography*, Vol. 137, July 1977, pp. 439-448.

[15] Pierce, W. O., Lamoreaux, T. C., Urry, F. M., Kopjak, L., and Finkle, B. S., "A New Rapid Gas Chromatography Method for the Detection of Basic Drugs in Post-mortem Blood, Using a Nitrogen Phosphorus Detector. Part I, Qualitative Analysis," *Journal of Analytical Toxicology*, Vol. 2, Jan./Feb. 1978, pp. 26-31.

[16] Adams, R. F., Schmidt, G. J., and Vandemark, F. I., "A Micro Liquid Column Chromatography Procedure for Twelve Anticonvulsants and Some of Their Metabolites," *Journal of Chromatography*, Vol. 145, No. 2, March 1978, pp. 275-284.

[17] Kabra, P. M., Stafford, B. E., and Marton, L., "Simultaneous Measurement of Phenobarbital, Phenytoin, Primidone, Ethosuxamide and Carbamazepine in Serum by High-Pressure Liquid Chromatography," *Clinical Chemistry*, Vol. 23, No. 7, July 1977, pp. 1284-1288.

[18] Soldin, S. J. and Hill, G. J., "Rapid Micromethod for Measuring Anti Convulsants in Serum by High-Performance Liquid Chromatography," *Clinical Chemistry*, Vol. 22, No. 6, June 1976, pp. 856-859.

[19] Finkle, B. S., McCloskey, K. L., Kopjak, L., and Carroll, J. M., "Toxicological Analyses in Cases of Sudden Infant Death: A National Feasibility Study," *Journal of Forensic Sciences*, Vol. 24, No. 4, Oct. 1979, pp. 775-789.

[20] Anthony, R. M., Bost, R. O., Thompson, W. L., and Sunshine, I., "Paraldehyde, Toluene, and Methylene Chloride Analysis by Headspace Gas Chromatography," *Journal of Analytical Toxicology*, Vol. 2, Nov./Dec. 1978, pp. 262-264.

[21] Davidow, B., Petri, N. L., and Ovame, B., "A Thin Layer Chromatographic Screening Procedure for Detection of Drugs of Abuse," *American Journal of Clinical Pathology*, Vol. 50, No. 11, Dec. 1968, pp. 714-719.

[22] Foltz, R. L., Fentiman, A. F., and Foltz, R. B., "GC/MS Assays for Abused Drugs in Body Fluids," Research Monograph, Vol. 32, National Institute on Drug Abuse, Rockville, MD, 1980, p. 202.

[23] Foltz, R. L., McGinnis, K. M., and Chinn, D. M., "Quantitative Measurement of Δ^9-Tetrahydrocannabinol and Two Major Metabolites in Physiological Specimens Using Capillary Column Gas Chromatography," *Biomedical Mass Spectrometry*, Vol. 10, No. 5, May 1983, pp. 316-323.

[24] Peat, M. A., Finkle, B. S., and Deyman, M. E., "High-Pressure Liquid Chromatographic Determination of Chlordiazepoxide and Its Major Metabolites in Biological Fluids," *Journal of Pharmaceutical Sciences*, Vol. 68, No. 11, Nov. 1979, pp. 1467-1468.

[25] Kopjak, L., Finkle, B. S., Lamoreaux, T. C., Pierce, W. O., and Urry, F. M., "A New Rapid Gas Chromatographic Method for the Detection of Basic Drugs in Postmortem Blood Using Nitrogen Phosphorus Detectors Part II, Quantative Analysis," *Journal of Analytical Toxicology*, Vol. 3, July/Aug. 1979, pp. 155-157.

[26] Chinn, D. M., Jennison, T. A., Crouch, D. J., Peat, M. A., and Thatcher, W., "Quantitative Analysis of Tricyclic Antidepressant Drugs in Plasma or Serum by Gas Chromatography-

Chemical/Ionization Mass Spectrometry," *Clinical Chemistry*, Vol. 26, No. 8, July 1980, pp. 1201-1204.

[27] Lebish, P., Finkle, B. S., and Brackett, J. W., "Determination of Amphetamines, Metamphetamine and Related Amines in Blood and Urine by Gas Chromatography with Hydrogen-Flame Ionization Detector," *Clinical Chemistry*, Vol. 16, No. 3, March 1970, pp. 195-200.

[28] O'Brien, J. E., Zazulak, W., Abbey, V., and Hensvark, O., "Determination of Amphetamine and Phentermine in Biological Fluids," *Journal of Chromatographic Science*, Vol. 10, May 1972, pp. 336-341.

[29] Jain, N. C., Sneath, T. C., and Budd, R. D., "Rapid Gas Chromatographic Determination of Amphetamine and Methamphetamine in Urine," *Clinical Chemistry*, Vol. 20, No. 11, Nov. 1974, pp. 1460-1462.

[30] Perez-Reyes, M., DiGuiseppi, S., Davis, K., Schindler, V., and Cook, E., "Comparison of Marijuana Cigarettes of Three Different Potencies," *Clinical Pharmacology and Therapeutics*, Vol. 31, No. 5, May 1982, pp. 617-624.

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