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Methaqualone is being encountered with increasing frequency throughout the nation. Both licit and illicit tablets and capsules have been seen. One exhibit from Canada contained methaqualone, diphenhydramine and LSD. Methaqualone has been abused for a number of years outside the United States and reportedly can cause addiction. It is not a controlled drug under the Controlled Substances Act in the U.S. Three U.S. trade names are "Quaalude", "Somnafac" and "Sopor". "Mandrax", a European preparation, has also been encountered.

Heroin and Benactyzine HCl in combination have recently been encountered in the New York area. The exhibit consisted of a white powder in glassine bags. Analysis shows 0.67% heroin and 0.48% benactyzine HCl, the remainder being quinine and lactose. This is the first encounter we have had with this combination.

"Liquid Hash" (See February 1972 Microgram) has recently been reported by our San Francisco Regional Laboratory. The three exhibits encountered weighed 77.6, 449 and 4042 grams and contained 33, 33 and 39% tetrahydrocannabinol (THC) respectively.

MDMA (3,4-methylenedioxymethamphetamine) has been encountered again by our Chicago Regional Laboratory. Only one previous encounter with this material has been reported to us. Of the three exhibits analyzed in this case, two were obtained by BNDD and one was from the State Crime Laboratory at Joliet, Illinois. MDMA is not under federal control.

MDA acetate (3,4-methylenedioxyamphelamphetamine acetate) has recently been reported from the Kansas City area. The exhibit was in the form of a white powder in a clear, unmarked plastic bag. This is the first encounter we have had with the acetate salt of MDA.

Heroin HCl (6.2%) and Phenylpropanolamine (12.8%) in combination are being found in red glassine bags. These bags measure 1 3/4 X 2 3/4 inches. This is the first encounter we have had with bags of this type.

Hashish in cheese has recently been encountered by police and U.S. Customs officials. The Southeast Missouri Crime Laboratory reports 1.8 pounds hashish in an 8 to 10 inch yellow ball, coated with paraffin and stamped as cheese. The ball was found among other packages of true cheese reported as originating in Amsterdam. The possibility of this type of shipment was noted in the February 1972 issue of Microgram.

Morphine HCl, 99% pure, has been reported from the West Coast. Allegedly originating in Singapore, this exhibit consisted of two rectangular pieces of a greenish-tan solid approximately 1/2 X 1 inch and apparently sawed from a larger block. Similar pieces of this material have also been encountered in Australia.

"Cokesnuff", a tobacco sniffing product aimed at the juvenile market, has recently become available in Minnesota. This product comes in a small, round container about the size of a silver dollar and has flowers and the word "Cokesnuff" imprinted on one side. The outer carton states: "TURN ON WITH COKESNUFF--SNIFF IT." The name apparently attempts to relate this product to cocaine. Product is believed to be imported from England through mail order.

Heroin HCl with benzoic acid, sugar and tetracaine is reported by our New York Regional Laboratory. This is our first encounter with benzoic acid being used as the primary diluent with heroin.

MEETINGS

Sixth International Meeting of Forensic Sciences, Edinburgh, Scotland--September 21-26, 1972. For further information, write to:

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Sixth International Meeting of Forensic Sciences
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Analysis of Cocaine, Procaine, Benzocaine Mixtures

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Introduction

This laboratory frequently receives illicit cocaine samples which have been adulterated with synthetic local anesthetics and sugar. Two local anesthetics commonly encountered are benzocaine and procaine.

Since cocaine, benzocaine and procaine have similar UV absorption characteristics, a means of separating all three components has been investigated. Milos and Porto[2] devised a procedure for the simultaneous spectrophotometric determination of cocaine and procaine mixtures. Canaff[3] separates cocaine from procaine or tetracaine by using a 2.0N HCl chromatographic column. Moore[4] separates the same mixture utilizing a 0.1N HNO_3 column.

The method below is a modification of Moore's procedure which can be utilized to quantitate and identify cocaine in the presence of benzocaine and/or procaine.

Method

Apparatus

Chromatographic Column
UV Spectrophotometer

Reagents

Nitric Acid - 0.1N
Sulfuric Acid - 0.1N
Chloroform - Reagent Grade
Ethyl Ether - Reagent Grade
Ammonia - conc.
Celite 545 - acid washed

Procedure

Pack a pledget of fine glass wool into the base of a chromatographic column (25 cm long, 2 cm diameter) with a tamping rod. Place 2 grams of diatomaceous earth (Celite 545, acid washed)* into a 100 ml beaker. Add 1 ml 0.1 Nitric Acid, and mix with a spatula until homogeneous. Transfer the mixture to the column, and tamp moderately to compress the material into a uniform mass.

* Johns - Manville, New York, New York

Into another 100 ml beaker weigh accurately a portion of sample equivalent to about 15-20 mgs cocaine. (Illicit cocaine samples are often damp and lumpy, therefore, sample mixture should be carefully ground before proceeding). Add 2 mls 0.1N Nitric Acid to the sample and swirl to wet powder thoroughly. To this solution add 3 grams of diatomaceous earth and mix until fluffy. Quantitatively transfer this mixture to the column and tamp moderately. Place a pledget of glass wool on top of the packing.

The benzocaine is eluted from the column into a 200 ml volumetric flask with 200 ml water washed ether. Dilute the flask to volumn with ether. Evaporate a 20 ml aliquot to dryness on a steam bath. Dissolve the residue in a known volume of 0.1N H_2SO_4 to give a final concentration of approximately 10 mcg/ml. Read the absorbance of the solution at 226 mμ and compare against a standard solution of benzocaine.

The cocaine may then be eluted by passing 100 mls water washed $CHCl_3$ into a 100 ml volumetric flask. Dilute flask to volume with $CHCl_3$. Evaporate a 10 ml aliquot to dryness on a steam bath. Dissolve residue in 0.1N H_2SO_4 to give a final concentration of approximately 15 mcg/ml. Read the absorbance of the solution at 233 mμ and compare against standard cocaine.

Procaine is eluted from the column into a 250 ml beaker by passing 100 mls of ammoniacal chloroform (prepared by vigorously mixing 2 ml concentrated ammonium hydroxide with 100 ml $CHCl_3$ and allowing the phases to separate) followed by 100 mls water saturated chloroform. Remove a 20 ml aliquot and evaporate to dryness on a steam bath. Dissolve the residue in 0.1N H_2SO_4 to give a final concentration of approximately 15 mcg/ml. Read the absorbance of the solution at 228 mμ and compare against standard procaine.

Identification

Methods most frequently used for the qualitative determination of mixtures of this type are infrared spectroscopy and thin layer or gas chromatography.

A - Infrared Spectroscopy

To obtain spectra for benzocaine and procaine, the remainder of the stock solutions eluted form the column are evaporated to dryness. The residue may then be deposited as a film on a sodium chloride window.

The cocaine that is eluted from the column must be re-extracted in order to obtain a satisfactory IR curve.

Evaporate the $CHCl_3$ stock solution to about 20 ml. Transfer to a 60 ml separatory funnel and shake with 20 mls 4% ammonium hydroxide. Evaporate the $CHCl_3$ extract on a steam bath (prior to doing so add 1 drop conc. HCl to solution). A KBr disk may now be prepared in the usual manner.

B - Thin Layer Chromatography

Mix a portion of powdered sample with methanol and apply to a silica gel G plate (Analtech). Use the solvent systems mentioned below and observe spots by spraying with iodoplatinate spray (prepared by mixing 0.25 gms Platinic Chloride and 5 grams Potassium Iodide in 100 ml water).

Solvent System A[5] - Cyclohexane: Chloroform: Diethylamine 5: 4: 1
Solvent System B[6] - Ethyl Acetate: Benzene: Ammonium Hydride (6:3.5:1)

	(System A) Rf	(System B) Rf
Cocaine	0.65	0.68
Procaine	0.34	0.60
Benzocaine	0.26	0.41

C - Gas Chromatography

Sample is dissolved directly in methanol and injected under the following conditions:

Instrument	Packard #7360	
Column	3% OV1	3% OV25
Temperature	210°C	140°C
Carrier Gas	Nitrogen	Nitrogen
Carrier Flow	40ml/min	25ml/min
Detector	Flame Ionization	Flame Ionization
Air Flow	500ml/min	500ml/min
Hydrogen Flow	30ml/min	25ml/min

The following results were obtained:

Retention Time Cocaine	5.9 min	4.7 min
Retention Time Procaine	4.3 min	2.4 min
Retention Time Benzocaine	0.7 min	0.5 min

Discussion

Cocaine samples should be subject to qualitative tests before quantitative analysis is performed. The presence of procaine or benzocaine may be detected using the following spot tests:

1 - Sanchez reagent (prepared by mixing 2.5 ml freshly distilled furfural, 22.5 ml 95% EtOH and 75 ml glacial acetic acid). A red color is obtained in the presence of benzocaine or procaine.

2 - p-dimethylaminobenzaldehyde (1 gm in 50 ml EtOH and 50 ml conc. hydrochloric acid). An intense yellow color is obtained in the presence of benzocaine or procaine.

Furthermore, chromatographic screening tests should be performed prior to quantitation to detect the presence of benzocaine and/or procaine. In cases where no benzocaine is present, the ether wash will not be necessary during the quantitation.

Quantitative results of better than 95% cocaine have been obtained using this procedure. Results obtained for the benzocaine and procaine ranged between 92 and 94%. The results obtained on simulated mixtures are tabulated as follows:

	mgs added				mgs found		
	Benz.	Pro.	Coc.		Benz.	Pro.	Coc.
1.	9.8	10.1	10.4	1.	9.3	9.2	10.1
2.	10.0	10.3	20.6	2.	9.2	9.8	19.6
3.	15.1	14.8	15.4	3.	14.0	14.1	14.9

References

1. E.G.C. Clarke, Isolation and Identification of Drugs Pharmaceutical Press, London, 1969

2. C. Milos, P. Porto, Spectrphotometric Determination of Cocaine in the Presence of Procaine and Benzocaine, IRS Publication, Alcohol and Tabacco Tax Laboratory, New York, N.Y.

3. R.F. Canaff, Ion Pairing Chromatographic Separation and Determination of Cocaine, Microgram Vol III, #4, 121 June 1970.

4. J. Moore, The Analysis of Cocaine in Illicit Preparations Microgram Vol III, #3, 89-95, May 1970.

5. Sunshine, Handbook of Analytical Toxicology, Chemical Rubber Company 1969, Reference #1A.

6. IRS Publication #341, June 1967, page 94, system S4

BNDD LABORATORY NOTES

DATE March 1, 1972

NO. 33

DRUG TYPE

METHODOLOGY

THE DETERMINATION OF BENACTYZINE HYDROCHLORIDE BY NMR SPECTROSCOPY

by

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NMR spectroscopy has been utilized for the rapid assay of a wide range of drug components (1,2). Its strength lies in its speed, specificity, and the ease with which it can be made to sidestep spectral interference from combined ingredients. Its chief limitation stems from its inherently low sensitivity, thereby requiring large sample sizes for analyses of greatest accuracy. This necessarily restricts NMR to the assay of those drugs that are either compounded at high concentrations or possessive of low equivalent weight.[1]

However, the forensic chemist, whose task it is to analyze the output of a clandestine laboratory, is far less concerned with problems of quality control than with the identification and reasonable estimation of the active ingredients in their products. Here, the applicability of NMR spectroscopy may be broadened to include many compounds not otherwise considered while enabling us to obtain results within reasonable bounds of accuracy for the intended purpose.

A case in point regards the recent analysis of two benactyzine samples in this laboratory using NMR spectroscopy. The results indicated that we were dealing with concentration levels previously deemed unsuitable for NMR analysis. However, a study of spectral data revealed that we were attaining much better precision than had been anticipated.

Experimental

100 mg. of sample powder and 20 mg. maleic acid (internal standard) were weighed accurately in a small G.S. test tube with 1 ml. graduation, then shaken well with about 1 ml. D_2O. After most of the undissolved material settled, about 0.4 ml. supernatant was transferred to an analytical NMR tube. The spectrum was scanned with the maleic acid (CH) absorption set at 6.4 ppmδ (by way of indirect reference to DSS (sodium 2,2-dimethyl-2-silapentane-s-sulfonate) at 0.0 ppm), then integrated several times. The NMR spectrometer used in our laboratory is a JEOL C60HL 60MHz unit with a signal-to-noise ratio averaging 40 to 1 (1% ethylbenzene convention).

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[1]Ratio of molecular weight to number of protons producing the absorption pattern used for quantitation.

$$\% \text{ Benactyzine HCl in Sample} = 100 \times (A_{ben} \times E_{ben} \times W_{mal}) / (A_{mal} \times E_{mal} \times W_{smp})$$

Where:

A_{ben}: absorption at 7.2-7.6 ppm

A_{mal}: absorption at 6.3-6.9 ppm

E_{ben}: NMR equivalent weight of benactyzine HCl (36.39)

E_{mal}: NMR equivalent weight of maleic acid (58.09)

W_{mal}: weight of standard

W_{smp}: weight of sample

Note: Precision was improved markedly in the analysis of small quantities by calculating A_{ben}/A_{mal} for each scan; the mean value of this ratio was then used in the final calculation. Normally, however, this device is unnecessary, as the mean absorption of each component may be used without detriment to the accuracy of the final result.

Discussion

Two samples analyzed by NMR for benactyzine hydrochloride were found to contain 7.4% and 1.9% of the active ingredient. The more dilute sample, showing a lower level than we had dared quantitate previously with other NMR instrumentation (specifically, a Varian A-60) was submitted for a check assay by GLC. The result obtained, 1.83%, was in excellent agreement with our findings, particularly so in light of the fact that we had rounded our result from 1.86%.

Preliminary results obtained with our NMR spectrometer indicate a relative standard deviation of 7-10% for five integral scans at a component level of only 0.05 to 0.1 milliequivalent per ml. In terms of controlled drugs this quantity is reflected by each of the following: 5-10 mg. MDA hydrochloride, 3-5 mg. meprobamate and gluthethimide, 2-3 mg. amphetamine sulfate, methamphetamine hydrochloride, mescaline sulfate, benactyzine hydrochloride and the JB's and 1-2 mg. ethchlorvynol and DMT. The relatively low variation in integral intensities attained at this level has been attributed to the superior sensitivity and integrator stability of this laboratory's spectrometer as compared with those predominating in the literature on quantitative applications. Further work is proceeding so that analytical guidelines may be formulated for the aforementioned compounds as well as others not previously considered.

References

1. Rackham, D. M., Talanta, 17, 895-906 (1970), and references cited therein.

2. Kram, T. C. and Turczan, J. W., Interbureau By-Lines (Food and Drug Adm.), 6 (5), 257-262.

BNDD LABORATORY NOTES

DATE February 16, 1972 -55-

NO. 34

DRUG TYPE

METHODOLOGY

THE PERKIN-ELMER 900 GAS LIQUID CHROMATOGRAPH EFFLUENT COLLECTION DEVICE USED AS AN AID TO PURIFY DRUGS FOR IDENTIFICATION TESTS

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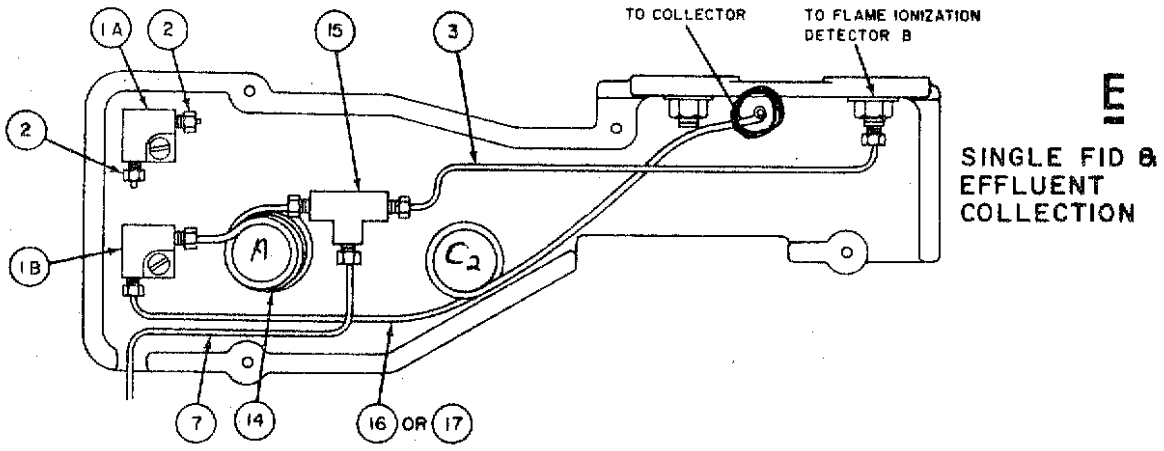
The Perkin Elmer 900 Gas Liquid Chromatograph equipped with a dual column oven and dual flame ionization detector system is conveniently designed to facilitate effluent collections. The restrictor tubes, splitters, and other parts of the complete device are located in the manifold chamber of the GLC unit. By removing the front panel of the instrument, the insulation block and the manifold chamber cover, the necessary manifold connections can be made for the mode of operation desired, such as one column can be used as the preparative column and the other column used as the analytical column. About $100.00 is required to purchase the parts for the effluent collection system. Refer to the diagram below.



E

SINGLE FID & EFFLUENT COLLECTION

Receiver fitting (1A) is plugged. Column B effluent entering receiver fitting (1B) is split between restrictor A, (14), and effluent collection restrictor B_2, (16), or C_2, (17). The split ratio for restrictors B_2 and A (i.e., flow through restrictor B_2: flow through restrictor A) is about 15:1; C_2:A is about 50:1. Effluent from restrictor A, (14), and hydrogen from tube (7) pass into tee (15), through tube (3) or (9), into flame ionization detector B.

(Reprinted from the instruction manual Model 900 Gas Chromatograph, Perkin Elmer, Norwalk, Connecticut).

After the assembly is installed, the collector tube extrudes through the front panel of the GLC unit approximately 1/16". A split ratio of about 15:1 (effluent: detector), is satisfactory for peak collection and detection.

For effluent collection a glass capillary tube or teflon tubing (1/16" O.D. x 0.031" I.D.) is inserted into the collector opening prior to elution. After elution the tubing is removed and the collected residue is washed from the tube with a suitable solvent.

Teflon tubing is recommended over glass because glass often breaks inside the collector and teflon, like glass, is inert to the drugs collected.

By inserting the teflon tube into the collector approximately 2/8", the eluting residue will crystallize about 3/8" from the tip of the collector. After drug elution, remove the tube and dissolve the residue by dipping the tube into a small volume of solvent several times. The collecting procedure can be repeated until enough residue is collected for an infrared analysis or other tests.

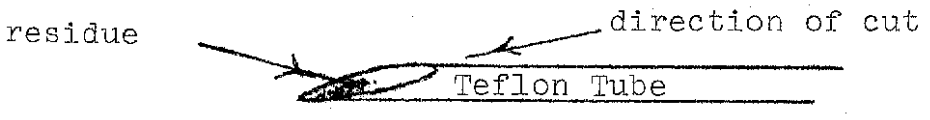
PROCEDURES

To separate Heroin in brown Mexican Heroin for infrared identification:

Dissolve a quantity of sample equivalent to 25 mg of Heroin in 20 to 30 ml Methylene Chloride. Filter the solution and concentrate to 1 ml or less. Inject 4 to 6 ul of solution onto the preparative column and collect the eluting peak. Repeat 5 to 7 more times to collect enough for a 1% KBr disk and I.R. analysis.

Purification of eluting drugs for Microcrystal tests:

A teflon tube is inserted into the collector about 2/8" into the collector opening. The drug is collected approximately 1/2" from the end of the teflon tube. A white residue is usually seen inside the thin walled teflon tube. After drug elution is complete the tube is removed and cut with a razor blade in the manner shown.



The exposed residue is mixed with a drop of microcrystal reagent on a glass slide to form crystals. Usually the amount of drug collected from one elution is enough to form a good crystal test.

Method for Thin Layer Chromatography:

A teflon tube is cut into a length of 8 cm and inserted into the collector tube until 1/8" teflon tube is exposed outside the collector tube. Just before the peak in question elutes a 1 ul Drummond Micro-pipette* is inserted approximately 1/4" into the teflon tube and held there until the peak has eluted. Remove the pipette and allow the pipette to self fill with a suitable spotting solvent. Spot the drug on a TLC plate and develop. For drugs sensitive to iodoplatinate or fast blue 2B, a sufficient amount of drug is collected (from a 20 ug injection), in the pipette to produce a visible spot on a TLC plate.

*Drummond "Micro-Caps", disposable micro-pipettes available from Drummond Scientific Company, Broomall, Pennsylvania.