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Benzoyltropeine, an unusual substance in street heroin samples

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ABSTRACT

Benzoyltropeine, an isomer of tropacocaine, was found in samples of heroin seized in Florence in 1981. Since there were no analytical data on benzoyltropeine, it was difficult to differentiate this substance from tropacocaine. In an effort to make the differentiation easier, the authors tried out various techniques and found thin-layer chromatography and high-resolution gas chromatography to be the most suitable for this purpose. A specific identification of isomers of these substances was obtained by using nuclear magnetic resonance and gas chromatography/mass spectrometry techniques.

Introduction

While analysing illicit heroin seizures in 1981 in Florence, an unusual substance, benzoyltropeine, was found for the first time [1]. With the exception of one report by the Mid-Atlantic Regional Laboratory of the Drug Enforcement Administration, United States of America, [2], the authors could not find any reported information on the presence of this substance in seized heroin.

Benzoyltropeine is an isomer of tropacocaine (benzoylpseudotropeine), the two substances differing only in the orientation of the groups on position 3 (figure I). Tropacocaine is a local anaesthetic. Benzoyltropeine also produces a mydriatic action. Differentiating between the two substances might be difficult because there are no available analytical data on benzoyltropeine. This paper reports the analytical data obtained when trying to differentiate these two substances using the following techniques: thin-layer chromatography (TLC), gas chromatography (GC), high-resolution gas chromatography (HRGC), nuclear magnetic resonance (NMC) and gas chromatography/mass spectrometry (GC/MS). This paper also describes a procedure that uses TLC, GC and HRGC to detect benzoyltropeine and tropacocaine in samples of seized heroin containing other drugs as well.

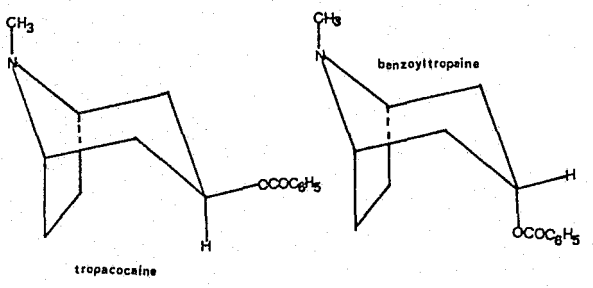

Figure I
Structures of tropacocaine and benzoyltropeine

Methods used

Thin-layer chromatography (TLC)

Substances under investigation (100 mg/dl): 10 mg of benzoyltropeine, tropacocaine, heroin, cocaine, procaine and lidocaine (as the free base) were each dissolved in 10 ml of ethanol.

Reference substances (100 mg/dl): 10 mg of morphine, phenmetrazine, methaqualone, strychnine, ethylmorphine (as the free base) and aminophenazone were each dissolved in 10 ml of ethanol.

Aliquots of all substances under investigation were spotted (10 µl) on each of two silica-gel precoated plates (Merck). On one plate, 10 µl of the morphine, phenmetrazine, methaqualone and aminophenazone reference solutions were also spotted. On the other plate 10 µl of the strychnine, ethylmorphine, phenmetrazine and methaqualone reference solutions were spotted. The developing solvents were:

System I. Acetone-toluene-ethanol-concentrated ammonium hydroxide (45:45:7:3) for the first plate.

System II. Methanol-concentrated ammonium hydroxide (100:1.5) for the second plate.

After a 10.0 cm development, both plates were dried and sprayed with iodoplatinate reagent (0.25 g of platinic chloride and 5 g of potassium iodide dissolved in water and diluted to 100 ml).

This TLC procedure was repeated five times using the reference compounds. An average R_f value was found for each compound. These averages were used as the abscissas of the reference curves that were subsequently generated. For each analysis, the R_f values of the developed reference compounds were used as ordinates and a reference curve was

plotted using the average R_f values described above as the abscissas. These reference curves were then used to determine the corrected R_f value of the analytes in question. For each of these analytes on a given plate, its R_f was used as the ordinate to locate a corresponding abscissa value which was designated as the corrected R_f value for that analyte. Five separate analyses of mixtures of analytes and reference compounds were made in each system [3]. The resulting corrected R_f values were statistically evaluated (table 1).

Table 1

Corrected R_f values[a] in the two developing solvents

Substance	*Solvent system I*	*Solvent system II*
Benzoyltropeine	40.8 ± 1.25	33.6 ± 0.45
Tropacocaine	60.3 ± 1.79	55.5 ± 0.77
Heroin	56.1 ± 1.25	59.6 ± 0.28
Procaine	65.9 ± 0.94	76.2 ± 0.48
Cocaine	89.3 ± 1.25	82.0 ± 0.53
Lidocaine	84.7 ± 1.30	88.8 ± 0.48

[a] Average for five values ± the standard deviation.

Gas chromatography (GC)

The retention index (I_r) values of benzoyltropeine, tropacocaine, heroin, cocaine, procaine and lidocaine were determined on a Carlo Erba series 4200 gas chromatograph, equipped with a flame ionization detector. The glass columns (2 m × 3 mm ID) were packed with:

System I. 2% SE-30 on Anakrom ABS 90 – 100 mesh.

System II. 2% XE-60 (one part) +2% OV-17 (two parts) on Chromosorb W 80 – 100 mesh.

Oven temperatures were 220° and 260° C for system I, 210° and 250° C for system II. Detector and injector temperatures were 300° C for both systems. The nitrogen flow rate was 50 ml/min.

Substances under investigation (10 mg/dl): 10 mg of benzoyltropeine, tropacocaine, heroin, cocaine, procaine and lidocaine (as the free base) were each dissolved in 100 ml of ethanol.

Hydrocarbon reference solutions (10 mg/dl): 10 mg of four hydrocarbons (chains of 20, 22, 24 and 26) were each dissolved in 100 ml of ethanol).

The substances under investigation were tested on each of the two GC systems at the two different temperatures by injecting 1 µl of each solution mixed within the syringe with 1 µl of each of two hydrocarbon reference solutions. The respective retention times were used to calculate the retention index I_r as described by Kovats [4]. The results are shown in table 2.

Table 2

Retention index values obtained by using the two gas chromatography (GC) systems

	GC System I		*GC System II*	
	Oven temperature (°C)		*Oven temperature (°C)*	
Substance	*220*	*250*	*210*	*250*
Lidocaine	1900	1850	2166	2139
Benzoyltropeine	1968	1930	2240	2304
Tropacocaine	1974	1940	2253	2313
Procaine	2029	2000	2393	2452
Cocaine	2200	2235	2565	2643
Heroin	2607	2643	...	3219

High-resolution gas chromatography (HRGC)

Mixture of substances under investigation (10 mg/dl): 10 mg of benzoyltropeine, tropacocaine, heroin, cocaine, procaine, lidocaine (as the free base) and caffeine were all dissolved in 100 ml of ethanol.

An aliquot of 1 µl of the mixture solution was injected into a Carlo Erba series 4160 chromatograph equipped with a capillary glass column (25 m × 0.4 mm ID) and a flame ionization detector. The stationary phase was SE-52. The hydrogen flow rate was 3.5 ml/min. Programmed temperatures were: initial 180° C (2 min), final 270° C (2 min). Detector and injector temperatures were 320° C. (See figure II.)

Nuclear magnetic resonance (NMR)

The proton NMR spectra of benzoyltropeine and tropacocaine were recorded at 30° C on a Varian CFT 20 operating at 80 MHz. The samples were dissolved in $CDCl_3$ (about 0.1 mol/l). Tetramethylsilane was added as an internal standard. (See figure III.)

Gas chromatography/mass spectrometry (GC/MS)

The benzoyltropeine and tropacocaine were analyzed on a LKB series 2091 apparatus. The glass column (2 m × 3 mm ID) was packed with 3% SE-30 on Chromosorb W 100 – 120 mesh. Temperatures of the oven, ion source and separator were 220°, 250° and 230° C respectively. The electron energy was 20 eV.

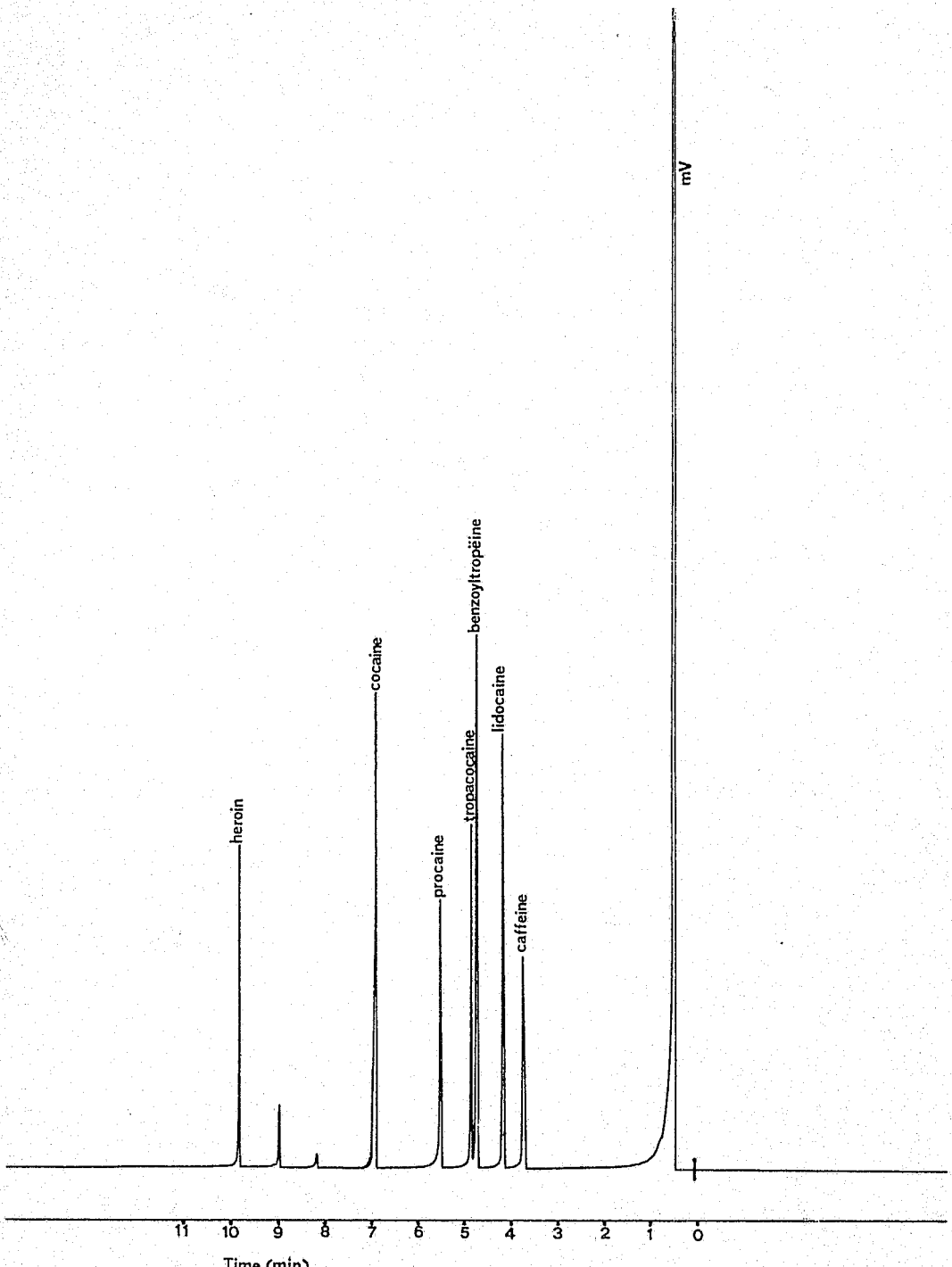

Figure II

High-resolution gas chromatogram of substances under investigation

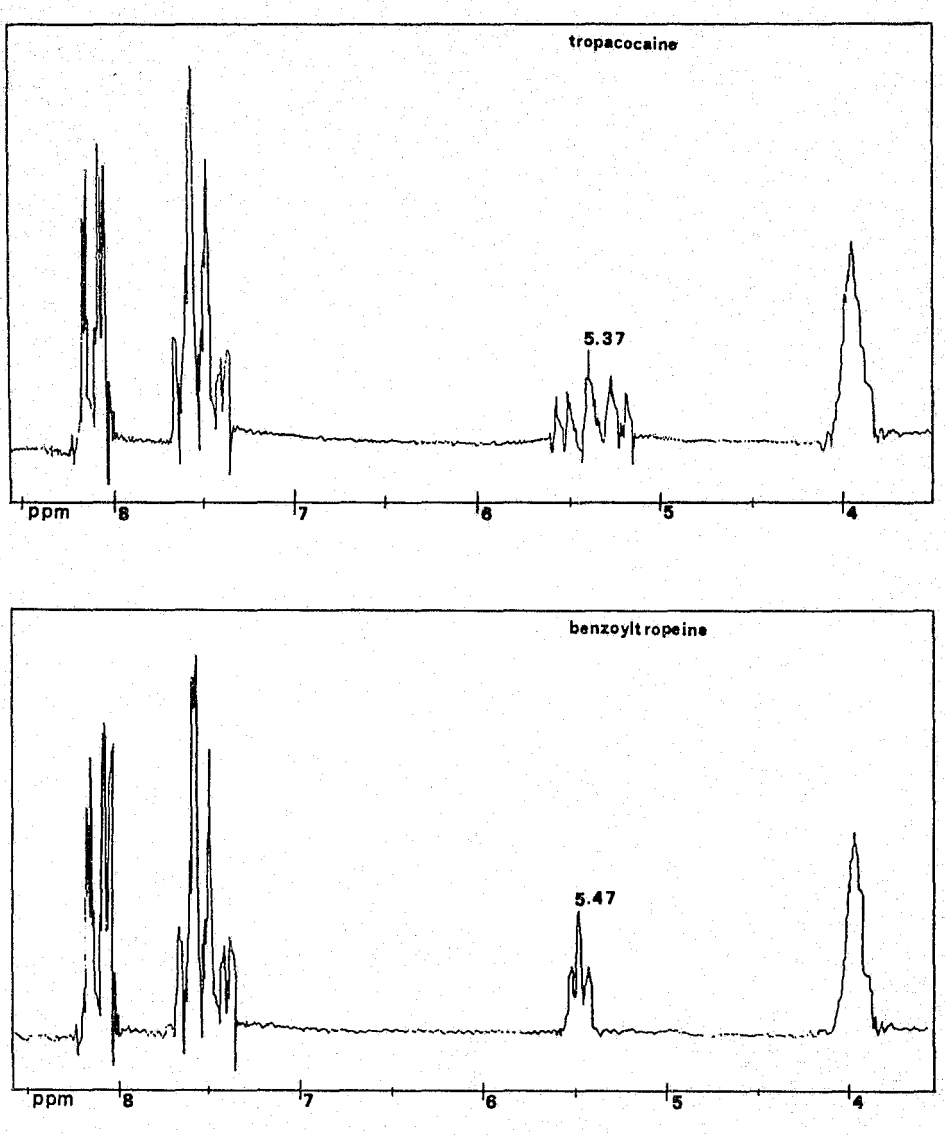

Figure III

The proton nuclear magnetic resonance spectra of tropacocaine and benzoyltropeine

Reference solutions (10 mg/dl): 10 mg of benzoyltropeine and tropacocaine were each dissolved in 100 ml of ethanol. 1—2 µl of each solution were injected into the column under the conditions described above.

The complete mass spectra of both substances is shown in figure IV.

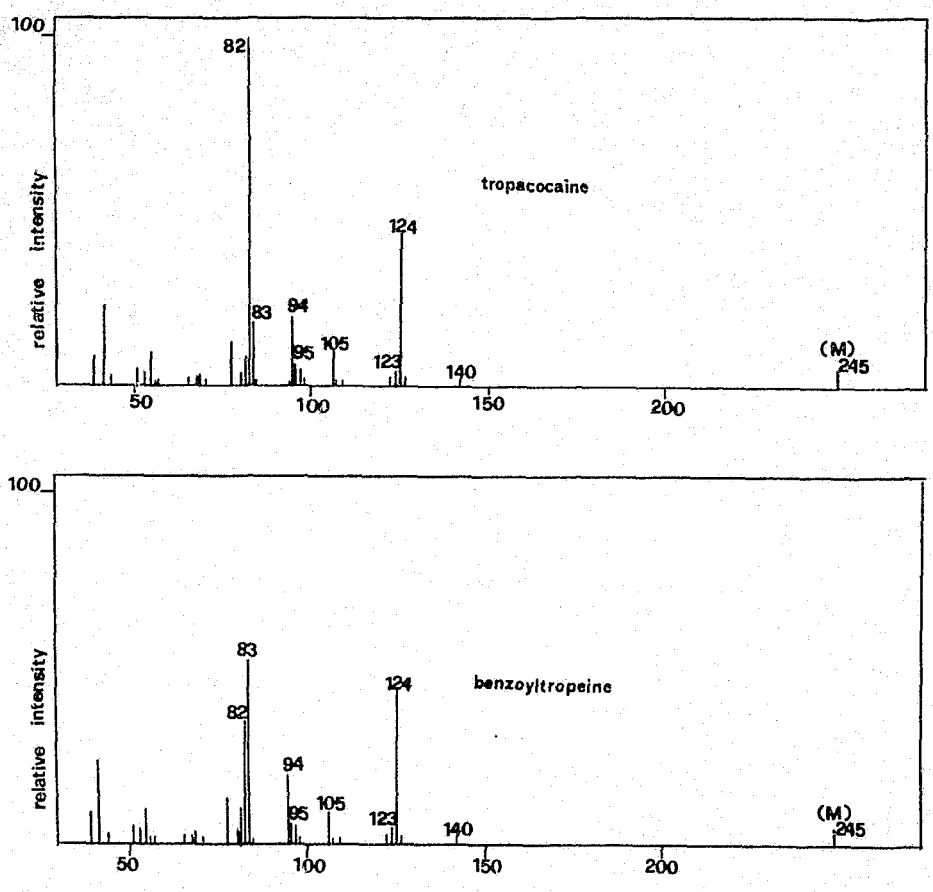

Figure IV

Mass spectra of benzoyltropeine and tropacocaine

Results and discussion

The corrected mobility data in TLC of benzoyltropeine and tropacocaine in comparison with heroin, cocaine, procaine and lidocaine (table 1) indicate that benzoyltropeine is easily differentiated from tropacocaine with both solvent systems. The GC results (table 2) indicate that the substances examined can be differentiated under the described conditions, but the benzoyltropeine and tropacocaine indices are so similar that their differentiation by GC presents some difficulty. On the other hand, HRGC analysis gives a good separation of both isomers and of all other drugs tested (figure II).

A further means of differentiating benzoyltropeine from tropacocaine is given by NMR measurement. The proton NMR spectra of both substances are similar except for the signal assigned to the H on position 3, which is a quintet (J = 9 Hz) centred at 5.37 ppm downfield from tetramethylsilane for tropacocaine and a triplet (J = 4.5 Hz) centred at 5.47 ppm for benzoyltropeine (see figure III). This difference has been ascribed to the respective equatorial or axial orientations of that H in benzoyltropeine and tropacocaine.

The complete mass spectra for benzoyltropeine and tropacocaine given in figure IV differ in the relative abundance of fragments of mass number m/e 82 and 83. A greater abundance of m/e 83 is indicative of benzoyltropeine in our system.

Conclusions

The TLC and HRGC methods, as applied in our study, were found to be the most suitable techniques for differentiating benzoyltropeine from tropacocaine. The NMR and GC/MS spectra of benzoyltropeine and tropacocaine showed particular differences in the structure of the two isomers and a good specific identification might be obtained with these techniques.

The positive differentiation of benzoyltropeine from tropacocaine and from other substances commonly present in street heroin samples is possible, using the analytical systems described above. This is important because benzoyltropeine has been found frequently in recent seizures of heroin in Italy. This heroin was mainly destined for the international illicit drug traffic, particularly for the market in North America.

Acknowledgements

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