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Heroin Abuse and a Gas Chromatographic Method for Determining Illicit Heroin Samples in Singapore

In the last few years the pattern of drug abuse in Singapore (an island city-republic with a land area of 584 km² and a population of 2.3 million) has undergone dramatic changes. The changing pattern resulted in the introduction in 1973 of the Misuse of Drugs Act (MDA) to replace the Dangerous Drugs Act and the Drugs (Prevention of Misuse) Act, which were found to be inadequate. The abuse of Mandrax (methaqualone) rose to a high point in 1973 and 1974 [1] but tapered off to almost nil in 1976. However, during this period there was an alarming increase in heroin abuse.

Table 1 shows the number of positive heroin, morphine, and Mandrax seizures and also the number of urines tested for drugs. The percentage of morphine-positive urines increased from 6% in 1972 to 40% in 1976. To a certain extent it is possible to differentiate the common narcotic drugs consumed by an abuser based on the ratio of the amounts of codeine/morphine excreted in the urine [2].

The upsurge in the abuse of heroin, one of the most potent of the narcotic drugs, prompted the incorporation of a number of amendments to the MDA in December 1975, the most noteworthy being the mandatory death sentence for traffickers caught with more than 15 g of diacetylmorphine or 30 g of morphine. The line drawn between possession and trafficking was lowered to 2 g for diacetylmorphine and 3 g for morphine (previously it had been 5 g each). Heavier penalties were introduced for drug offenses in general, the degree of severity of punishment rising with increasing amounts of drug implicated. For trafficking there is no option of a fine, and whipping of the buttocks with a cane is also mandatory. A simplified presentation of these penalties is shown in Table 2.

These are drastic measures, and the first conviction under the death penalty was obtained in May 1976. Since then a dozen more heroin traffickers have been sentenced to death, and a further 35 are still awaiting court trials. But, despite all these measures, the heroin problem continues to escalate unabated. In April 1977, the government stepped in with a massive campaign to ferret out all abusers and traffickers or, at the least, to contain the problem. The narcotics laboratories and the various enforcement agencies, such as the police, army, customs, immigration, social services, and drug rehabilitation centers, were coordinated and their resources and expertise mobilized in an all-out war against the sources of supply and demand for the drug. The effect of this operation will not be known until later.

The drug scene in Singapore over the past several decades did not fluctuate until the last eight years. In terms of the number of drug seizures, opium had been most prevalent since the late 19th century, a legacy of the early immigrants from China where opium smoking was then widespread. It remained the predominant drug of abuse through the

Received for publication 18 July 1977; revised manuscript received 23 Sept. 1977; accepted for publication 27 Sept. 1977.

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first half of the 20th century to the year 1969. Prior to World War II, licensed opium smokers were permitted by what was then the British Colonial Government to purchase prepared opium from Customs and Excise shops. From 1970 to 1972, the most abused drug was *Cannabis*; then for a two-year span (1973 to 1974), methaqualone was the biggest problem before the beginning of the increased abuse of heroin from 1975 onwards (Table 3).

The illicit heroin samples encountered in Singapore are either in powder or granular form. Sometimes the associated paraphernalia such as syringes, spiked cigarettes, and containers are also found. The granules in plastic bags come in shades of light brown or pinkish brown. The powder is packed in plastic vials (one full vial containing about 1 g) and, more recently, stuffed in 4-cm-long plastic drinking straws (containing about 0.1 g each) ready for use. This type of heroin is known locally as "No. 3" or "Asian" heroin. Similar types have been found in North America [3] and more recently in Europe [4,5], where it is termed "Chinese" heroin. It differs from the types normally found in North America [6,7], where the diacetylmorphine content is lower (5 to 10%) and a greater variety of diluents and contaminants (such as quinine, procaine, caffeine, methaqualone, and sugars) is present.

Heroin abusers and addicts in Singapore, mostly youths below the age of 24, almost invariably consume the drug by inserting the powder into a cigarette (with the aid of a grooved wooden needle). If the cigarette is smoked tilted upwards the process is called "firing the ack-ack (antiaircraft) gun"[8]. Other modes of smoking have been observed; the one fast gaining popularity is the Hong Kong style "chasing the dragon," which was reported in 1958 [9]. In this method, the abuser tries to inhale as much as possible (chasing)

TABLE 1—Number of drug seizures and urines tested for drugs of abuse.

Samples	1972	1973	1974	1975	1976
Drug seizures, <i>n</i>					
Methaqualone	38	185	111	38	1
Heroin	3	8	47	387	1 672
Morphine	34	54	81	142	87
Urines tested for drugs of abuse, <i>n</i>					
Total samples tested	372	902	1420	3042	10 555
Samples positive for morphine ^a	22	48	213	1254	4 235
Samples positive for methaqualone	113	554	671	360	33

^a Mostly from heroin abusers.

TABLE 2—Misuse of Drugs Act Amendment 1975, Singapore.

Drug	Possession	Trafficking	Trafficking	Trafficking
Heroin, g	0 to 2	> 2 to 10	> 10 to 15	> 15
Morphine, g	0 to 3	> 2 to 20	> 20 to 30	> 30
Punishment	0 to 10 years jail and/or fine	5 to 20 years jail, 5 to 15 strokes of the cane	20 to 30 years jail, 15 strokes of the cane	death

TABLE 3—Pattern of the predominant drug of abuse in Singapore.

Drug	Period
Opium	late 19th century through 1969
<i>Cannabis</i>	1970 to 1972
Methaqualone	1973 to 1974
Heroin	1975 to present

of the column of curled smoke (dragon) emanating from the charred heroin powder placed on top of a piece of silvery foil (usually from a cigarette pack) heated by means of a lighted candle below it. Heroin injection, either intramuscularly or intravenously, is not a common practice in Singapore.

Heroin Estimation

Because under the amendments to the MDA the penalties depend on the quantities of diacetylmorphine involved, a precise method for the quantitation of diacetylmorphine in an illicit heroin sample is important. Several gas chromatographic (GC) methods have been reported [10-14] with a number of agents chemically unrelated to heroin being used as internal standards; some methods require the formation of derivatives, which involves an extra step in the procedure. Methods using related narcotic compounds as internal standards and which do away with derivative formation were explored. The present paper describes such a method, with codeine as the internal standard. The procedure is simple and rapid, one chromatogram taking 15 min to complete. The amount of O⁶-acetylcodeine and O⁶-monoacetylmorphine, both of which are invariably present in illicit heroin samples, can be estimated by a further step involving acetylation, which converts the monoacetylmorphine to diacetylmorphine.

Experimental Procedure

Apparatus

The gas chromatograph was a PE Model 900 equipped with a flame ionization detector. A PE Model 2 integrating calculator was used. The column was a 1-m by 6.35-mm outside diameter coiled glass column, prepacked with 3% OV-17 on 80-100 mesh Gas Chrom Q. The column temperature was 235°C, and the injector and manifold temperatures were both 250°C. The carrier gas was nitrogen at a flow rate of 55 ml/min; attenuation was 80; and the chart speed was 5 mm/min.

Reagents

Diacetylmorphine hydrochloride, codeine phosphate, and caffeine were obtained from the Singapore Pharmaceutical Department and complied with British Pharmacopeia 1973 specifications. Acetic anhydride, pyridine, and methanol were analytical-grade reagents obtained from British Drug Houses, Ltd.

Stock Solutions

Codeine standard solution (1 mg base/ml) was prepared as the internal standard by dissolving 138.8 mg of codeine phosphate in 100 ml of methanol.

Diacetylmorphine standard solutions of 5, 4, 3, 2, and 1 mg base/ml were prepared by dissolving appropriate amounts of the diacetylmorphine hydrochloride in 20 ml of ethanol.

Codeine and caffeine standard solutions were prepared in a manner similar to the diacetylmorphine standard solutions.

Acetylcodeine standard solutions were prepared from the standard codeine solutions by acetylation, as described later in this report.

Preparation of Standard Calibration Curves

Pipette 4 ml of the codeine internal standard into each of five stoppered 10-ml cylinders containing an equal volume of the five diacetylmorphine solutions. Mix and inject 1 μ l

each into the GC. Calculate the ratios of peak areas of diacetylmorphine/codeine by means of the integrator and then plot the graph of diacetylmorphine concentration (1 to 5 mg/ml) against the ratios of peak areas. Prepare similar calibration plots for caffeine and acetylcodeine. Figure 1 illustrates the excellent linearity of responses.

Sample Procedure

Estimation of Diacetylmorphine and Caffeine—Homogenize the illicit heroin sample by grinding it in a mortar. Add a weighed aliquot (about 25 mg) of the powder to a 10-ml glass stoppered centrifuge tube and dissolve in 4 ml of methanol. Pipette 2 ml into a second (similar) tube and inject 1 μ l into the GC. Reserve the solution in the first centrifuge tube for monoacetylmorphine and acetylcodeine determinations. Figure 2a shows a typical chromatogram. Then add 2 ml of the internal standard into the second tube, mix, and again inject 1 μ l into the GC (Fig. 2b). Calculate the diacetylmorphine content of the sample from the following equation:

$$\% \text{ w/w diacetylmorphine} = 200A/SW$$

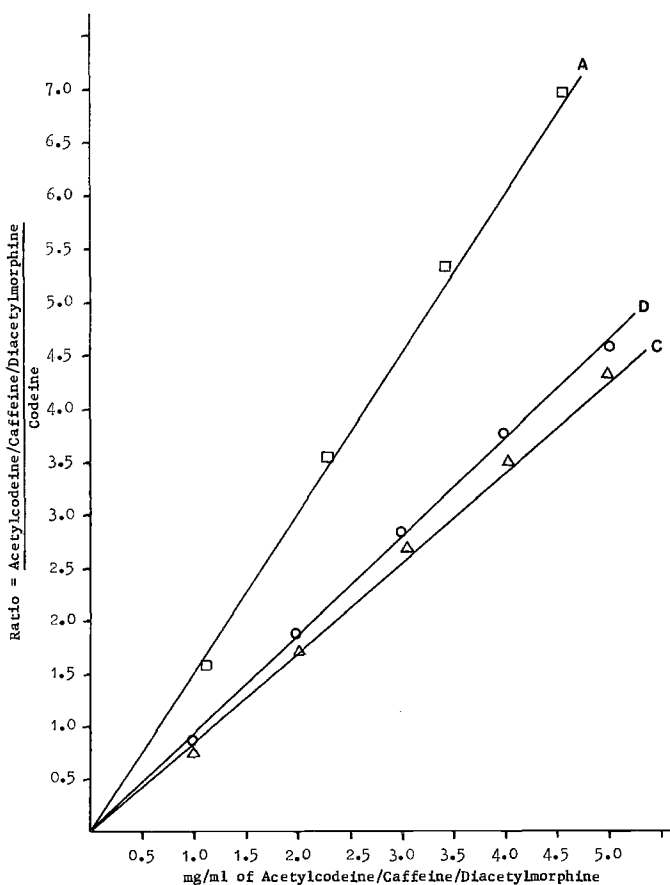


FIG. 1—Calibration curves for the determination of diacetylmorphine, acetylcodeine, and caffeine in illicit samples. A = acetylcodeine; C = caffeine; and D = diacetylmorphine.

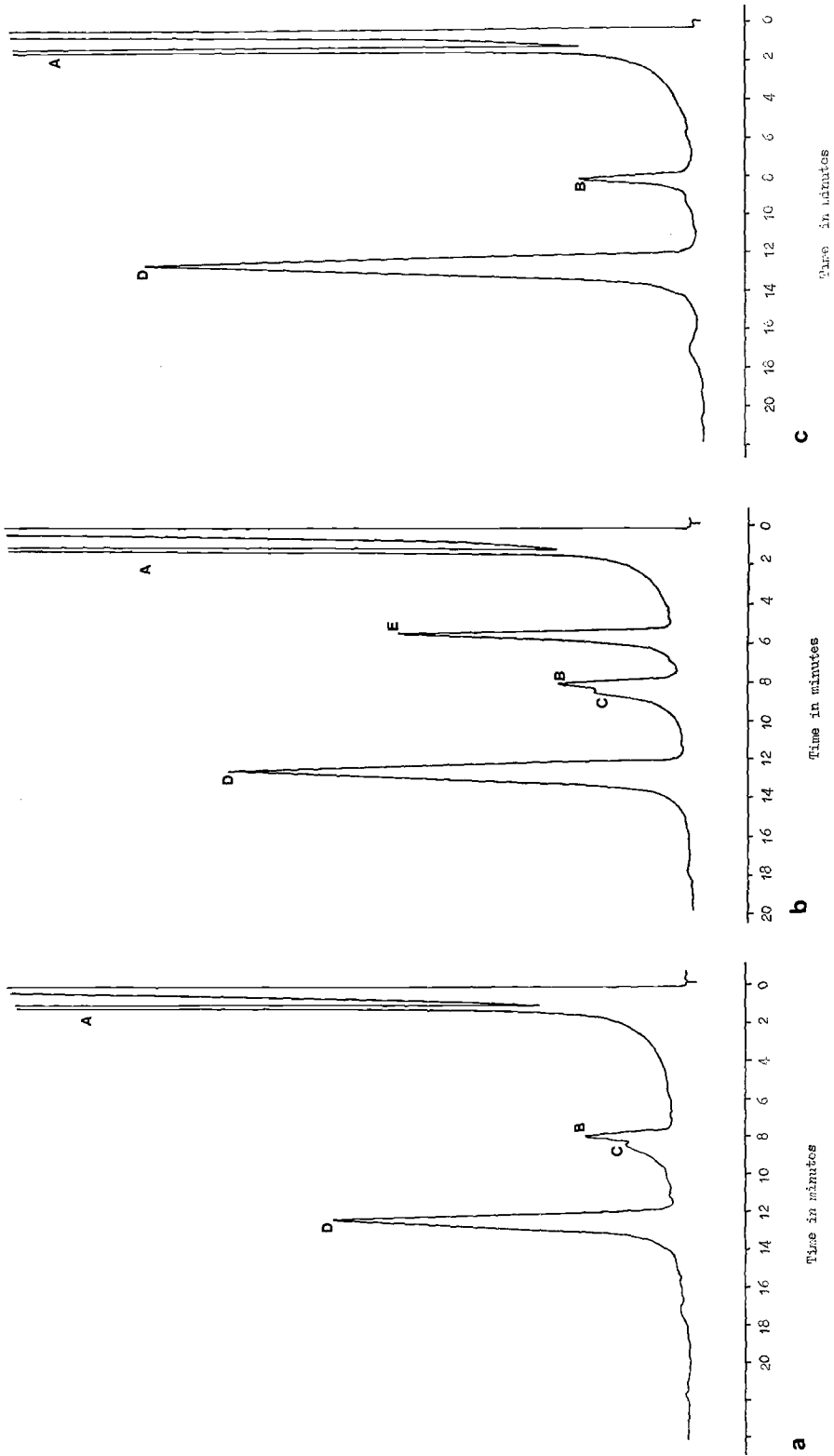


FIG. 2.—Chromatograms of an illicit heroin sample; (a) typical chromatogram; (b) with codeine internal standard; and (c) after acetylation. A = caffeine; B = acetylcodeine; C = monacetylmorphine; D = diacetylmorphine; and E = codeine internal standard.

where

- A = ratio of the peak areas of diacetylmorphine to codeine internal standard,
 S = slope of the calibration plot for diacetylmorphine (Fig. 1), and
 W = weight of the sample, mg.

The caffeine content may be similarly estimated. If, however, the chromatogram shows that codeine is present (as in Fig. 2a) the following corrected equation may be used:

$$\% \text{ w/w diacetylmorphine} = 400ab/SW(2a - b)$$

where

- a = ratio of the peak areas of diacetylmorphine to codeine before the addition of the codeine internal standard, and
 b = ratio of the peak areas of diacetylmorphine to codeine after the addition of the codeine internal standard.

This corrected equation need not be applied if the amount of codeine present in the sample is insignificant (that is, if $a > 100$, an error of $< 1\%$ of the diacetylmorphine content is involved).

Estimation of Monoacetylmorphine and Acetylcodeine—Evaporate the remaining 2 ml of sample solution in the first centrifuge tube to dryness under a stream of nitrogen and add 2 ml acetic anhydride and 0.5 ml pyridine. Stopper the tube and heat in a water bath at 80°C for 1 h to effect complete acetylation. The solution will become brownish. Remove the stopper and evaporate the excess reagents under a stream of nitrogen in the same water bath. Cool, dissolve the residue in 2 ml methanol, and inject 1 μ l into the GC (Fig. 2c). Then add 2 ml of the codeine internal standard, mix, and inject 1 μ l of the solution into the GC. The increased diacetylmorphine content is a measure of the monoacetylmorphine present in the sample. The acetylcodeine, which is now free from monoacetylmorphine, may then be determined from the calibration curve (Fig. 1).

Results and Discussion

The choice of codeine phosphate as an internal standard was substantiated by the following considerations: (1) no interfering peak was observed in the chromatogram before or after acetylation; (2) it is chemically related to the drugs being analyzed; (3) the pure standard is readily available and the methanolic stock solution is stable over an extended period of time; and (4) the elution of codeine well before that of diacetylmorphine in the chromatogram allows for a shorter time of analysis. In the other methods reported [11-14] the retention times of the internal standards used were greater than that of diacetylmorphine.

The accuracy and reproducibility data for diacetylmorphine and caffeine contents based on ten determinations of different weights of the same illicit heroin sample are shown in Table 4. The standard deviation and coefficient of variation values show that the accuracy and reproducibility of the method is good and comparable with the GC [14] and high-pressure liquid chromatography [5] methods.

Table 5 shows the retention time data of the four components of illicit heroin samples and codeine and Table 6 the results of analysis of twelve heroin samples.

Derivative formation by means of acetylation was required to quantitate the monoacetylmorphine and acetylcodeine since both were fused together in the unresolved doublet peak. In most samples the acetylcodeine was present to a larger extent than monoacetylmorphine. The shape of the doublet peak in Fig. 2a is that of a sample with about equal amounts of monoacetylmorphine and acetylcodeine. An example of a sample in which the

TABLE 4—Accuracy and reproducibility data for the GC method.

Weight of Sample, mg	Diacetylmorphine, % w/w	Caffeine, % w/w
10.0	36.8	26.8
15.0	36.3	26.8
20.0	36.6	26.6
25.0	35.5	25.6
30.0	35.9	26.3
35.0	35.3	25.2
40.0	35.5	25.1
45.0	35.6	25.2
50.0	35.4	24.9
55.0	35.7	25.0
Mean	35.9	25.8
Standard deviation	0.52	0.78
Coefficient of variation, %	1.4	3.0

TABLE 5—Gas chromatographic retention time data for codeine and the components of illicit heroin samples.

Drug	Retention Time, min	Relative Retention Time
Caffeine	1.25	0.23
Codeine	5.45	1.00
O ⁶ -acetylcodeine	7.92	1.45
O ⁶ -monoacetylmorphine	8.33	1.53
Diacetylmorphine	12.33	2.26

monoacetylmorphine content is much larger than the acetylcodeine content is illustrated in Fig. 3. In fact, the characteristic shape of this doublet peak can provide an indication of the proportion of monoacetylmorphine vis-à-vis acetylcodeine.

Analysis of more than a thousand illicit heroin samples seized in Singapore revealed that all of them contained diacetylmorphine, monoacetylmorphine, acetylcodeine, and the diluent caffeine (Fig. 2a). Thin-layer and paper chromatography confirmed the absence of morphine, codeine, and other drugs. Sugars and starch were also not detected. In most of the samples the diacetylmorphine was in the form of the hydrochloride, although in several instances only the base was present. The diacetylmorphine content of most of the illicit samples was within the range of 30 to 50%. There were a number of cases in which the diacetylmorphine content exceeded 70%, with correspondingly low values for caffeine.

The total diacetylmorphine content after acetylation (Table 6, Column *b*) was in good agreement with the results of the nitrite colorimetric method (British Pharmacopeia 1973) for diacetylmorphine after hydrolysis. This confirmed the complete conversion of monoacetylmorphine to diacetylmorphine by the acetylation procedure. There was less variation in the acetylcodeine (4 to 10%) than monoacetylmorphine contents. The greater range of monoacetylmorphine values (1 to 14%) could be the result of incomplete acetylation of morphine from the use of wet acetic anhydride during preparation, or partial hydrolysis of diacetylmorphine by moist air during storage, or both. Table 6 shows that the ratios of total diacetylmorphine to acetylcodeine for all the samples (except Sample 2) give an average of 9.6:1. This is in agreement with the findings of Nakamura and Ukita [15] and Nakamura [16]. It also approximates the morphine/codeine ratio found in illicit morphine samples analyzed by us in the laboratory. It could be inferred that these morphine samples were the starting material for the preparation of the illicit heroin samples found in Singapore.

Several analysts in Europe [4,5,17] have reported the detection of up to 10% strychnine

TABLE 6—Results of analysis of twelve illicit heroin samples, % w/w.

Sample	Column a	Column b	Column c	Column d	Column e	Column f	Column g
	Diacetyl- morphine	Total Diacetyl- morphine After Acetylation	Monoacetyl- morphine, b - a	Acetylcodeine	Caffeine	Total Diacetyl- morphine ^a	Diacetylmorphine b Acetylcodeine d
1	40.7	42.6	1.6	4.7	27.6	40.5	9.1
2	35.8	38.0	1.8	6.9	25.6	39.0	5.5
3	31.1	48.1	14.3	4.3	23.9	46.8	11.2
4	54.4	56.9	2.1	6.6	19.1	55.7	8.6
5	41.0	42.0	0.8	5.0	17.2	41.9	8.4
6	36.2	42.0	4.9	4.0	21.3	43.5	10.5
7	39.3	42.4	2.6	5.0	20.9	43.9	8.5
8	15.3	27.2	10.0	3.7	29.1	26.4	7.4
9	72.2	78.0	4.9	7.3	2.0	79.6	10.4
10 ^b	78.0	83.3	4.5	10.2	2.8	80.6	8.2
11 ^b	73.8	80.5	5.6	7.1	3.4	78.6	11.3
12 ^b	42.3	46.2	3.3	3.9	25.4	45.7	11.8

^aBritish Pharmacopeia 1973 nitrite method.^bNo chloride or other salts were detected in these samples.

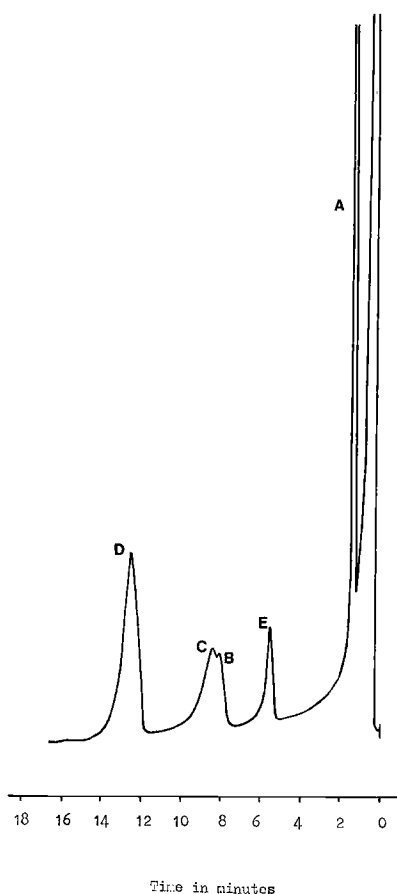


FIG. 3—Chromatogram of another illicit heroin sample with codeine internal standard. A = caffeine; B = acetylcodeine; C = monoacetylcodeine; D = diacetylmorphine; and E = codeine internal standard.

in some of the similar-type "Chinese" heroin samples. However, we found not strychnine but significant amounts of acetylcodeine in all the samples analyzed; acetylcodeine was not reported by other workers [3,4,5,17]. The presence of acetylcodeine in illicit heroin preparations had been previously demonstrated by paper, thin-layer, and partition chromatography [15,16,18].

Summary

The abuse of heroin (diacetylmorphine) in Singapore escalated sharply in 1975 and 1976, as indicated by the 35-fold increase in the number of heroin seizures and the 20-fold increase in the urine samples containing morphine since 1974. A rapid and simple GC method has been described to estimate diacetylmorphine (and caffeine). Monoacetylmorphine and acetylcodeine may be ascertained by an additional step involving acetylation. All gas chromatograms of a large number of samples analyzed consistently had the same pattern, indicating that they possibly had a common origin. This GC "fingerprint," together with the quantitative data, appears to be characteristic of the illicit Asian or Chinese type of heroin found in Singapore. The proportions of the four major ingredients in some twelve typical samples have been tabulated. Statistical data confirming the accuracy and reproducibility of the analytical method have also been presented.

Acknowledgment

The authors would like to thank the acting director, Department of Scientific Services, Mr. M. C. Dutt, for permission to publish this paper and the senior laboratory technician, Mr. K. L. Tham, for drawing the figures.

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