UNITED NATIONS

SCIENTIFIC AND TECHNICAL NOTES

SCITEC/5
February 1989

Some Aspects of the Gas Chromatographic (GC) Analysis of Heroin

Henk Huizer and Anneke J. Poortman

Forensic Science Laboratory, Rijswijk, The Netherlands

V.89-51669

Introduction

Several GC methods have been described for the analysis of heroin, and some reviews have been published on the subject (1, 2, 3). Mostly non-polar or slightly polar stationary phases and packed columns have been used in combination with FID. However, for the analysis of illicit heroin samples containing acetylcodeine and O^6-Monoacetylmorphine (6MAM) (sometimes also morphine), derivatization of the samples was performed -- mostly by trimethylsilylation, acetylation or propionylation - to enable the quantification of the compounds mentioned (4, 5, 6). For the determination of O^3-monoacetylmorphine (3MAM), derivatization with heptafluorobutyric anhydride (HFBA), in combination with electron capture detection has also been applied (7). In recent years, capillary columns have been introduced in the GC analysis of heroin (8, 9, 10) using the same stationary phases as used for packed columns. Capillary columns have also been used for studies of the profiles of illicit heroin samples together with derivatization with MSTFA (11), and for the detection and determination of minor impurities, formed during the manufacture of heroin, using HFBA as derivatizing agent (12).

For routine quantitative determination of heroin, GC using packed columns without derivatization has very extensively been used and this method is still widely applied, although many laboratories have started to use high pressure liquid chromatography (HPLC). However, GC is not a method without problems. In fact, Brochmann-Hanssen and Baerheim Svendsen (13), studying GC separation of alkaloids, using on-column injection on packed columns, mentioned decompositions (cotarnine), adsorptin (morphine), dehydration in the injection port (atropine), and transesterifications (heroin in the presence of codeine or morphine). For the last two phenomena, the amount of glass wool was observed to be an important factor. For the analysis of illicit heroin, it is important to note the authors' observation that, in the presence of glass wool, both 3MAM and 6MAM could be converted to morphine and heroin.

It is well known that many compounds degrade when they come into contact with hot metal surfaces. Even nickel, which was claimed to be little reactive, proved to be insufficiently inert for heroin analysis. Most authors applied glass columns (14). Much attention has also been paid to the deactivation of the solid support of the glass wall and the glass wool.

Gough and Baker (15) discussed problems of adsorption and thermal instability of heroin during GC. They compared several columns, each containing the same solid support coated with another stationary phase. Their results directly related to the stationary phase used, without paying attention to the many other important factors that determine the quality of a column. Therefore, their conclusion that some stationary phases (like OV-1) were not suited because of adsorption, may not be correct, especially since only one column per stationary phase was investigated. However, the non-ideal GC behaviour of heroin was, again, clearly demonstrated.

Dybowski and Gough (16) found differences in the results obtained with HPLC and GC, which they attributed to transacetylation. It was demonstrated that the main route of transacetylation occurred via the 3-acetyl group.

Illicit heroin samples are often cut with other substances and the influence of some diluents like sugars and mannitol, on the results of the analysis of heroin has been reported (17, 18).

In this paper several phenomena that can be expected to occur during the GC analysis of heroin samples, are summarized. Data were obtained from the literature, from discussions with colleagues dealing with the analysis of heroin, and from our own experiments and experience.

All phenomena described may occur; however, in practice not all of them will actually occur and certainly not all of them at the same time or in the same gas chromatograph.

Experimental

Apparatus

Gas chromatograph: Perkin Elmer Sigma 3. Autosampler: Perkin Elmer AS 100. Data station: Perkin Elmer Sigma 15. Detector: FID.
Conditions:

A. Injector/detector temp. 300°, oven 260°, glass column, 6 ft x 2 mm ID, suited for on-column injection, carefully deactivatized as described under "Methods". Carrier gas nitrogen, 30 ml/min.

B. As described under A, but with a standard glass column and an injection port equipped with a glass liner.

C. Injector/detector temp. 300°, oven 250°, split-splitless injection port. Fused silica capillary column, 25 m x 0.24 mm ID, with a chemically bonded methyl silicone as stationary phase, film thickness 0.11 um (CP-Sil 5 CB, Chrompack, Middelburg, the Netherlands). Carrier gas nitrogen; inlet pressure 100 kPa, split 1:100.

Packings

Packings were 3% OV-17 on Chromosorb W HP, and 3% OV-1 on Chromosorb W HP, 80-100 mesh, commercially obtained, pretested, (Chrompack).

Methods

Quantitative analysis of heroin

1. 20-30 mg of heroin in 10.0 ml of methanol, containing 0.5 mg/ml codeine as internal standard.
2. 20-30 mg of heroin in 10.0 ml of chloroform, containing 0.5 mg/ml octacosane as internal standard.

Silylation of glass columns (19)

The columns were filled with a mixture of hexamethyldisilazane, trimethylchlorosilane and pyridine (2:1:10), heated in a water bath during 20 min at 75°C and rinsed with ethanol.

Injections

A. Manual injections were made with a syringe SGE type A-RN, using two different injection methods.

Method 1 consisted of filling the needle + barrel up to the 0.5 ul mark. Since the needle was 0.8 ul, the syringe contained 1.3 ul. After injection the volume of the liquid left behind was about 0.3 ul; thus, about 1 ul of chloroform was introduced into the GC, half a microliter being sprayed, and half a microliter by evaporation from the needle.

Method 2 ("solvent flush" method) consisted of the suction of 1.5 ul chloroform, 0.5 ul air, 1 ul sample, 1 ul air, respectively. In this way about 1 microliter of sample was introduced into the GC, all by spraying.

B. Autosampler injection principle is determined by the construction of the autosampler. In the autosampler used by us, the syringe barrel + needle are flushed with the sample solution, that is entering the back of the syringe due to overpressure; the injection is achieved by the forward movement of the barrel and needle, followed by a movement of the barrel over the needle.

Results and discussion

Transacetylation

1. In GC analysis of heroin metal column connectors should be avoided because catalytic transacetylation may take place. Although injectors with glass liners can be used, on-column injection offers less risk. In our experiments, using the conditions under A (on-column injection), the injection of a methanolic solution of heroin (base or hydrochloride) showed no MAM formation, whereas the same solutions yielded under conditions B, (glass lined injector) a small but distinct peak of MAM (MAM is not specified as 3MAM or 6MAM even if the formation of 6MAM is most probable because the separation of the monoacetylmorphines is insufficient for discriminating between them using standard OV-1 and OV-17 columns).

2. When chloroform was used as solvent instead of methanol under conditions B, the MAM formation was considerably less, suggesting that transacetylation is also dependent on the solvent used.

3. Although a low injection temperature is usually recommended, we observed no distinct MAM formation when using on-column injectin at 300°C. Even at an injection temperature of 400° no MAM formation from heroin hydrochloride was observed; however, for the methanolic heroin base solution an increase of MAM took place.

4. Under on-column conditions, a methanolic solution of heroin hydrochloride containing codeine showed a slight formation of acetylcodeine whereas under the same conditions methanolic solution of heroin base gave a substantial increase of acetylcodeine as well as MAM (see Figure 1). Therefore, transacetylation depends also on the form in which heroin is present in the sample.

5. A methanolic solution of heroin hydrochloride containing morphine hydrochloride showed under on-column injection conditions some transacetylation, resulting in a modest peak of MAM. Since morphine can be present in illicit heroin samples in considerable amounts, the influence of morphine must be considered. Dybowski and Gough (16) showed that the amount of MAM formed depended on the proportions of heroin hydrochloride and morphine hydrochloride. We obtained similar results for codeine. Although codeine is usually not present in substantial amounts in illicit heroin samples, it is sometimes used as internal standard (20). It can be concluded that, because of the risk of transacetylation, codeine should preferably not be used as internal standard in a GC determination of heroin.

Figure 1

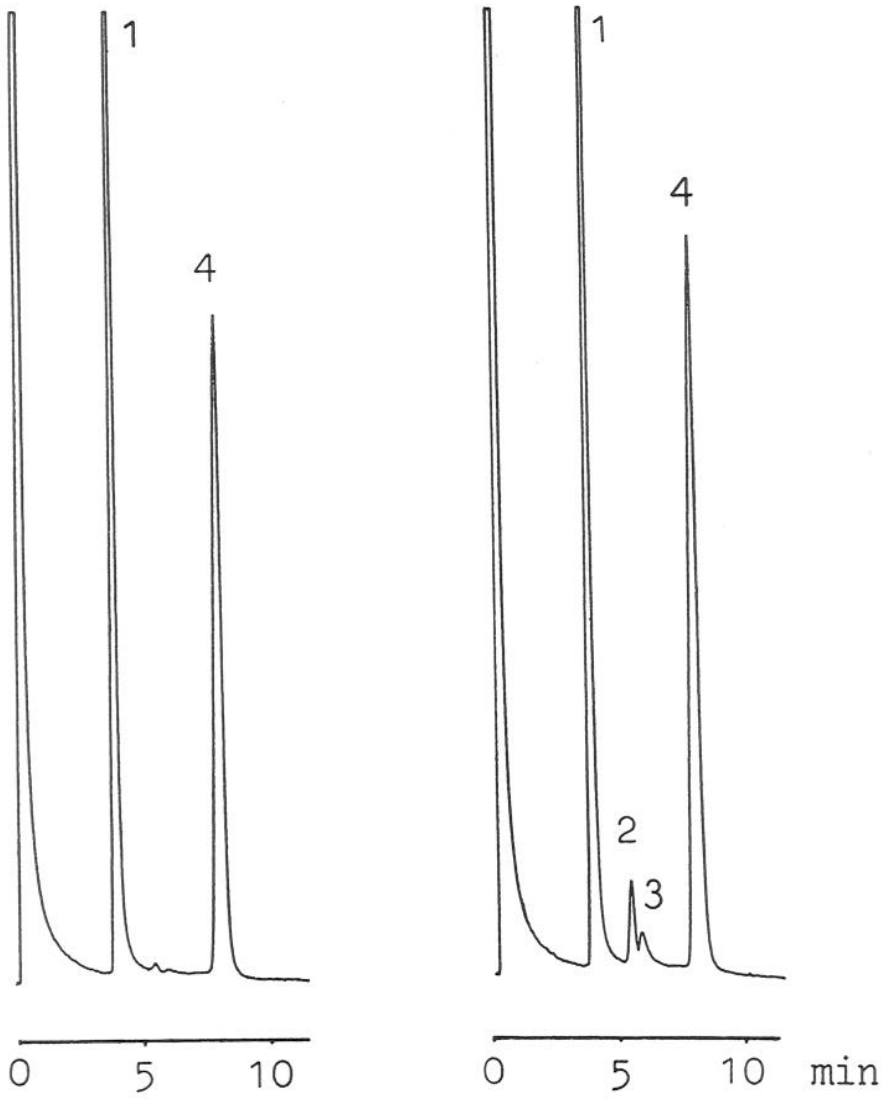

Fig. 1. Chromatogram showing the influence of heroin base/heroin hydrochloride on transacetylation. Left: codeine and heroin hydrochloride in methanol (1 mg/ml). Right: codeine and heroin base in methanol (1 mg/ml).

1 = codeine; 2 = acetylcodeine; 3 = 6MAM; 4 = heroin.

A summary of the above experiments on transacetylations, using GC conditions A, is as follows:

Table 1

Heroin hydrochloride Added compound	Solvent	Acetylcodeine	MAM
-	chloroform		-?
-	methanol		-?
codeine	methanol	+	+
morphine hydrochloride	methanol		+
morphine (base)	chloroform		++
codeine	chloroform	-	-
Heroin base Added compound			
-	chloroform		-
-	methanol		+
codeine	methanol	++	++
morphine hydrochloride	methanol		++

Strongest transacetylation reactions were observed for methanolic heroin base solutions, when morphine was present in the sample and the injection technique B (liner injection port) was applied. With chloroform solutions and on-column injection, transacetylation was minimum (see Table I).

6. The decomposition of heroin to MAM may be promoted by the presence of other compounds. Since illicit heroin samples are often diluted with a wide variety of substances, their influence on the quantitative determination of heroin should be considered.

We investigated the influences of procaine hydrochloride and paracetamol (acetaminophen) because these substances were considered as "acetylacceptors", and they have frequently been found in illicit heroin samples. Chromatography of a methanolic solution of heroin hydrochloride and paracetamol (1 resp. 2 mg/ml), even under on-column conditions, resulted in a decreased heroin peak, a distinct MAM peak, and peaks of paracetamol and acetylparacetamol. Also, the effect was dependent on the paracetamol concentration.

However, a similar experiment carried out with procaine hydrochloride did not give any acetylprocaine or MAM. In the contrary, procaine hydrochloride appeared to prevent the reaction between heroin hydrochloride and paracetamol, as shown in Figure 2. It was also noticed that procaine hydrochloride inhibited the MAM formation during GC of heroin base in methanol.

The behaviour of procaine hydrochloride must be considered as unusual, since procaine is easily acetylated by acetic anhydride, even at room temperature.

Figure 2

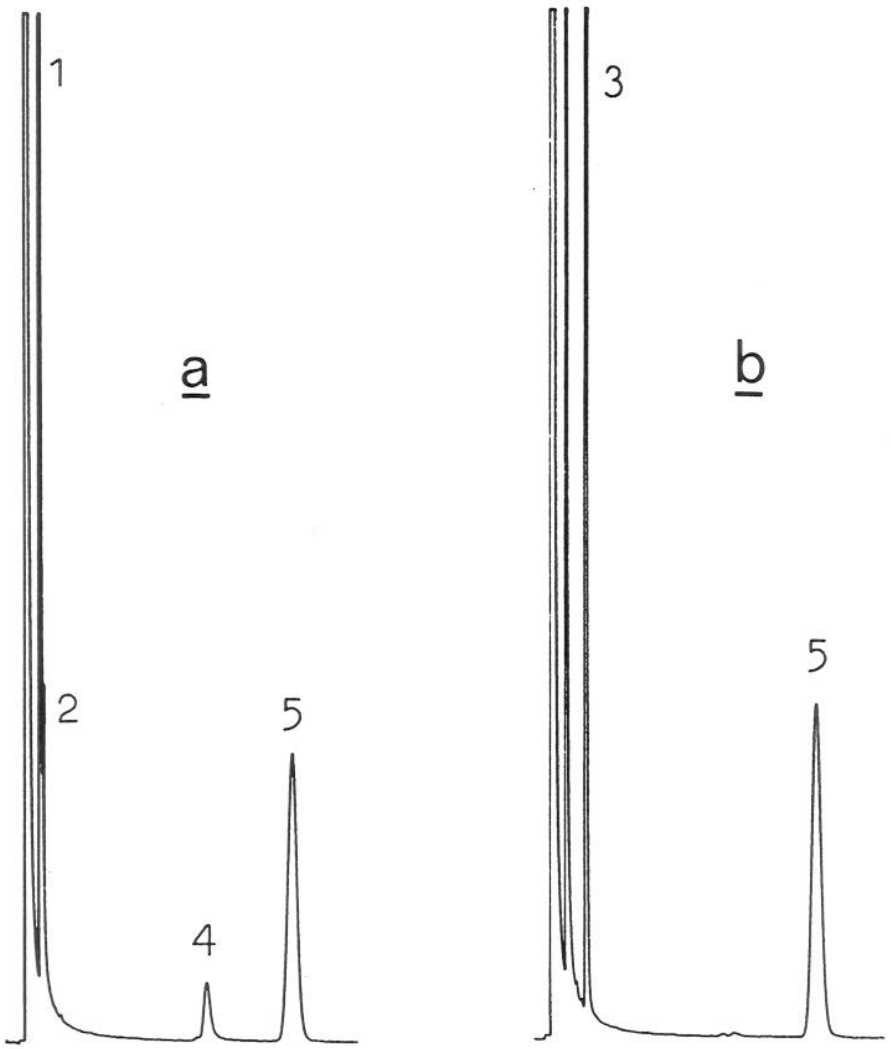

Fig. 2. Influence of procaine hydrochloride on the transacetylation between paracetamol and heroin hydrochloride.
a. paracetamol and heroin hydrochloride (1 mg/ml); b. paracetamol and heroin hydrochloride in the presence of procaine hydrochloride (2 mg/ml).
1 = paracetamol; 2 = acetylparacetamol; 3 = procaine; 4 = 6MAM; 5 = heroin.

Various sugars, mannitol (17) and ascorbic acid (16) have been found to influence heroin determinations. Whereas these influences can be explained by transacetylation reactions, also other - less easily explainable - influences have been found. For example, if lidocaine hydrochloride was present in a five-fold excess in a cocaine sample, a 20% decrease of the cocaine hydrochloride values was observed (18); we obtained similar results with heroin. While the influence of identified cutting agents on the quantitative determination of heroin can be investigated, described and eventually compensated for, if the sample has been cut with unidentified substances, it seems advisable to apply a second quantitative method, for example HPLC.

Figure 3

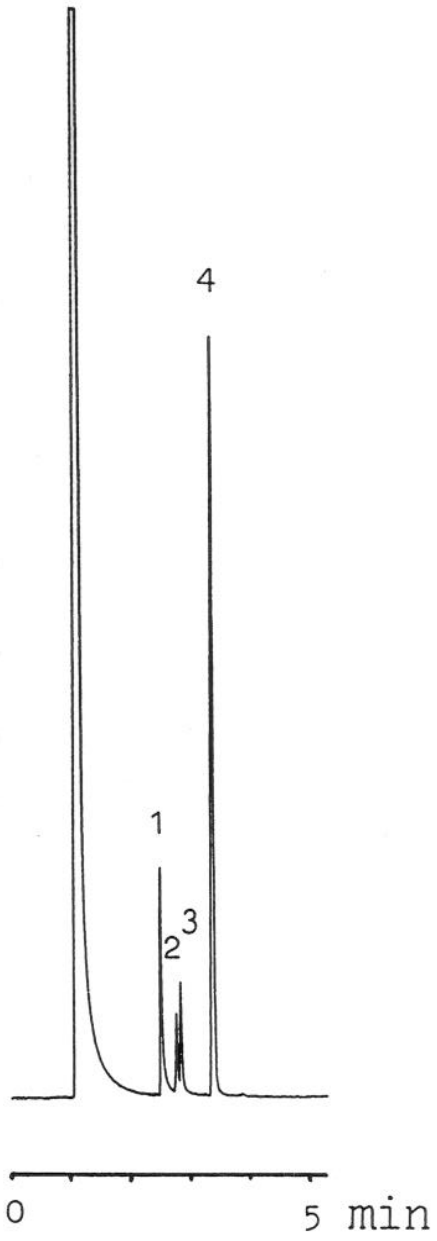

Fig. 3. Transacetylation between morphine hydrochloride and heroin hydrochloride (1 mg/ml each in methanol) on capillary system.
1 = morphine; 2 = 3MAM; 3 = 6MAM; 4 = heroin.

Protection of heroin against transacetylation can be achieved by means of silylating agents. After silylation of a paracetamol-heroin mixture in chloroform/methanol (9:1) with BSA no transacetylation could be observed.

7. Usually transacetylation will lead to loss of heroin in favour of formation of 6MAM. Also the reverse reaction, i.e. formation of heroin could be observed when 6MAM was injected together with acetylsalicylic acid in methanolic solution.

8. Transacetylation in the injection port was also observed under capillary GC conditions. Figure 3 shows the chromatogram obtained when heroin hydrochloride was chromatographed together with morphine in methanol. Both 3MAM and 6MAM can be observed. When a mixture of heroin and paracetamol in methanol were injected, only 6MAM was found. The results agree with those obtained by Dybowski and Gough who found that transacetylation predominantly involves the 3-acetyl group (16). The strongly protective influence of procaine was also observed in the capillary injector.

Adsorption

1. Gough and Baker (15) observed losses of heroin on packed columns with various stationary phases. They found 40% loss of response using an OV-1 column, and no loss on an OV-17 or an OV-210 column and ascribed the phenomena to differences in the properties of the stationary phases. It was considered useful to reinvestigate adsorption on OV-1 and OV-17. Six glass columns were treated and filled as described under Experimental; three of them were filled with 3% OV-1 and the other three with 3% OV-17 packing. The OV-17 columns gave about 4500 theoretical plates/6 ft while the OV-1 columns gave about 5000 theoretical plates/6 ft. The adsorption of the columns was compared by determining the relative responses of heroin (base) vs. octacosane. A column temperature of 250° was used for both phases and the results are presented in Table II.

Table II

OV-17	OV-1
2.76	2.95
2.78	2.95
2.66	3.06

Table II. Response ratios obtained for heroin/octacosane in chloroform, using an OV-1 and an OV-17 packing; three columns per packing.

The differences found between the two packings were small which is in disagreement with the results obtained by Gough and Baker (15). It is therefore concluded that adsorption is mainly determined by the effectiveness of the deactivation of the soiid support and the efficiency of the coating with the stationary phase, and not by the stationary phase itself. A good method for deactivation of the solid support is given by Street et. al (21), who showed that treatment of the support with benzoylchloride in pyridine before coating with the stationary phase results in columns with a marked reduction of adsorption - even for morphine.

2. Because procaine hydrochloride was frequently found in a certain period in illicit heroin samples, we used for heroin quantitation method No. 1, with methanol as solvent and codeine as internal standard (20). We found a variation in the response factors that was larger than what could be explained by variation in the FID response. Adsorption was considered as the most probable cause, especially since in this method codeine which can be easily adsorbed because of its alcoholic hydroxyl group, was used as internal

standard. Method No.2 , using chloroform as solvent and an alkane as internal standard, offers the advantage that transacetylation is minimum, and that adsorption of the internal standard is negligible. By regularly monitoring the heroin/alkane response ratio, a good impression of the quality of the column can be obtained. It is important to note that deviations in the linearity of the calibration curve, especially near the origin, may be strongly indicative for adsorption phenomena.

3. When analysing a series of heroin samples, it is important to reanalyse the standard at regular intervals. In ideal cases 100% should be found.

However, often an increase during the run is observed, which is indicative for adsorption phenomena. Usually the increase is small and then the use of an appropriate correction factor during the series seems permitted.

Typical results, obtained by automatic injection of a solution of hexacosane (C26), octacosane (C28) and heroin hydrochloride in chloroform during 6 hours are present in Table III.

Table III

Inj.No.	C26/C28	Heroin/C28	Inj.No.	C26/C28	Heroin/C28
1.	1.066	1.631	11.	1.067	1.700
2.	1.071	1.672	12.	1.059	1.702
3.	1.067	1.689	13.	1.057	1.705
4.	1.065	1.689	14.	1.061	1.711
5.	1.062	1.687	15.	1.062	1.701
6.	1.066	1.692	16.	1.056	1.692
7.	1.061	1.692	17.	1.058	1.704
8.	1.063	1.695	18.	1.055	1.701
9.	1.061	1.700	19.	1.058	1.704
10.	1.062	1.707	20.	1.062	1.704

Table III. Response ratios for hexacosane/octacosane and heroin hydrochloride/octacosane obtained by automatic injection.

An increase in the heroin/octacosane response is seen; after about 10 injections a stabilization is observed. The RSD's for heroin/octacosane were 1% for the series as a whole, whereas in the last 10 injections 0.3% was obtained. For hexacosane and octacosane the values were 0.4 and 0.3% respectively. The results indicate a saturation of the column with heroin. Some workers advise the saturation of the column by repetitive injections an excessive amount of compound (22) before the analysis .

The fused silica columns used in capillary GC are highly inert with respect to adsorption. However, adsorption may take place in the injection port, when support material or glass beads are used in the injection liner.

Deterioration

After an extensive use of a packed column, the increase in heroin response during a run was often considerable; also the variation between duplicate determinations showed sometimes big and inexplainable variations; the calibration line was not linear. On old OV-17 columns sometimes broad peaks were formed, eluting immediately after the heroin peak (the identity of the compounds responsible for these peaks has not yet been elucidated). In general, the beginning of the column appeared to be heavily deteriorated after injection of a great number of samples, leading to discolouration of the column, dark brown deposits and (sometimes) the presence of small rubber particles from the septa. Usually, the original column performance can be reproduced by emptying the first centimeters of the column, and refilling with fresh packing material. Such a refill may have a strong effect on the response factors obtained.

Injection

1. The reliability of a quantitative determination depends strongly on the reliability of the injection. Basically the injection may consist of two steps:

A. A number of small liquid particles is sprayed from the needle into the injection port.
B. If the needle is still filled with liquid after step A, additional evaporation of solvent, heroin and/or internal standard may take place from the needle. It can be assumed that in the injection spray, obtained in step A, the ratio heroin/internal standard is the same as in the solution to be analysed. In step B, problems can be expected concerning this point. When using manual injections, step B can be avoided by using the so called "solvent flush" method (Experimental, Method 2). However, when using autosamplers the "needle evaporation" can not always be avoided.

In order to investigate the influence of the injection technique on the quantitative determination of heroin, two different manual injection techniques were used, as described under Experimental. The results obtained for an injection time of about 4 sec. are given in Table IV.

Table IV

Method 1 (spray+needle evaporation)				Method 2 ("solvent flush" method)			
Areas		Ratios		Areas		Ratios	
C28	Heroin	C24/C28	Heroin/C28	C28	Heroin	C24/C28	Heroin/C28
815	2357	1.02	2.88	1610	4292	1.02	2.66
1025	2822	1.06	2.75	1434	3805	1.02	2.65
945	2684	1.00	2.84	1536	4089	1.02	2.66
895	2596	1.04	2.90	1717	4616	1.03	2.69
1006	2782	1.06	2.76	1492	3942	1.00	2.64
905	2774	1.01	3.06	1542	4190	1.01	2.71

Table IV. Areas and response ratios obtained for heroin hydrochloride/tetracosane in chloroform, using two different injection methods; (in both methods 1 ul chloroform on column).

The results show a large variation in relative responses for injection method 1, whereas this ratio is more stable with the "solvent flush" method. Furthermore, the absolute areas of the alkanes and of heroin using method 1 are only about 60% of what would be expected from the volume of evaporated chloroform solution (see Experimental). So, when using injection method 1, chloroform evaporates from the filled needle, without giving a proportional evaporation of heroin hydrochloride and the internal standard, octacosane; a major part of the substances stays behind.

Under the given circumstances, injection method 1 resulted in a somewhat higher ratio for heroin hydrochloride/octacosane than the "solvent flush" method. This would suggest higher evaporation of heroin than of octacosane. Indeed, when the residue left in the needle was taken up in chlororform and reinjected, a relative increase of the alkane response was observed. The different behaviour of heroin hydrochloride and the alkane can be attributed to differences in physical properties, like solubility and volatility.

The evaporation from the needle was investigated by three injections with only the needle filled; in these cases 0.5-0.6 ul of chloroform evaporated in the injection port. The amounts of heroin hydrochloride detected were 19, 14 and 21% of the "proportional" amount; for octacosane respectively 7, 11 and 14% were found. Thus, a large variation is observed for the absolute amounts and for the heroin/octacosane ratio as well. As a consequence, the best results in a quantitative determination can be expected from the "solvent flush" injection method.

2. Using our autosampler, the portion of the substance brought onto the column by needle evaporation is very important due to the large volume of the needle. The result obtained for the evaporation of the needle contents is given in Table V as a "0" ul injection. The injection volumes given as 0.5, 1.0 and 1.5 ul mean the amounts in addition to the volume present in the needle.

Table V

volume (µl)	areas		ratio heroin/octacosane
	octacosane	heroin	
0	1217	2289	1.88
0.5	2297	4870	2.12
1	3366	7402	2.20
1.5	4500	10080	2.24

Table V. Areas and ration heroin/octacosane (mean of 4 injections) obtained by autosampling, using different injection volumes.

The ratio strongly varies with the injection volume. The fault caused by the evaporation from the needle is enclosed in all values, but its portion decreases as the injection volume increases. Due to the influence of evaporation from the needle, calibrations may show differences from system to system. Therefore, ratios obtained by one injection technique can not be used for a determination using another injection technique.

3. When analyzing a standard solution of tetracosane, octacosane and heroin hydrochloride in chloroform by autosampling, variation of the injection time (namely the time when the needle stays in the injection port) between 1, 2 and 3 sec. did not result in a significant difference for the ratio tetracosane/octacosane. For the heroin hydrochloride/octacosane response ratio, no difference was found between 3 and 2 sec. However, an injection time of 1 sec. resulted in a 5% lower response. With heroin base no effect of the injection time was observed.

4. The response for heroin base and heroin hydrochloride was investigated by preparing a solution of heroin hydrochloride and octacosane (2 and 0.5 mg/ml respectively) in chloroform. The solution was divided into two parts; one part was shaken with sodium hydrogen carbonate solution. When both solutions were analysed using autosampling injection, 0.5 ul under GC conditions A, ... a 3% higher response was obtained for heroin base.

Such higher responses for bases have been described for cocaine (17, 22). Cooper (17) attributed the differences to acid hydrolysis of cocaine hydrochloride, although no proof for hydrolysis was given. In experiments with heroin, no indication of hydrolysis was obtained. Therefore the different response of salt and base was attributed to the needle evaporation of the injection. By repeating the experiment with an injection volume of "0" ul, the difference between salt and base could be increased; under these conditions the base gave a 5-8% higher response.

Also in capillary GC strong differences between the responses of salt and base were found. These may also be attributed to discrimination in the split/splitless injector (23, 24).

As a conclusion it is suggested that, when possible, a method should be used in which the results are independent of the form in which heroin is present.

One approach to solve the problem of the different responses for salt and base is the extraction of the illicit sample from a slightly alkaline solution into chloroform. This, however, is quite laborious for routine laboratories, and there is a risk of hydrolysis of heroin.

Another approach could be to use the base as reference when the base has to be analysed, and the hydrochloride when the salt has to be analysed. This method is good when only a few samples have to be analysed; for a series of samples it is quite unpractical. Sometimes -- especially in "cut" samples - it is not known whether the base or the salt is involved. Furthermore, the illicit samples may consist of mixtures of salt and base. Probably the simplest approach to solve the problem is to use more diluted sample solutions, and to inject larger volumes; in this way, the effect of the evaporation from the needle is minimized. The effects are also avoided by using the manual "sample flush" injection technique, or very short injection times.

Solubility

Usually the heroin in the illicit samples is present as base or hydrochloride, thus direct dissolution in chloroform (or methanol) is possible. However, occasionally heroin may occur as tartrate or citrate. In these cases the quantitative method has to be modified in order to achieve dissolution.

Internal standard

A number of internal standards have been recommended for the quantitative GC determination of heroin, e.g. tetracosane, octacosane, triacontane, or benzopinacolone, tetraphenylethylene, amitriptyline, diacetylnalorphine, codeine, squalane, cinchonine, cholesterol. (3, 4, 6, 8, 20, 25, 26, 27, 28, 29). Problems have been described above that can be expected to occur in the injection needle when the physical properties of the internal standard differ from those of heroin. In principle, it is preferable to use internal standards which are chemically related to the compound to be analysed. From this point of view, alkanes and benzopinacolone are not attractive. On the other hand, a related compound like codeine also showed some disadvantages. Diacetylnalorphine has to be synthesized from nalorphine and it may also undergo transacetylation. Thus, although each internal standard will show some disadvantages, a choice should be made depending on the aim of the analysis and the circumstances. There is always a risk that an internal standard coelutes with another compound in the sample. The use of two internal standards may, therefore, be useful.

Conclusion

The quantitative determination of heroin by means of GC is connected with a number of problems, such as adsorption, transacetylation, influence of other substances, as well as the form in which heroin occurs (salt or free base). The injection volume as well as the injection technique may also have influence on the results. However, by recognizing the problems most of them can be solved or avoided.

References

1. Gough T.A., Baker P.B., Identification of Major Drugs of Abuse Using Chromatography, J. Chromatogr. Sci. 20, 289 (1982).

2. Soni S.K., Dugar S.M., Separation of Standard Opiates and Their Analysis in Pharmaceutical and Illicit Preparations by Paired-ion Reverse-phase High-pressure Liquid Chromatography, J. Forensic Sci. 294, 297 (1984).

3. Huizer H., Analytical Studies in Illicit Heroin. Thesis, (1988).

4. Recommended Methods for Testing Heroin. ST/NAR/6, New York, United Nations, (1986).

5. Machata G., Vycudilik W., Gas Chromatographic Analysis of Illicit Heroin Samples, J. Anal. Toxicol. 4, 318 (1980).

6. Van Vendeloo F., Franke J.P., De Zeeuw R.A., Fingerprint Analysis of Illicit Heroin Samples by Gas Chromatography. Pharm. Weekbl. (Sci) 2, 129 (1980).

7. Moore J.M., Klein M., Identification of 03-Monoacetylmorphine in Illicit Heroin Using Gas Chromatography-Electron Capture Detection and Mass Spectrometry, 154, 76 (1978).

8. Demedts P., Van der Verren J., Heyndrickx A., Recent Developments in GC Column Technology. An Illustration of its Interest in Forensic Toxicology. Forensic Sci. Int. 23, 137 (1983).

9. Gloger M., Neumann H., Analysis of Heroin Samples by Capillary Gas Chromatography. Comparison of Glass Capillary Column and Packed Column. Forensic Sci. Int. 22, 63 (1983).

10. Mari F., Bertol E., Tosti M., Benzoyltropeine, an Unusual Substance in Street Heroin Samples. Bull. Narc. 36(1):59 (1984).

11. Neumann H, Gloger M., Profiling of Illicit Heroin Samples by High Resolution Capillary Gas Chromatography for Forensic Application. Chromatographia 16, 269 (1982).

12. Moore J.M., Allen A.C., Cooper D.A., Determination of Manufacturing Impurities in Heroin by Capillary Gas Chromatography with Electron Capture Detection after Derivatization with Heptafluorobutyric Anhydride. Anal. Chem. 56, 642 (1984).

13. Brochmann-Hanssen E., Baerheim Svendsen A., Gas Chromatography of Alkaloids, Alkaloidal Salts and Derivatives. J. Pharm. Sci. 51, 1095 (1962).

14. Verpoorte R., Baerheim Svendsen A., Chromatography of Alkaloids. Part B: Gas-liquid Chromatography and High-performance Liquid Chromatography. Amsterdam - Oxford - New York - Tokyo, Elsevier, (1984).

15. Gough T.A., Baker P.B., The Selection of Gas Chromatographic Stationary Phases and Operating Conditions for the Separation and Quantitation of Heroin and Structurally Related Compounds. J. Chromatogr. Sci. 29, 227 (1981).

16. Dybowski R., Gough T.A., A Study of Transacetylation between 3, 6-Diacetylmorphine and Morphine. J. Chromatogr. Sci. 22, 465 (1984).

17. Cooper D.A., A Problem in GLC Quantitation. Microgram 11, 88 (1978).

18. Kiser W.O., Cocaine Hydrochloride/Lidocaine Hydrochloride Mixtures by GLC. Microgram 15, 4 (1982).

19. Pierce A.E., Silylation of Organic Compounds. Rockford Ill: Pierce Chemical Company, 1968.

20. Lim H.Y., Chow S.T., Heroin Abuse and a Gas Chromatographic Method for Determining Illicit Heroin Samples in Singapore. J. Forensic Sci. 23, 349 (1978).

21. Street H.V., Vycudilik W., Machata G., Gas-liquid Chromatography of Submicrogram Amounts of Drugs. V. Preparation of Low-Activity Packed Columns and their Application to the Toxicological Analysis of Underivatized Polar Drugs in the Low Nanogram Range. J. Chromatogr. 168, 117 (1979).

22. Clark C., Gas-liquid Chromatographic Quantitation of Cocaine. HCL in Powders and Tablets: Collaborative Study. J. Assoc. Off. Anal. Chem. 61, 683 (1978).

23. Bayer E., Liu G.H., New Split Injection Technique in Capillary Column Gas Chromatography. J. Chromatogr. 256, 201 (1983).

24. Verzele M., Verstappe M., Sandra P., Van Luchene E., Vuye A., Glass Capillary columns. J. Chromatogr. Sci. 10, 668 (1972).

25. Recommended Method for the Quantitative Characterization of Heroin. Collaborative Australian Study, 1976.

26. Analysis of Drugs. Analytical Manual, Supplemental Transmittal. Washington D.C. Drug Enforcement Administration, 1986.

27. Davey E.A., Murray J.B., Determination of Diamorphine in the Presence of its Degradation Products using Gas Liquid Chromatography. Pharm. J. 207, 167 (1971).

28. DeZan P., Fasanello J., The Quantitative Determination of Heroin in Illicit Preparations by Gas Chromatography. J. Chromatogr. Sci. 10, 333 (1972).

29. Moore J.M., Bena F.E., Rapid Gas Chromatographic Assay for Heroin in Illicit Preparations, Anal. Chem. 44, 385 (1972).