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Note

Application of a gas chromatographic capillary-to-capillary column-switching system to the analysis of complex illicit drug samples

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Progress in the analysis of complex drug samples using capillary columns in gas chromatography (GC) is well documented[1–3]. In this area we have studied in detail the trace impurity profiles of illicit heroin[4,5] and the determination of alkaloids in opium and crude morphine[6]. However even when using highly efficient and perfectly deactivated dimethylsiloxane capillary columns, some problems such as insufficient separation of certain parts of the impurity profiles, decomposition during the GC process and total masking (overlap) of important components by interfering matrix compounds, remained unsolved.

To address these problems thoroughly, we made use of two capillary columns of different selectivity coupled by a switching device, which should permit separations and determinations that are impossible with a single column[7–10]. The heart-cutting mode, *i.e.*, the transfer of timed cuts from the first to the second column, with enhanced resolution on the second column was applied to improve the separation of certain parts of a heroin impurity profile, to study the GC decomposition of thebaine and to the unmasking of important impurity components. Preliminary results are reported in this paper.

EXPERIMENTAL

All chromatography was performed on a Sichromat 2 GC system (Siemens, Karlsruhe, F.R.G.). The dual-oven gas chromatograph was equipped with a Siemens double T-piece for column-switching purposes (Deans' principle of pneumatic switching). With regard to the flow resistance, we prepared the double T-piece with a 0.23 mm O.D. plantinum–iridium coupling capillary. A 20 m × 0.25 mm I.D. fused-silica capillary column coated with OV-1 or SE-54 (see the legends of the figures) with a 0.15-μm film thickness was installed in the first oven. In order to optimize the switching conditions, the end of this column was coupled with a 5 cm × 0.32 mm I.D. uncoated fused-silica tube by a column-connecting unit (Gerstel, Mülheim, F.R.G.). In the second oven, OV-17 cross-linked fused-silica columns with a film thickness of 0.25 μm and different dimensions (5 m × 0.32 mm I.D. and 20 m × 0.32 mm I.D.) were installed. Helium was used as the carrier gas.

Trapping on the second column was considered essential for peak focusing and to avoid mixed polarity in the retention behaviour within the second column.

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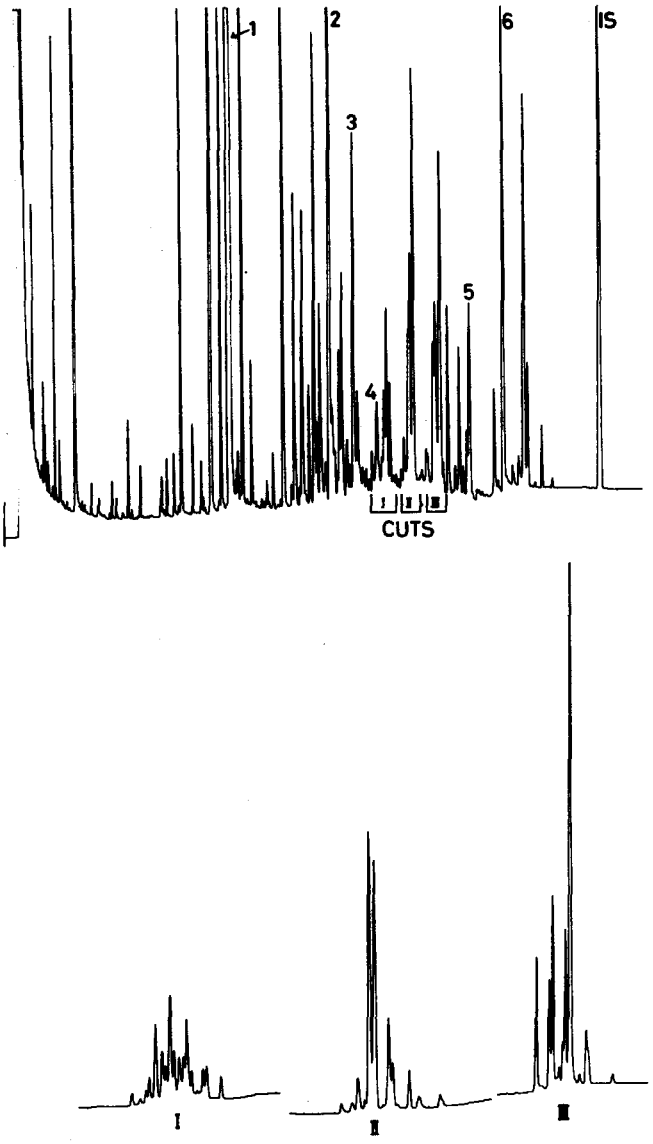

Fig. 1. Chromatograms generated by the trace impurities of an illicit heroin sample. Top: complete chromatogram generated on the first column (SE-54). Oven temperature programme: initial temperature 160°C, raised at 12°C/min to 240°C, 5°C/min to 280°C, then 20°C/min to 330°C. Bottom: separations of selected cuts I–III on the second column (5 m OV-17). Oven temperature programmes: (I) initial temperature 150°C, raised at 8°C/min to 290°C; (II) initial temperature 150°C, raised at 20°C/min to 240°C, then 5°C/min to 290°C; (III) initial temperature 150°C, raised at 20°C/min to 240°C, then 8°C/min to 290°C. Peaks: 1 = acetylthebaol; 2 = 4-acetoxy-3,6-dimethoxy-5-[2-(N-methylacetamido)]ethylphenanthrene; 3 = N-acetylnorlaudanosine; 4 = narcotine; 5 = N-acetylnornarcotine; 6 = (*E*)-N-acetylanhydronornarceine; IS (internal standard) = dotetracontane.

Therefore, a liquid carbon dioxide cold trap (Siemens) was used. Trapping started 2 min before column switching and stopped with the start of the temperature pro-

gramme of the second oven. Switching times and the trapping period were automatically controlled by the controlling device of the Sichromat 2.

Sampling was carried out with a split injector (temperature 300°C; splitter flow-rate 60 ml/min), and for monitoring the effluent from both the first and second columns two flame-ionization detectors (335°C) were used. Further experimental details are given in the legends of the figures. .

Samples were prepared as described previously[4–6]. Standard thebaine was obtained from Boehringer-Ingelheim (Ingelheim, F.R.G.), Merck (Darmstadt, F.R.G.) and Knoll (Ludwigshafen, F.R.G.).

RESULTS AND DISCUSSION

Enhanced resolution of heroin trace impurity profiles

The identification of compounds in certain parts of the trace impurity profiles of illicit heroin is still difficult, mainly owing to incomplete chromatographic resolution of these parts of the chromatogram, as indicated by overlapping of peaks in regions I–III in Fig. 1 (top).

Column-switching capillary GC permitted this problem to be addressed by cutting these parts of the profile to a second column with a more polar stationary phase, OV-17 (Fig. 1). Peak group I, which contained the one previously identified peak in this area of the chromatogram (peak 4 = narcotine on the first column coated with SE-54) was separated from 6 peaks into 17, peak group II from 5 into 13, and peak group III from 6 into 12. A comparison of the results of the statistical theory of multi-component chromatograms, which showed that a random chromatogram will never contain more than 37% of its potential peaks[11], supports the considerable progress made here. Fig. 1 also demonstrates that some major peaks with good shapes and without signs of overlapping separate into more peaks on the second column. The major peak in peak group II is an example.

The combination of a non-polar SE-54 first column for an overall good separation of the complex mixture with a medium-polarity OV-17 column for further separation of the problematic parts of the chromatogram therefore offers new approaches to this problem. As indicated by similar work on tobacco smoke samples[12], this technique will improve the ability to identify the impurity compounds in question by mass spectrometry, which is being studied separately.

Study of a decomposition problem in the GC analysis of opium

Capillary GC proved to be a good method for the direct determination of major and minor constituents of opium after silylation without the need for prior extraction or column separation[6]. We used two capillary columns to study further the problem of thebaine decomposition during normal GC analysis, studied previously by a combination of GC and thin-layer chromatographic (TLC) experiments[13].

Fig. 2 (top) shows that on non-polar phases such as OV-1, thebaine chromatographs at lower concentrations as a single peak without obvious signs of decomposition. However, when the alkaloid group is "cut" to a second column, a different picture is obtained. Whereas morphine (peak 3) and codeine (peak 1) again result in single peaks, the "pure" thebaine peak obtained on the first column (peak

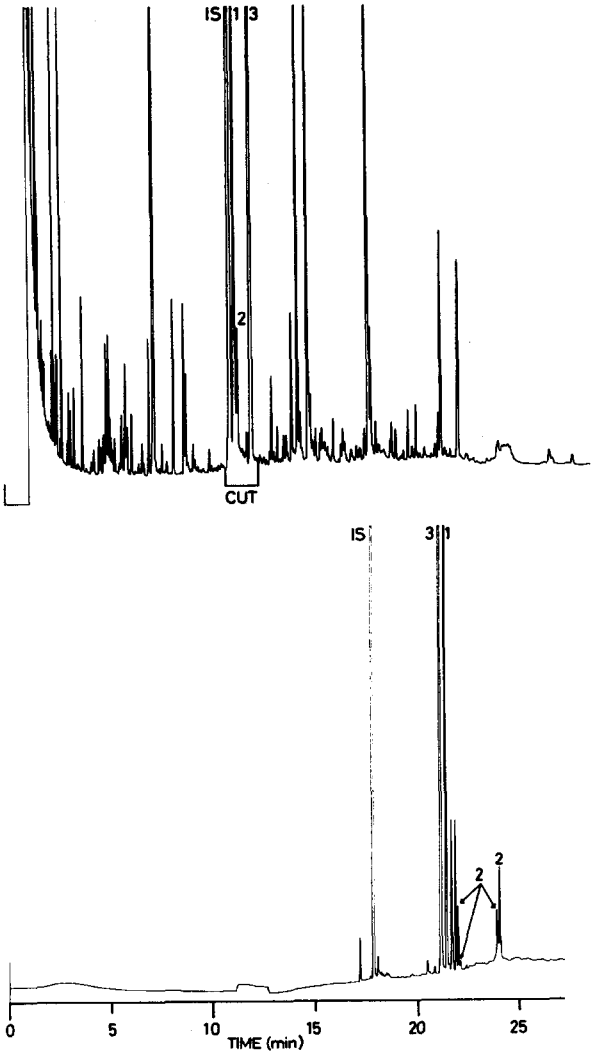

Fig. 2. Top: gas chromatogram of an opium sample on the first column (OV-1). Oven temperature programme: initial temperature 150°C, raised at 9°C/min to 320°C. Bottom: separation of the marked cut fraction on the second column (20 m OV-17). Oven temperature programme: initial temperature 150°C, raised at 25°C/min to 240°C, 4°C/min to 270°C, 25°C/min to 290°C. Peaks: 1 = codeine-TMS; 2 = thebaine; 3 = morphine-TMS; IS = tetracosane (TMS = trimethylsilyl derivative).

2) is separated to four major peaks [Fig. 2 (bottom), peak group 2]. This result was also obtained with different samples of standard thebaine. It is in substantial agreement with previous work[13] in which TLC identified four major decomposition products generated under normal GC conditions. Fig. 2 demonstrates that the instrumental set-up used, with an independent second oven, is capable of complete separation of the cut fraction on the second column within the normal running time of the sample on the first column. It should also be noted that only a combination of

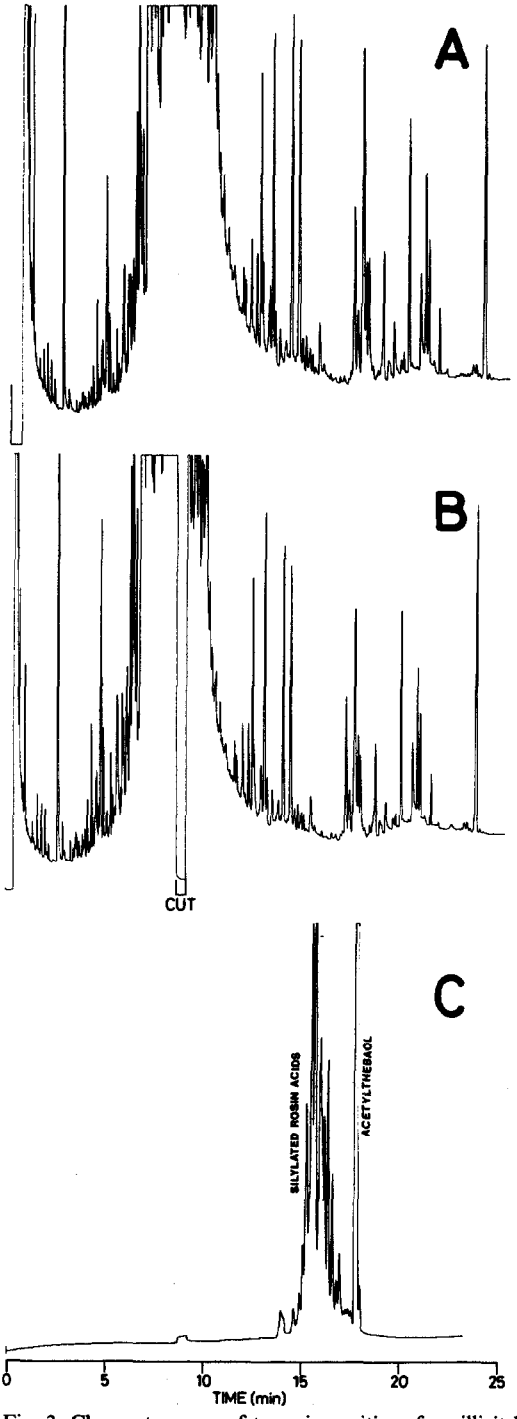

Fig. 3. Chromatograms of trace impurities of an illicit heroin sample diluted with rosin. (A) Complete chromatogram generated on the first column (SE-54). Oven temperature programme as in Fig. 1 (top). (B) Chromatogram of the cut run on the first column (conditions as in A). (C) Separation of the selected cut on the second column (5 m OV-17). Oven temperature programme: initial temperature 150°C, raised at 8°C/min to 290°C.

two columns with different selectivities can solve the problem, as the OV-17 capillary column alone is not suitable for the analysis of high-boiling components such as narcotine[14].

As shown here, the technique used is capable of indicating efficiently if a "pure" peak represents an intact compound or some degradation occurs during the chromatographic process.

Separation and determination of totally masked heroin impurity components

Recently, rosin or colophony was identified in illicit heroin samples from Southwest Asia[15]. Because this diluent consists mainly of rosin acids, it is enriched in the trace impurity extracts obtained by extraction of a slightly acidic aqueous solution of the heroin sample[4,5]. The result, as demonstrated in Fig. 3A, is that an important part of the impurity chromatogram is masked by these compounds. In this region, for instance, the impurity component acetylthebaol[16] is eluted. Fig. 3B shows that this part of the chromatogram can be transferred to a second column, and here (Fig. 3C) acetylthebaol could be separated nearly quantitively from the accompanying rosin matrix. For sample comparisons it is therefore possible to determine the interesting components, even if they are masked by large amounts of an interfering substance or group of substances.

CONCLUSION

A commercially available capillary-to-capillary column-switching instrument has been applied successfully to achieve a better resolution of certain parts of very complex mixtures of opium and heroin impurities and diluents. The superior characteristics of this technique in comparison with capillary GC on a single column have been demonstrated by three different examples. At present, however, the application of column-switching capillary GC on a routine basis is difficult owing to the extreme complexity of the technology involved.

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