CHROMATOGRAPHIC INVESTIGATION OF THE ALKALOIDS OF THE OPIUM POPPY AND THEIR ACETYL DERIVATIVES

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The composition of the alkaloids in narcotic agents of domestic production (khanke) has been investigated by thin-layer and gas chromatographies. The retention times in GLC and the retention indices in TLC of the initial alkaloids and their acetylated derivatives have been determined. The rates of acetylation of the alkaloids have been evaluated with the aid of the GLC method.

Of the five main alkaloids of the opium poppy, morphine has two hydroxy groups — an alcoholic group in position 6 and a phenolic one in position 3, while codeine has one alcoholic hydroxy group, in position 6. All these groups may take part independently of one another in acetylation reactions, giving four derivatives: 6-acetylmorphine, 3-acetylmorphine, 3,6-diacetylmorphine (heroin), and acetylcodeine. Thebaine, papaverine, and narcotine, which have no hydroxy groups, are not acetylated.

Narcotic agents of domestic production (khanke) contain all nine bases in larger or smaller amounts. On the TLC of extracts of opium raw material the five spots of the initial alkaloids can be seen clearly (Table 1) [1]. Analysis of acetylated samples of opium raw material shows the presence of additional spots having R_f 0.52, 0.62, and 0.72. The spot with R_f 0.52 can be assigned to an intermediate in the acetylation of morphine, since its intensity decreases sharply, together with that of morphine, on the analysis of a sample heated with an excess of acetic anhydride and rises again on the partial saponification of an acetylated sample by KOH in ethanol. On complete saponification in an excess of alkali this spot again practically disappears. From its chemical properties the substance with R_f 0.52 must be ascribed the structure of 6-acetylmorphine, since an alcoholic hydroxyl is acetylated more readily than a phenolic one, and the acetyl derivative is saponified with greater difficulty. It was impossible to detect a second intermediate, 3-acetylmorphine, by this method.

The product with R_f 0.62 is acetylcodeine, as was shown by comparison with an authentic sample. The spot with R_f 0.72 is that of heroin since it appears most distinctly in fully acetylated samples of opium raw material and of morphine itself. Its fluorescence in UV light – a weak greenish blue may sometimes be masked by the intense blue coloration of the closely located narcotine. The results obtained enable a contamination of acetylated opiates to be identified in urinanalysis from spots with R_f 0.52, 0.62, and 0.72.

Additional information on the quantitative composition of the alkaloids is given by gas chromatography. By this method, using specimens of partially acetylated products from the extraction of opium, partially saponified acetyl derivatives, and individual preparations of morphine, codeine, papaverine, and narcotine it has been possible to determine and show the positions of all the nine bases mentioned above (see Table 1).

By studying the dynamics of the acetylation of the alkaloids of opium raw material it has been possible to evaluate the relative rates of the reactions of the hydroxy groups in morphine and codeine.

Table 2 gives the relative amounts of alkaloids during the acetylation of opium raw material, obtained as the result of integrating chromatograms.

The rate of acetylation of morphine is about one-and-a-half times to twice as great as for codeine. The hydroxy group in position 6 of morphine is acetylated approximately 20 times faster than that in position 3.

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TABLE 1. Results of Analysis of the Alkaloids

Alkaloids	R_f	Fluorescence in UV	Retention time, min		Amount in the initial substance, %
			290°C	270°C	
	TLC analysis		GLC analysis		
Morphine	0,22	Blue	2,73	5,10	57,20
Codeine	0,44	—	2,35	3,98	12,29
Thebaine	0,57	Yellow	3,64	6,55	7,75
Papaverine	0,66	Greenish Yellow	8,64	19,0	17,00
6-Acetylmorphine	0,52	Bluish Green	3,80	8,40	—
3-Acetylmorphine	—	—	2,08	3,52	—
Narcotine	0,76	Blue	13,50	28,0	5,76
Acetylcodeine	0,62	Yellow	2,42	4,60	—
Heroin	0,72	Bluish Green	2,86	5,86	—

TABLE 2. Composition of the Reaction Mixture during the Acetylation of Opium Raw Material

Alkaloid*	Relative amount in the sample after the addition of acetic anhydride					
	0 min	2 min	12 min	22 min	40 min	50 min
Morphine	60,01	35,40	14,32	6,12	0,60	0,12
Codeine	12,89	10,41	5,16	2,14	1,71	0,4
Thebaine	7,05	8,14	7,26	7,91	8,72	8,21
Papaverine	19,05	18,80	17,90	17,97	20,44	19,60
6-Acetylmorphine	—	15,94	26,70	18,41	8,14	2,76
3-Acetylmorphine	—	0,4	0,16	0,14	—	—
Acetylcoeine	—	1,06	5,80	8,14	10,91	11,22
Heroin	—	8,4	22,90	40,94	48,14	54,82

*Narcotine as not taken into account.

Thus, from the results of GLC analysis it may be concluded that a reliable and rapid method has been found for the quantitative determination of heroin and other products of the acetylation of opiates in preparations of domestic origin.

EXPERIMENTAL

Extraction [2]. The opium raw material (0.2 g) was treated with 1 ml of hot aqueous ethanol (1:1) acidified with sulfuric acid to pH 3-4 to give a homogeneous mixture. Then the solvent was evaporated off, and 0.1 ml of ethanol was added. The pH was brought to 9-10 with the aid of K_2CO_3 and the mixture was heated to 70°C and was used for chromatography and acetylation.

Acetylation. The ethanol was evaporated off from the solution obtained as described in the preceding section, 0.1 ml of acetic anhydride was added, and, with the gradual heating of the solution the change in composition was observed with the aid of thin-layer and gas chromatographies.

Saponification of the Acetyl Derivatives. The whole of the acetic acid was evaporated off from the solution obtained as described above, and 0.1 ml of a saturated solution of KOH in ethanol was added to the solid residue. The change in composition on gradual heating was observed with the aid of thin-layer chromatography.

Thin-Layer Chromatography. Samples of solutions of the substances to be analyzed were deposited with the aid of a glass capillary at points 1 cm apart on a Silufol UV-254 plate with dimensions of 5 × 15 cm. The whole starting line was 1 cm from the lower edge of the plate. The plates were chromatographed twice in benzene–ethanol–diethylamine (9:1:1). After drying, the plates were examined under UV irradiation, and they were then treated with iodine vapor and were again examined under UV.

Gas Chromatography. GLC analysis was conducted on a Chrom-5 chromatograph. Glass column, 0.3 cm × 1 m, filled with Inerton Super 0.125-0.160 mm, impregnated with 3% of OV-17. The carrier gas was helium (40 ml/min). Flame-ionization detector. The temperature of the evaporator and the detector was 280°C. The column temperature was 270°C for the identification of the alkaloids and 290°C for the study of the kinetics of acetylation.

LITERATURE CITED

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