

DETERMINATION OF NARCOTINE AND PAPAVERINE BY INFRA-RED SPECTROPHOTOMETRY AND NON-AQUEOUS TITRATION

BY LEE KUM-TATT, RUSSELL A. ROCKEBIE AND LEO LEVI

From the Government Chemistry Department, Singapore, Crime Detection Laboratory, Royal Canadian Mounted Police, Regina, and the Food and Drug Laboratories, Department of National Health and Welfare, Ottawa, Canada

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An infra-red spectrophotometric method for the determination of narcotine in the presence of papaverine in carbon tetrachloride or chloroform solution is described. The carbonyl group of the lactone ring present in narcotine displays strong absorption at 1760 cm.^{-1} and the intensity of the band observed at this wavelength provides an index of the concentration of the narcotic. By conventional non-aqueous titration the amount of both alkaloids may be estimated quantitatively and the papaverine content of a mixture obtained readily by difference.

THE determination of narcotine and papaverine has been the subject of several publications. Most of the methods reported use Anneler's procedure¹ for the preliminary separation of the two alkaloids before their determination by either gravimetric² or spectrophotometric analysis³. The process described by Anneler involves heating the substrate with both strong acid and alkali. This treatment was found to destroy some of the opium alkaloids and only low recoveries of narcotine were obtained⁴.

Lee and Farmilo recently reported a method for the isolation of narcotine and papaverine from raw opium⁵, the *isoquinoline* alkaloid being removed as the reineckate from a two-phase water-chloroform system. During this study it was observed that the infra-red spectrum of narcotine reineckate exhibits strong absorption at 1760 cm.^{-1} (C = O stretching vibrations of the lactone carbonyl group of the molecule), whereas papaverine reineckate shows no band in this region.

A further study of the infra-red spectra of the alkaloidal bases in both chloroform and carbon tetrachloride solutions revealed the same phenomenon—see Figure 1. This observation suggested a simple method of determining narcotine by an infra-red technique without prior separation of the alkaloid from papaverine. Since, furthermore, the total amount of these alkaloids in a binary mixture can be determined by conventional non-aqueous titration procedures the weight of papaverine present may readily be obtained by difference.

Apparatus, Reagents and Solutions

Perkin-Elmer Model 21 Recording infra-red spectrophotometer; sodium chloride cells, 1 mm. light path; narcotine, T. and H. Smith, Ltd., M.P. 174° ; papaverine, T. and H. Smith, Ltd., M.P. 146° ; carbon tetrachloride, Fisher Spectroanalyzed Grade, chloroform, Fisher Spectroanalyzed Grade, glacial acetic acid, Fisher Reagent Grade, acetous perchloric acid, 0.05N.

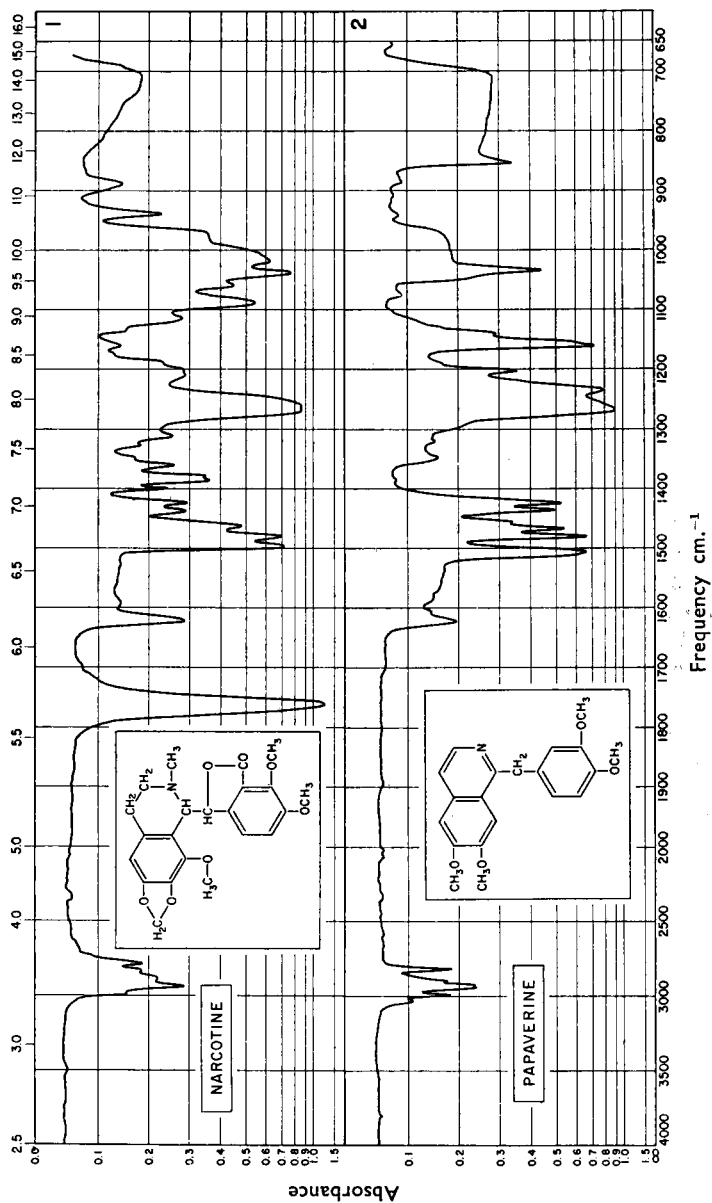


FIG. 1. Infra-red absorption spectra of narcotine and papaverine in carbon tetrachloride.

DETERMINATION OF NARCOTINE AND PAPAVERINE

EXPERIMENTAL PROCEDURES AND DISCUSSION OF RESULTS

Preparation of Calibration Curve for Narcotine

Quantities of about 5, 10, 15, 20 and 25 mg. of narcotine were weighed accurately and dissolved in carbon tetrachloride or chloroform in 10-ml. volumetric flasks and the solutions made up to volume. The infra-red spectra of these preparations were measured from 1900 to 1650 cm^{-1} using slit schedule 927 and the instrument zeroed at 0.05 on the absorbance scale. The absorbance of each solution ($A_{\text{corr.}}$) was then computed by means of the following equation:

$$A_{\text{corr.}} = A_{1760 \text{ cm}^{-1}} - \frac{A_{1900 \text{ cm}^{-1}} + A_{1650 \text{ cm}^{-1}}}{2} \quad \dots \quad (1)$$

where A denotes the absorbance measured at the given wavelength.

The calibration curve thus obtained reveals that the absorbance of narcotine solutions at 1760 cm^{-1} is linear for concentrations up to approximately 2.5 mg./ml. when using cells of 1 mm. light path.

It was observed that on standing, solutions of narcotine in carbon tetrachloride gradually turned yellowish. Their absorbances at 1760

TABLE I
ANALYSIS OF SYNTHETIC MIXTURES OF NARCOTINE AND PAPAVERINE

Composition		Narcotine found (mg.)	Total volume of titrant used (ml.) (X)	0.05N Perchloric acid equivalent		Papaverine found (mg.)
Narcotine (mg.)	Papaverine (mg.)			Narcotine (ml.)* (Y)	Papaverine (ml.) (X-Y)	
23.9	8.0	23.0	1.60	1.11	0.49	8.3
30.4	8.0	29.7	1.94	1.44	0.50	8.5
47.0	20.0	48.0	3.43	2.32	1.11	18.8
105.0	40.0	101.0	7.37	4.89	2.42	41.0
138.0	40.0	140.0	9.10	6.77	2.33	39.5

* Calculated from infra-red data.

cm^{-1} remained, however, unchanged and since, furthermore, this solvent was found to serve advantageously for the extraction of narcotine and papaverine in a relatively pure state from crude opium⁵ it was used throughout these experiments. Chloroform proved equally satisfactory for the infra-red measurements and may therefore also be employed as a solvent.

Determination of Narcotine and Papaverine in Binary Mixtures

Solutions containing both narcotine (0.4–3.0 mg./ml.) and papaverine (0.2–0.8 mg./ml.) were prepared by dissolving the alkaloids in carbon tetrachloride. Their infra-red spectra were recorded as described and the absorbances, measured at 1760 cm^{-1} in accordance with equation 1, expressed as narcotine with reference to a calibration graph. It was found that absorbances of the mixtures at the critical wavelength of 1760 cm^{-1} were independent of the amount of papaverine present and therefore provided an accurate index of the narcotine content.

For the determination of papaverine, solution aliquots were diluted with 20 ml. of glacial acetic acid and titrated with 0.05N acetous perchloric acid

in accordance with the procedure described by Levi and others⁶. The experimental data were expressed in terms of papaverine using the following equation:

$$W = (X - Y) \times N \times M$$

where W = mg. of papaverine present, X = ml. of titrant used, Y = ml. of titrant equivalent to weight of narcotine as derived from infra-red measurements, N = normality of titrant and M = molecular weight of papaverine = 339.4.

Results obtained by this method on mixtures of pure narcotine and papaverine are recorded in Table I. The compositions were chosen so as to cover fully the proportions in which the two alkaloids occur in raw opium and the experimental data suggest that the method described should find practical application in the field of drug and opium analysis.

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