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Short Communication

Spectrophotometric determination of meperidine hydrochloride in pharmaceutical preparations by complexation with bromocresol green*

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Introduction

Numerous analytical procedures have been described for meperidine hydrochloride. These procedures are mostly screening tests used for detection and identification of meperidine hydrochloride in drug combinations and biofluids, or developed for the separation, isolation and determination of meperidine hydrochloride in biological materials. Among the quantitative methods described for the determination of meperidine hydrochloride in pharmaceutical preparations are those based on UV-spectrophotometry [1, 2], colorimetry [3], colorimetry and volumetric analysis [4], fluorimetry [5], gas-chromatography [6] and high-performance liquid chromatography [7].

The USP XX [8] and BP 1973 [9] describe a non-aqueous titration for meperidine hydrochloride in pharmaceutical preparations. The BP 1980, Addendum, 1982 [10] suggests infra-red spectroscopy of meperidine hydrochloride after extraction by chloroform and further physical manipulation.

These methods mostly lack simplicity and selectivity for routine analysis. Bromocresol green (BCG) has been used for the determination of small amounts of long-chain tertiary and quaternary ammonium salts [11]. It has also been used for the spectrophotometric determination of thebaine [12], diphenylhydramine hydrochloride [13], sparteine sulphate [14] and codeine [15].

The present paper describes a spectrophotometric determination for meperidine hydrochloride in pharmaceutical preparations using BCG as a reagent. The method is

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based upon a complexation reaction of meperidine hydrochloride and BCG, followed by extraction with chloroform and measurement of the absorbance of the complex at 425 nm.

Experimental

Reagents and chemicals

All solutions were prepared from AnalaR grade chemicals. BP standard pH 3 buffer solution was prepared by diluting 250 ml of 0.2 M potassium hydrogen phthalate and 101.6 ml of 0.2 M HCl to 1 l with water. The pH of all buffers was controlled using a Beckman type H-3 pH meter. Meperidine hydrochloride was 10^{-4}M in buffer solution. BCG 10^{-4}M (69.80 mg) was first dissolved in 2 ml of 0.1 M NaOH and diluted to 1 l with buffer solution.

General procedure

An aliquot of 3.00 ml of meperidine hydrochloride solution was pipetted into a 50-ml separating funnel and then 20 ml of BCG solution was added. The yellow complex was extracted by vigorous shaking with successive volumes of 5, 3 and 2 ml of chloroform. The extracts were combined in a 10-ml volumetric flask and adjusted to volume with chloroform. The absorbance was measured at 425 nm against chloroform as blank, using a Beckman DB-GT spectrophotometer with 1-cm glass cells.

Results and Discussion

In the present study meperidine hydrochloride reacted with BCG to form a yellow complex. The meperidine hydrochloride–BCG complex in chloroform showed maximum absorbance at 425 nm (Fig. 1). The complex formation and extraction were studied in the pH range from 1 to 11. Complex extraction was quantitative at pH 3 as shown in Table 1.

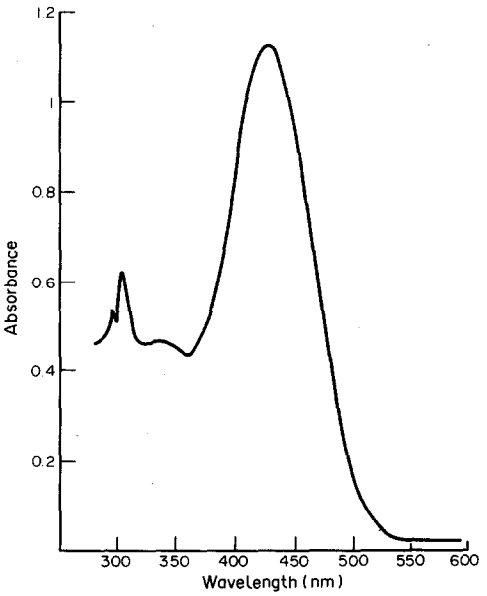

Figure 1
Absorption spectrum of chloroform solution of meperidine HCl–bromocresol green complex.

Table 1
pH effect on the formation and extraction of meperidine HCl–BCG complex*

pH	Complex extracted in $CHCl_3$ (%)	D†
1	66.30	1.97
2	93.48	14.34
3	100.00	∞
4	97.83	45.08
5	94.56	17.38
6	93.48	14.35
7	84.78	5.57
8	24.35	0.32
11	1.08	0.01

* Amount of meperidine HCl = 56.8 μg.
† Distribution ratio.

The absorbance of the complex was measured at selected intervals of time after extraction; six estimates on the first day and two estimates on each day for four days. The range of absorbance was 0.87% of the initial value and the relative standard deviation (RSD) was 0.30%.

Nature of complex

The composition of meperidine hydrochloride–BCG complex was studied by the continuous variation method [16–18] and the mole ratio method [18, 19]. In the first method the total concentration of BCG–meperidine HCl was kept constant at two different concentrations. The method was carried out by following the general procedure. The maxima occurred at a mole ratio of 0.5 for BCG–meperidine HCl, indicating a 1:1 ratio of BCG–meperidine HCl in the complex (Fig. 2). In the second

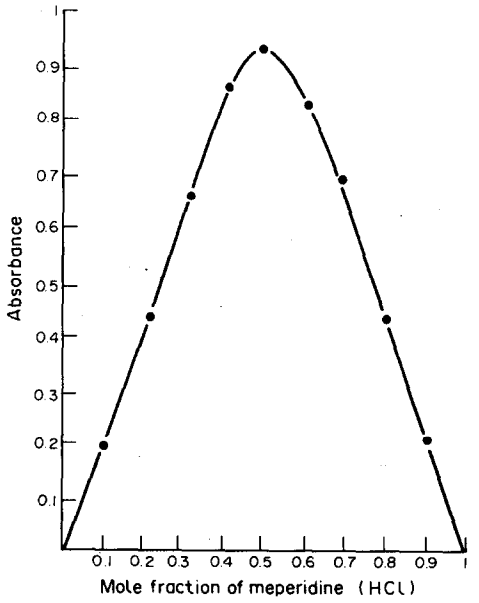

Figure 2
Composition of meperidine HCl–BCG complex by continuous variation method: 3.2×10^{-4}M meperidine HCl.

method, the concentration of meperidine HCl was kept constant while the BCG concentration was varied. The determination was carried out as for the general method. The ratio of the BCG–meperidine HCl complex was 1:1 as shown in Fig. 3. However, the required ratio for complete complexation and quantitative extraction was 2:5.

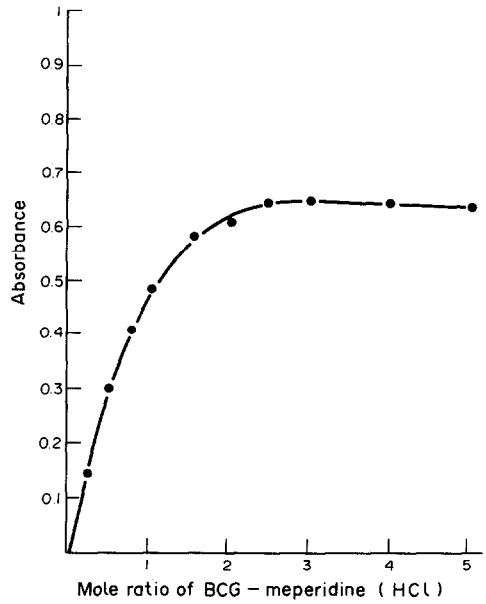

Figure 3
Composition of meperidine HCl–BCG complex by the mole ratio method. The total concentration of meperidine HCl and BCG was 10×10^{-4}M.

Conformity to Beer's law

Standard curves of six samples, ranging in concentration from 2 to 14 μg/ml, were analysed according to the procedure described. Each measurement was replicated 5 times. The linearity of the absorbance (y) as a function of concentration (x) was calculated by the least mean square method:

$$y = 0.084x + 0.020.$$

The correlation coefficient, $r = 0.99$; the standard deviation of the slope, $s = 9.13 \times 10^{-4}$. The concentration range over which Beer's law was obeyed at 425 nm corresponded to 2–10 μg/ml, as expressed in the regression equation above.

The molar absorptivity of the complex in solution was 2.36×10^6. The relative standard deviation (RSD) of the absorptivities in the optimum concentration range was 0.68% ($n = 4$).

Interference by other compounds

A standard solution of meperidine hydrochloride, plus the various compounds likely to be present in pharmaceutical preparations, was analysed by the described method. The following compounds did not interfere up to the indicated amounts: sodium sulphite (50 mg), sodium metabisulphite (50 mg), sodium citrate (20 mg), hydroquinone (100 mg), amidone (10 mg), glucose (80 mg), lactose (80 mg), caffeine (10 mg), acetylsalicylic acid (12 mg), acetaminophen (80 mg), phenobarbital (70 mg), saccharin sodium (24 mg),

sodium benzoate (12 mg), benzoic acid (21 mg), ammonium chloride (70 mg), glycerol (10 ml), ethyl alcohol (5 ml).

To test the validity of the method, meperidine hydrochloride was added to the locally available pharmaceutical preparations and the recovery determined by the described method. Recovery of the added amounts of meperidine hydrochloride is given in Table 2.

Table 2
Determination and recovery of meperidine hydrochloride in pharmaceutical preparations

Preparation	μg meperidine HCl/sample taken			Recovery (%)	RSD* (%)
	Manufacturer's claim	Added amount	Amount found		
Ampoule A†	40	40	39.5	98.75	1.2
Ampoule B‡	40	40	39.75	99.25	1.6
Tablet A§	50	40	40.7	101.75	1.5
Tablet B‖	50	40	39.0	97.50	2.0

* $n = 4$.

† Dolantin, (Hoechst, Germany); Meperidine HCl 100 mg in a 2 ml ampule; 0.8 ml aliquot taken for analysis.

‡ Pethidine HCl, (Antigen Ltd., Ireland); Meperidine HCl 50 mg in a 1 ml ampule; 0.8 ml aliquot taken for analysis.

§ Demerol, (Winthrop Laboratories, USA); Meperidine HCl 50 mg/tablet; one tablet taken for analysis.

‖ Pethidine HCl, (Ammino Ltd., Switzerland); Meperidine HCl 25 mg/tablet; 2 tablets taken for analysis.

The advantages of the proposed method are its simplicity and validity: it can be used for the determination of meperidine hydrochloride in pharmaceutical preparations.

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