59 (1988).
8) M. Pujol, V. Girona, J. Prat and J. Cots, **Int. J. Pharm.**, 58, 103 (1990).
9) **"United States Pharmacopeia"**, XXII, US Pharmacopeial Convention, Rockville, MD, P. 258 (1990).
10) D. B. Bowman, M. K. Aravind, J. N. Miceli and R.E. Kauffman, **J. Chromatogr. Biomed. Appl.**, 34, 209 (1984).
11) H. Auterhoff, **Dtsch. Apoth. Ztg.**, 102, 765 (1962).
12) O. Matousova and M. Peterkova, **Cesk. Farm.**, 30, 189 (1981); through **Anal. Abstr.**, 42, 1E35 (1982).
13) F. I. Sengun and K. Ulas, **Talanta**, 33, 363 (1986).

Received: Oct. 28, 1993.
Accepted for Publ.: Nov. 28, 1993.

Spectrophotometric Determination of Mequitazine and Thiopentone Sodium in Dosage Forms

MAGDI M. ABDEL-KHALEK and HODA G. DAABEES

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Alexandria, Alexandria, Egypt.

Abstract ❑ A simple and sensitive spectrophotometric method is described for the determination of mequitazine and thiopentone sodium. The method is based on the formation of ferroin upon reaction of these drugs with iron(III)-o-phenanthroline reagent. The colored product is quantitated spectrophotometrically at 510 nm. Beer's law is obeyed over concentrations ranging from 0.2-0.8 mg% and 2-6 mg% for mequitazine and thiopentone sodium, respectively. The proposed method has been applied successfully to the determination of the investigated drugs in dosage forms.

Keyphrases ❑ Mequitazine, thiopentone sodium, spectrophotometric determination, iron(III)-o-phenanthroline, dosage forms.

Mequitazine, 10-(quinuclidin-3-ylmethyl)phenothiazine, is a phenothiazine derivative with the properties and uses of the antihistamines (1). Thiopentone sodium, sodium 5-ethyl-5-(1-methylbutyl)-2-thiobarbiturate, is a barbiturate which is used for the induction of general anaesthesia or the production of complete anaesthesia of short duration (1). Several methods have been reported for the determination of these drugs including titrimetric (2,3), gravimetric (2), spectrophotometric (4-7), coulometric (8), fluorimetric (9), polarographic (10), GC (11,12) and HPLC (13) methods.

In the present work, a simple, rapid and sensitive spectrophotometric method for the estimation of mequitazine and thiopentone sodium in pure samples and dosage forms is described. The proposed method is based on the interaction of the investigated drugs with iron(III)-o-phenanthroline reagent to form ferroin.

Experimental:

Apparatus: UV-VIS spectrophotometer (Shimadzu, Model 160A), was used for spectroscopic analysis.

Materials: Mequitazine authentic sample and Primalan^R tablets (labelled to contain 5 mg mequitazine, Amriya, Egypt). Thiopentone sodium authentic sample and Nesdonal^R vials (labelled to contain 1 g thiopentone sodium, Specia, France).

Reagents:

Iron(III)-o-phenanthroline reagent was freshly prepared by mixing 0.198 g of o-phenanthroline monohydrate with 2 ml of 1 N HCl and 0.266 g of ferric ammonium sulfate

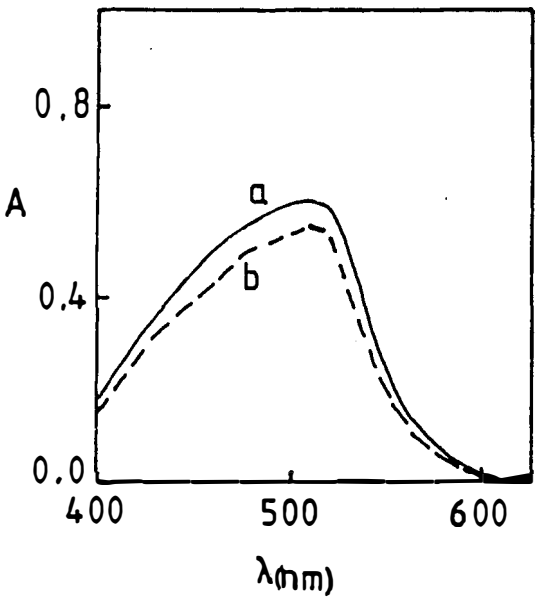

Fig. 1: **Absorption spectra of the colored products of: (a) thiopentone sodium (4 mg%); (b) mequitazine (0.5 mg%).**

and diluted with H_2O to 100 ml.

Standard solutions: Separate standard solutions were prepared in EtOH in the concentration range of 2-8 mg% and 20-60 mg% for mequitazine and thiopentone sodium, respectively.

General procedure: A solution of the standard preparation in 2 ml EtOH, containing 0.02-0.08 mg mequitazine or 0.2-0.6 mg thiopentone sodium, was transferred into a 10 ml calibrated flask, treated with 2 ml reagent and heated in a boiling water-bath for 5 min. The flask was then cooled and diluted to volume with EtOH. The developed red color was measured at 510 nm against a reagent blank treated similarly ***(Fig. 1.).***

Primalan^R tablets analysis: Twenty tablets were weighed and powdered. A quantity of the powdered tablets equivalent to 50 mg of the drug was transferred into a 100 ml calibrated flask, followed by the addition of about 70 ml of EtOH. The mixture was shaken for 15 min., diluted to volume with EtOH, mixed well and filtered. A 8-ml volume of the filtrate was transferred into a 100 ml calibrated flask and diluted to volume with the same solvent. This solution was used for the determination of mequitazine as mentioned under the general procedure.

Nesdonal^R vials analysis: From the mixed contents of vials, a quantity of powder equivalent to 40 mg thiopentone sodium was transferred into a 100 ml calibrated flask, dissolved and diluted to volume with EtOH. The assay was completed as described under the general procedure.

RESULTS and DISCUSSION

Iron(III)-o-phenanthroline reagent was used for the determination of some drugs (14,15). The proposed method is based on the interaction of mequitazine or thiopentone sodium with iron(III)-o-phenanthroline reagent to form iron(II)-salt complex with phenanthroline. The reaction proceeds through the reduction of iron(III) to iron(II) and subsequent formation of the intensive orange-red coloration of the ferroin complex (14).

Investigation of Assay parameters:

Effect of reagent concentration: Various volumes (0.5-3 ml) of iron(III)-o-phenanthroline were added to a fixed concentration of the investigated drugs. The maximum color intensity was reached upon using 2 ml of the reagent in the final measured volume.

Effect of diluting solvent: Ethanol gave maximum sensitivity with the reagent. In addition, it was a good solvent for the investigated drugs.

Table I: **Determination of Mequitazine and Thiopentone Sodium in Pure Form and Pharmaceutical Preparations.**

Compound	Sample	Recovery, % ± s. d. [+] Proposed method	Reference method[++]
Mequitazine	Powder	100.2 ± 0.4	99.9 ± 0.2
		t* =	1.37
		F** =	3.84
	Primalan^R tablets	100.4 ± 0.4	100.2 ± 0.3
		t =	0.64
		F =	1.06
Thiopentone sodium	Powder	99.5 ± 0.5	99.3 ± 0.5
		t =	0.61
		F =	1.00
	Nesdonal^R vials	101.2 ± 0.4	101,1 ± 0.3
		t =	0.54
		F =	1.31

(+) Mean of 5 determinations ± standard deviation. (++) References 6 and 16. (*) Theoretical value for t = 2.31 (p = 0.95). (**) Theoretical value for F = 6.39 (p=0.95).

Reaction time and stability of the color: Complete color development was attained after 5 minute heating in a boiling water-bath. The color remained stable for at least 30 minutes. Under the above mentioned experimental conditions, calibration graphs were constructed at 510 nm for both drugs. Beer's law was valid over the concentration range 0.2-0.8 mg% of mequitazine and 2-6 mg% of thiopentone sodium. The sandell sensitivities of the reactions, as calculated from the Beer's law data, were 8.9 and 64.4 ng cm^{-2} and the corresponding molar absorptivities were $3.6x10^4$ and $4.1x10^3$l $mol^{-1}cm^{-1}$ for mequitazine and thiopentone sodium, respectively. The correlation coefficients were between 0.9994-0.9995. Regression equations derived using the method of least squares were:

$A = - 0.0116 + 1.150C$ (mequitazine)

$A = 0.0240 + 0.148C$ (thiopentone sodium)

where C is mg%.

Five replicate determinations were carried out to test the reproducibility of the proposed method. The relative standard deviation was found to be less than 0.53%. The accuracy of the developed procedure was evaluated by assaying mequitazine and thiopentone sodium in pure form and in pharmaceutical preparations. In ***Table I,*** the results obtained for mequitazine were compared with the published spectrophotometric method (6) using p-chloranilic acid. Moreover, ***Table I*** shows the results of analysis of thiopentone sodium by the proposed method, and by the reported method (16) using zinc/hydrochloric acid, to liberate sulfide

ions, which react with p-phenylenediamine in the presence of ferric ions to give thionine. Statistical analysis of the obtained results showed comparable accuracy (t-test) and precision (F-test).

In conclusion, the suggested method has the advantage of being simple, accurate and rapid and may be considered for routine quality control of mequitazine and thiopentone sodium.

References:

1) **"Martindale",** The Extra Pharmacopoeia, J.E.F. Reynolds (Ed.), **The Pharmaceutical Press,** London, 30th ed., pp. 920, 942 (1993).
2) **"British Pharmacopoeia",** HM Stationary, Office, London, UK, p. 668 (1993).
3) Z. Bezakova, M. Bachrata, J. Subert, L. Knazko and E. Kokaiova, **Cesk. Farm.,** 26, 278 (1977), through **Anal. Abstr.,** 35, 2E32 (1978).
4) **"United States Pharmacopeia",** XXII, US Pharmacopeial Convention, Rockville, MD, p. 1364 (1990).
5) C.S.P. Sastry, P. Satyanarayana, A.R.M. Rao and N.R.P. Singh, **Indian Drugs,** 26, 84 (1988).
6) M. M. Ayad, H.M. Saleh, M. El-Maamli, S. El-Adl and M. El-Henawee, **Alex. J. Pharm. Sci.,** 6, 173 (1992).
7) M.M. Abdel-Khalek, M.S. Mahrous and H.G. Daabees, ***ibid.,*** 7, 201 (1993).
8) C.A. Mairesse-Ducarmois, J.L. Vandenbalck and G. J. Patriache, **J. Pharm. Belg.,** 28, 300 (1973).
9) G. Miles and G. Schenk, **Anal. Lett.,** 4, 61 (1971).
10) Z. Han and Z. Yuan, Huaxue Tongbao, 6, 14 (1982); through **Anal. Abstr.,** 44, 2E43 (1983).
11) J.B. Fourtillan, J. Girault, S. Bouquet and M.-A. Lefévre, **J. Chromatogr. Biomed. Appl.,** 34, 391 (1984).
12) L.T. Sennello and F.E. Kohn, **Analyt. Chem.,** 46, 752 (1974).
13) B.P. Vesnovski, G.N. Merlis and Y.I. Yashin, **Zh. Anal. Khim.,** 40, 939 (1985), through **Anal. Abstr.,** 48, 5E35 (1986).
14) A. Besada, **Anal. Lett.,** 20, 427 (1987).
15) M.S Mahrous, H.G. Daabees, Y.A. Beltagy and M.M. El-Semary, **Egypt J. Pharm. Sci.,** 33, 453 (1992).
16) M. Sharaf El-Din, F. Belal and S. Hassan, **Zentralbl. Pharm. Pharmakother. Laboratoriumsdiagn.,** 127, 133 (1988), through **Anal. Abstr.,** 50, 8E35 (1988).

Received: Oct. 28, 1993.
Accepted for Publ.: Nov. 27, 1993.

Spectrofluorimetric Determination of Mebeverine Hydrochloride in Tablets and in Biological Fluids

AZZA ABDEL-KADER GAZY

Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, University of Alexandria, Alexandria , Egypt.

Abstract ❑ A sensitive and rapid spectrofluorimetric method is described for the determination of mebeverine hydrochloride in tablets, in spiked human serum and urine samples. The method is based on measuring the intrinsic fluorescence of mebeverine hydrochloride in water:acetonitrile (1:1) mixture at 355 nm (excitation at 295 nm). The proposed method has been successfully applied to the determination of mebeverine hydrochloride in biological fluids after selective extraction. The method proved to be accurate and reproducible as indicated by relative standard deviation of less than 2%. The limit of detection is 0.02 μg/ml.

Keyphrases ❑ Mebeverine hydrochloride, intrinsic fluorescence, spiked urine, spiked serum, tablets.

Mebeverine, 4-[ethyl(4-methoxy-α-methylphenethyl)amino]butyl veratrate has a spasmolytic activity of the musculotropic type (1,2). Mebeverine is effective in relieving irritable bowel syndroms. It acts on gastrointestinal smooth muscle and colon (3,4). Other papers have been published concerning the mode of action and the activity (5,6). The use of mebeverine in pharmacotherapy necessitates the need of a sensitive and selective method for the assay of the drug in tablets and in biological fluids. Very few attempts have been reported for mebeverine assay using high performance thin layer chromatography (7) and high performance liquid chromatography (HPLC) (8). Mebeverine hydrochloride has been determined in plasma using HPLC with fluorescence detection (9). In the presence of its degradation products, mebeverine hydrochloride has been assayed using derivative spectrophotometry (10).

In the present work, a rapid, sensitive and accurate