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Short Communication

Spectrophotometric determination of some antiallergic agents with 3-methyl-2-benzothiazolinone hydrazone

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Introduction

Phenothiazines (isothipendyl, ID; trimeprazine, TM; promethazine, PM; and methdilazine, MD), pyridoindole (mebhydrolin, MH) and pyrrolidinyl (triprolidine, TP) are extensively used as antiallergic agents. They have been officially determined by titrimetry (TP [1, 2], TM [1, 2], PM [1, 2] and MH [3]) and spectrophotometry (TP [1, 2], MD [1], TM [1, 2], PM [1, 2] and ID [18]). Few spectrophotometric methods have been reported for the determination of ID [4], TM [5,6], PM [7–9], MD [10, 11], MH [12, 13] and TP [14, 15] in the visible region. 3-Methyl-2-benzothiazolinone hydrazone (MBTH) [16, 17] with appropriate oxidizing agent has been reported as chromogenic agent for the determination of aromatic amines and iminohetero aromatic compounds in microgram amounts. In the present paper we have utilized the MBTH for the determination of ID, TM, PM, MD, MH and TP in bulk samples and pharmaceutical preparations.

Experimental

Apparatus

Systronics 105 (MK 1) spectrophotometer with 1 cm matched glass cells was used for all absorbance measurements. All pH measurements were performed on an Elico model LI-120 digital pH meter.

Reagents

All chemicals were of analytical reagent grade. MBTH hydrochloride solution, 0.2% m/v (8.56×10^{-3} M) prepared in distilled water. Iron(III) chloride hexahydrate solution, 0.4% m/v (1.48×10^{-2} M) freshly prepared in distilled water. Potassium persulphate solution, 0.27% m/v (1×10^{-2} M) prepared in distilled water. Sodium hypochlorite solution (3.45×10^{-3} M) prepared in distilled water. All three oxidant solutions were standardized.

Standard drug solutions

Aqueous solutions (500 μg ml^{-1}) of ID hydrochloride, TM tartrate, PM hydrochloride, MD hydrochloride and TP hydrochloride were prepared separately. MH napadisylate solution (250 μg ml^{-1}) was prepared by dissolving 25 mg initially in minimum volume of warm HCl solution and diluted to 100 ml with distilled water after bringing the pH to 6.5 with sodium hydroxide. Standard solution (100 μg ml^{-1} for TM or MD, 200 μg ml^{-1} for PM or ID, 25 μg ml^{-1} for MH and 50 μg ml^{-1} for TP) was prepared in each instance by appropriate dilution of the stock solution with distilled water.

Procedures

Method A. Aliquots of aqueous solutions of TM (0.2–2.0 ml, 100 μg ml^{-1}), MD (0.2–2.0 ml, 100 μg ml^{-1}) or MH (0.4–4.0 ml, 25 μg ml^{-1}) were placed in a series of 25-ml calib-

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rated tubes. Iron(III) chloride solution (1 ml for TM or MD, 2 ml for MH), hydrochloric acid (1 ml of 1 M HCl for TM or MD, 1 ml of 0.1 M HCl for MH) and MBTH (0.5 ml for TM or MD, 2 ml for MH) were added successively at 1 min interval to each tube. The contents were diluted to the mark with distilled water after 5 min. The absorbances were measured at 680 nm (TM or MD) or at 630 nm (MH) against a reagent blank during the stability period (2 min–12 h for TM or MD, 10 min–40 h for MH). The amount of TM, MD or MH was computed from its calibration graph.

Method B. Aqueous solutions of PM (100–800 μg) or ID (100–700 μg) were delivered into a series of 25 ml calibrated tubes. Potassium persulphate (1 ml) and MBTH (1 ml) were added successively at 1-min interval and kept in a waterbath at 70°C for 5 min (PM) or 10 min (ID). The contents were cooled and diluted to the mark with distilled water. The absorbances were measured at 630 nm against a reagent blank after 5 min and before 5 h. The amount of PM or ID was computed from its calibration graph.

Method C. Aliquots of TP (20–200 μg) were delivered into a series of 25-ml calibrated tubes. Sodium hypochlorite (1 ml) and MBTH (3 ml) were added to each tube at 1-min intervals. The volume was made up to the mark with methanol after 5 min. The absorbances were measured at 390 nm against a reagent blank after 5 min and before 1 h. The amount of TP was computed from its calibration graph.

Procedure for the assay of dosage forms

Powdered tablets or syrups equivalent to 25 mg of antiallergic agent were treated as in standard solution preparation and analysed as per the assay procedure.

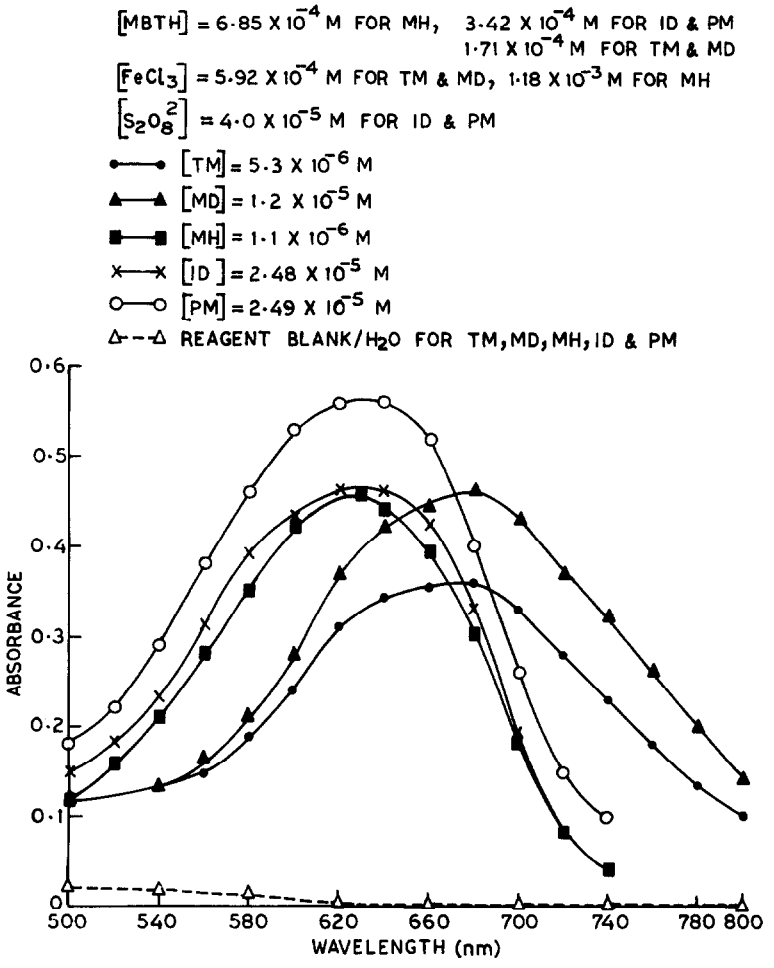


Figure 1

Table 1
Optical characteristics and precision data

	TM	MD	MH	PM	ID	TP
λ_{max} (nm)	680	680	630	630	630	390
Beer's law limits ($\mu g\ ml^{-1}$)	0.8–8.0	0.8–8.0	0.4–4.0	4–32	4–28	0.8–8.0
Molar absorptitivy (1. $mol^{-1}cm^{-1}$)	4.48×10^4	2.57×10^4	1.30×10^5	1.12×10^4	1.2×10^4	2.03×10^4
Sandell's sensitivity ($\mu g/cm^2$/0.001 absorbance unit)	0.0167	0.0129	0.0065	0.0286	0.0267	0.0163
Correlation coefficient (r)	0.9999	0.9999	0.9999	0.9998	0.9999	0.9999
Regression equation (A)*						
Slope (b)	0.05956	0.07584	0.15167	0.03467	0.02871	0.06071
Intercept (a)	0.00278	0.00446	0.00446	−0.00137	−0.00357	0.00274
% RSD	0.95	0.74	0.74	0.59	0.69	0.88
% Range of error (95% confidence limit) (±)	0.97	0.76	0.76	0.61	0.71	0.90
Stability (h)	12	12	40	5	5	1

$A^* = a + bc$, where c is the concentration in $\mu g\ ml^{-1}$.

Results and Discussion

As the antiallergic agents under investigation possess tertiary amino group in cyclic form, the suitability of MBTH reagent for the determination was examined. The applicability of MBTH in conjunction with various oxidizing agents [iron(III), $S_2O_8^{2-}$, OCl^-, Ce(IV), IO_4^-, CAT, $Fe(CN)_6^{3-}$ or $Cr_2O_7^{2-}$) for the determination of antiallergic agents was examined and the appropriate combination with MBTH, iron(III) (TM, MD or MH), $S_2O_8^{2-}$ (PM or ID) or OCl^- (TP) were included in the procedures. The effects of reagent concentrations (MBTH with suitable oxidizing agents), pH, temperature, time, order of addition of reagents and solvents with respect to maximum sensitivity, minimum blank, adherence to Beer's law and stability have been studied through control experiments. The optimum conditions were incorporated in the procedures. Beer's law was found to be valid over the concentration ranges given in Table 1 at appropriate λ_{max} (Figs 1 and 2). The molar absorptivity, slope, intercept and correlation coefficients obtained by a linear least-squares treatment of the results are also given in Table 1. The precision of each method was tested by measuring six replicate samples of antiallergic agent (150 μg of TM, 150 μg of MD, 150 μg of TP, 50 μg of MH, 300 μg of PM, 300 μg of ID). The relative standard deviation (RSD) and the range of error obtained are given in Table 1.

The other components usually present in dosage forms did not interfere. The pharmaceutical dosage forms were analysed by the previously reported [1, 3, 4] and the proposed methods (Table 2) to confirm the accuracy of the proposed methods for the determination of antiallergic agents.

The proposed procedures were found to be simple, rapid, accurate and sensitive for the analysis of antiallergic agents and its dosage forms.

Mechanism

The coloured species obtained in these pro-

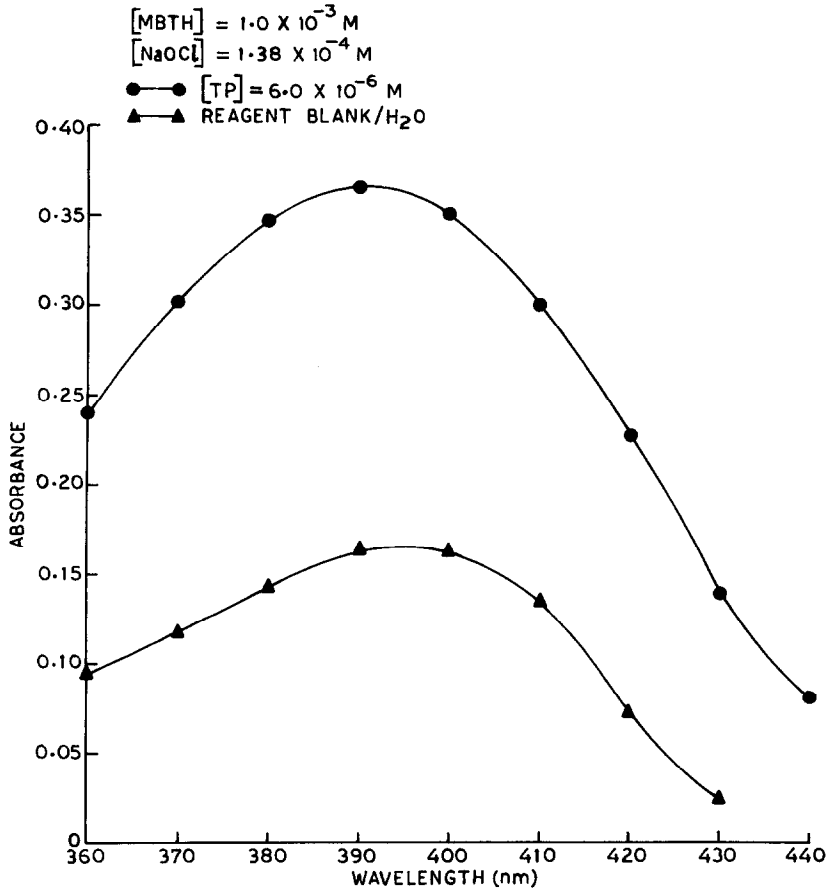
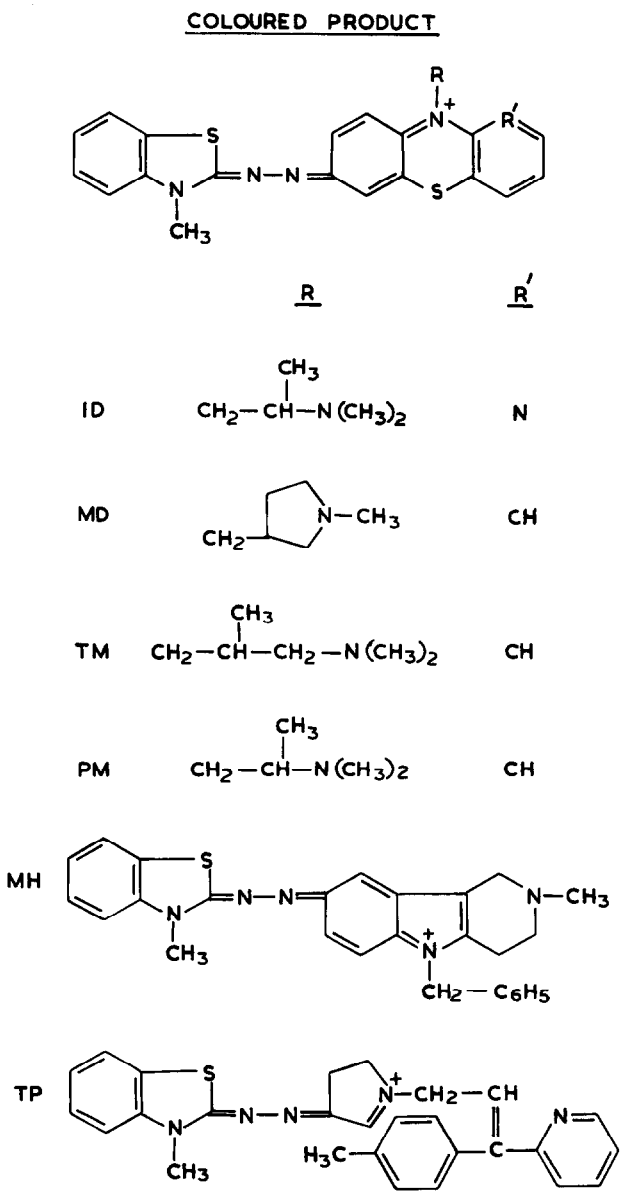


Figure 2

Table 2
Determination of antiallergic agents in pharmaceutical preparations

Pharmaceutical preparations	Labelled amount (mg)	Amount (mg) found by methods Proposed	Reported [1, 3, 4]	% Recovery* (proposed method)
Tablets				
PM	25	24.80	24.52	99.4
MD	8	7.64	7.56	100.6
TM	10	9.78	9.69	100.2
ID	8	7.78	7.67	99.8
MH	10	9.86	9.74	99.6
TP	2.5	2.28	2.25	99.9
Syrups (mg ml^{-1})				
PM	1	0.98	0.97	100.2
TM	6	5.85	5.79	99.2
MD	0.8	0.76	0.75	99.7

*Added 10 mg to each sample. Average of three determinations.



Scheme 1

cedures can be considered as an oxidative coupling product between the anti-allergic agent and MBTH analogues to the products obtained by reaction of MBTH with hetero-amines [17].

Probable structure of coloured product in each instance (TM, MD, ID, PM, TP or MH) are shown in Scheme 1. The reagent would be expected to attack phenothiazine (TM, MD, PM or ID) and carbazole (MH) in the position *para* to the ring nitrogen as substitutions in these compounds take place more readily in those positions. However, in pyrrolidine compounds (TP) the 3-position is the most active. The variation in λ_{max} and ϵ_{max} of the coloured species formed in the case of different anti-allergic agents links to the extent of conjugation, inductive, mesomeric and steric effect exhibited by the other substituents.

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References

[1] *U.S. Pharmacopeia* (XXI Revn), pp. MD, 656; PM, 893; TM, 1091 and [XX Revn. 1980] pp. TP, 830. Mack Publishing Co., Eastern PA (1985).

[2] *British Pharmacopoeia* (13th edn), pp. PM, 372, 813; TM, 465, 830; TP, 467, 831. HMSO University Press, Cambridge (1980).

[3] *British Pharmaceutical Codex*, pp. MH, 468, 1298. The Pharmaceutical Press, London (1968).

[4] S.S. Zarapker, R.V. Rele and V.J. Doshi, *Ind. Drugs* **24**, 560–564 (1987).

[5] R.T. Sane, S.S. Kamat, V.S. Narkar, A.Y. Sathey and J.H. Mhales, *Ind. Drugs* **18**, 19–22 (1980).

[6] S.R. El-Shabouri, *Talanta* **32**, 999–1001 (1985).

[7] P.G. Ramappa and K. Basavaiah, *Ind. J. Pharm. Sci.* **47**, 125–127 (1985).

[8] A.F. Youssef, S.R. El-Shabouri, F.A. Mohamed and M.I. Abdel Rageh, *J. Assoc. Off. Anal. Chem.* **69**, 513–518 (1986).

[9] Jayarama, M. Violet D'Souza, H.S. Yathirajan and Rangaswamy, *Talanta* **33**, 352–354 (1986).

[10] O.S. Kamalapurkar and C. Menezes, *Ind. Drugs* **22**, 97–98 (1984).

[11] J. Emmanuel and R. Mathew, *Ind. Drugs* **22**, 602–603 (1985).

[12] R.G. Bhatkar and D.C. Madkaiker, *Ind. J. Pharm. Sci.* **43**, 20–21 (1981).

[13] O.S. Kamalapurkar and J.J. Chudasama, *Ind. Drugs* **21**, 404–405 (1984).

[14] J. Emmanuel and T.V. Yagnanarayanan, *Ind. Drugs* **19**, 77–79 (1981).

[15] R.T. Sane, V.M. Vaidya, V.G. Nayak, A.Y. Dhamankey, S.K. Joshi, V.J. Doshi, S.V. Sawant, V.B. Malkar, V.K. Pandit, A.Y. Sathey and A. Swatipurkar Nadkarni, *Ind. Drugs* **19**, 398–403 (1982).

[16] M. Pays, R. Bourdon and M. Belgean, *Analytica Chim. Acta* **47**, 101–111 (1969).

[17] E. Sawicki, T.W. Stanley, T.R. Hauser, W. Elbert and J.L. Noel, *Anal. Chem.* **33**, 722–725 (1961).

[18] *British Pharmaceutical Codex*, pp. ID, 256, 812. The Pharmaceutical Press, London (1973).

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