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A spectrophotometric method for the determination of metoclopramide HCl and dapsone

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Abstract

A rapid, sensitive and selective spectrophotometric method has been developed for the quantitative determination of metoclopramide hydrochloride (MCP) and dapsone (DAP) in both pure and dosage forms. The method is based on the diazo coupling reaction of the drugs with a new coupling agent, dibenzoyl methane in an alkaline medium. The resulting coloured azo dyes exhibit maximum absorption at 440 nm for MCP and at 470 nm for DAP with a molar absorptivity of 2.85×10^4 and 1.71×10^4 l mol^{-1} cm^{-1} for MCP and DAP, respectively. All variables have been optimized. No interferences were observed from excipients and the validity of the method was tested against reference method.

Keywords: Metoclopramide; Dapsone; Spectrophotometry; Drug analysis

1. Introduction

Metoclopramide hydrochloride (MCP), chemically 4-amino-5-chloro-[2-(diethyl amino) ethyl] — 2-methoxy benzamide hydrochloride has a wide range of clinical applications in fields as diverse as gastroenterology, surgery, gynaecology, radiology and cardiology. Dapsone (DAP), 4,4-diamino diphenyl sulfone, is an antileprotic drug. In view of their pharmacological importance considerable work has been done for the detection and quantification. Various analytical techniques have been developed for the determination of these drugs include HPLC [1,2] and electron-capture gas liquid chromatography [3] but involve expensive experimental setup. Official methods used for the determination of these drugs in pharmaceutical preparations are usually based on extraction as a free base and subsequent determination by UV-spectrophotometry [4–6]. Many organic compounds, drug excipients and diluents as well as various organic bases, strongly interfere.

The determination of these drugs by spectrophotometric methods has been proposed based on diazotization [7–10], ion-pair complexes [11,12], charge-transfer complexes [13], and the formation of coloured dye by the coupling reaction between the oxidation product of MBTH [14] and catechol [15]. Other chromogenic reactions use sodium vanadate [16], ammonium meta vana-

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date [17] and 9-chloroacridine [18]. These methods involve a time-consuming extraction step or heating and require strictly controlled reaction conditions. Many of these methods are less sensitive. For routine quality control, development of a simple, rapid and sensitive spectrophotometric method is highly desirable.

The aim of the present work is to provide a simple, accurate, precise and inexpensive method for the assay of MCP and DAP in bulk and pharmaceutical formulations, employing dibenzoyl methane as a new coupling agent.

2. Experimental

2.1. Apparatus

All spectral measurements were carried out with a Jasco (Model UVIDEC-610) and Elico (Model CL-27) spectrophotometers with 1 cm matched cells.

2.2. Reagents

All chemicals were of analytical-reagent grade.
Dibenzoyl methane (*DBM*, *1% m/v*)*:* Prepared by dissolving 1 g of DBM in 100 ml of methanol.
Sodium nitrite (*0.1% m/v*)*:* Prepared by dissolving 1 g of sodium nitrite in water and diluting to 1000 ml with water.
Sulphamic acid (*3% m/v*)*:* Freshly prepared by dissolving 3 g of sulphamic acid in 100 ml of distilled water.
Sodium hydroxide (*4 M*)*:* Prepared by dissolving 16 g of sodium hydroxide pellets in 100 ml of distilled water.
Hydrochloric acid: 1 M solution was used.

2.3. Standard solution

Separate aqueous solution of metoclopramide hydrochloride (MCP, IPCA Laboratories Ltd, India) and methanolic solution of dapsone (DAP, Intas Laboratories Ltd., India) were prepared daily by dissolving 100 mg of the sample in 100 ml standard flask (1000 μg ml^{-1}). Working solutions were prepared as required by dilution.

2.4. Standard procedure

An aliquot of a standard solution containing 0.5–6.0 ml (50 ppm) of MCP or 0.5–7.0 ml, (50 ppm) of DAP was transferred into a series of 25 ml standard flasks. To this solution was added 2 ml of 0.1% sodium nitrite and the acidity was adjusted with 1 ml of 1 M hydrochloric acid. The solution was shaken thoroughly for 2 min to allow the diazotization reaction to go to completion. Then, 3 ml of 3% sulphamic acid was added to each flask. A volume of 2 ml of 1% DBM and 2 ml of 4 M sodium hydroxide solutions were added and the contents were diluted to the mark with methanol and mixed well. After 10 min, absorbance of the coloured azo dye was measured at 440 nm for MCP and at 470 nm for DAP against the corresponding reagent blank.

2.5. Procedure for pharmaceutical formulations

A quantity of the sample (Perinorm, Reglan, Dapsone) equivalent to 20 mg of the drug was weighed accurately and transferred into a 100 ml standard flask and the volume made up with distilled water (methanol for Dapsone) (the contents were thoroughly shaken for about 30 min) and filtered. Requisite amount (200 μg/25 ml) of the drug solution was taken and the above standard procedure was followed for the assay of drug content.

For the analysis of injection solution, the requisite volume was transferred into a 100 ml standard flask and diluted to the mark with distilled water. The drug content in the diluted solution was assayed as described above. The results of the analysis are given in Table 1.

3. Results and discussion

The method involves the diazo coupling reaction of MCP or DAP with DBM in an alkaline medium to give an orange coloured azo dye with a maximum absorption at 440 nm for MCP and

at 470 nm for DAP. The absorption spectra of the above dyes are presented in Fig. 1. Two steps are involved in the reaction that produces the coloured dye. In the first step, MCP or DAP are treated with nitrite solution in acidic medium, undergoes diazotization to give the diazonium chloride ion. In the second step, the diazonium ion is coupled with the active methylene group of DBM to form an azo dye in an alkaline medium. The reaction can be represented in Scheme 1. Here MCP as the model compound, since the other compound behaved similarly to it (Scheme 1).

3.1. Effect of dibenzoyl methane

The effect of the concentration of dibenzoyl methane was studied by measuring the absorbance at specified wavelengths in the standard procedure for solutions containing a fixed concentration of drugs and varying amounts of dibenzoyl methane.

Table 1
Analysis of metoclopramide and dapsone in various dosage forms

Samples	Proposed method*				Reference method [a]	*t*-test [b]	*F*-test [c]
	Amount taken (μg ml^{-1})	Amount found (μg ml^{-1})	% Rec ± SD	% CV	% Rec ± SD		
MCP							
Perinorm tab (10 mg)	4	3.99	99.8 ± 0.6	1.23	100.2 ± 0.5	1.7	1.44
	6	5.97	99.5 ± 0.6	0.75	99.9 ± 0.4	1.4	2.25
	8	8.04	100.5 ± 0.4	0.64	100.9 ± 0.6	2.7	2.25
Reglan tab (10 mg)	4	3.96	99.1 ± 0.7	3.92	99.8 ± 0.4	2.4	3.06
	6	6.03	100.6 ± 0.5	1.71	100.9 ± 0.6	1.6	1.44
	8	7.97	99.6 ± 0.4	0.57	99.9 ± 0.4	1.7	1.00
Emenil tab (10 mg)	4	3.99	99.7 ± 0.4	1.67	99.8 ± 0.5	0.6	1.56
	6	5.99	99.8 ± 0.5	1.58	99.6 ± 0.5	1.1	1.00
	8	7.92	99.9 ± 0.4	0.86	100.5 ± 0.4	3.0	1.00
Perinorm inj (5 mg/5 ml)	4	4.01	100.3 ± 0.5	0.85	99.6 ± 0.4	1.4	1.56
	6	6.01	100.1 ± 0.1	0.68	99.9 ± 0.2	0.3	4.00
	8	7.98	99.8 ± 0.5	0.31	100.9 ± 0.8	1.0	2.56
Reglan inj (5 mg/5 ml)	4	3.96	99.1 ± 0.7	2.06	99.8 ± 0.5	1.4	1.96
	6	5.97	99.6 ± 0.5	1.72	99.7 ± 0.4	3.0	1.56
	8	7.99	99.9 ± 0.4	0.69	100.3 ± 0.2	2.6	4.00
DAP							
Dapsone tab (25 mg)	4	3.98	99.6 ± 0.5	1.65	99.9 ± 0.5	0.2	1.00
	8	8.02	100.3 ± 0.4	1.17	99.5 ± 0.6	0.9	2.25
	12	11.97	99.8 ± 0.5	0.84	98.8 ± 0.7	1.6	1.96
Dapsone tab (100 mg)	4	3.99	99.7 ± 0.4	2.01	100.3 ± 0.5	2.7	1.56
	8	8.01	100.2 ± 0.5	1.82	99.7 ± 0.4	1.5	1.56
	12	11.87	98.9 ± 0.6	1.61	99.9 ± 0.4	2.3	2.25

[a] Average of five determinations.
[b] Tabulated value 2.78.
[c] Tabulated value 6.39.

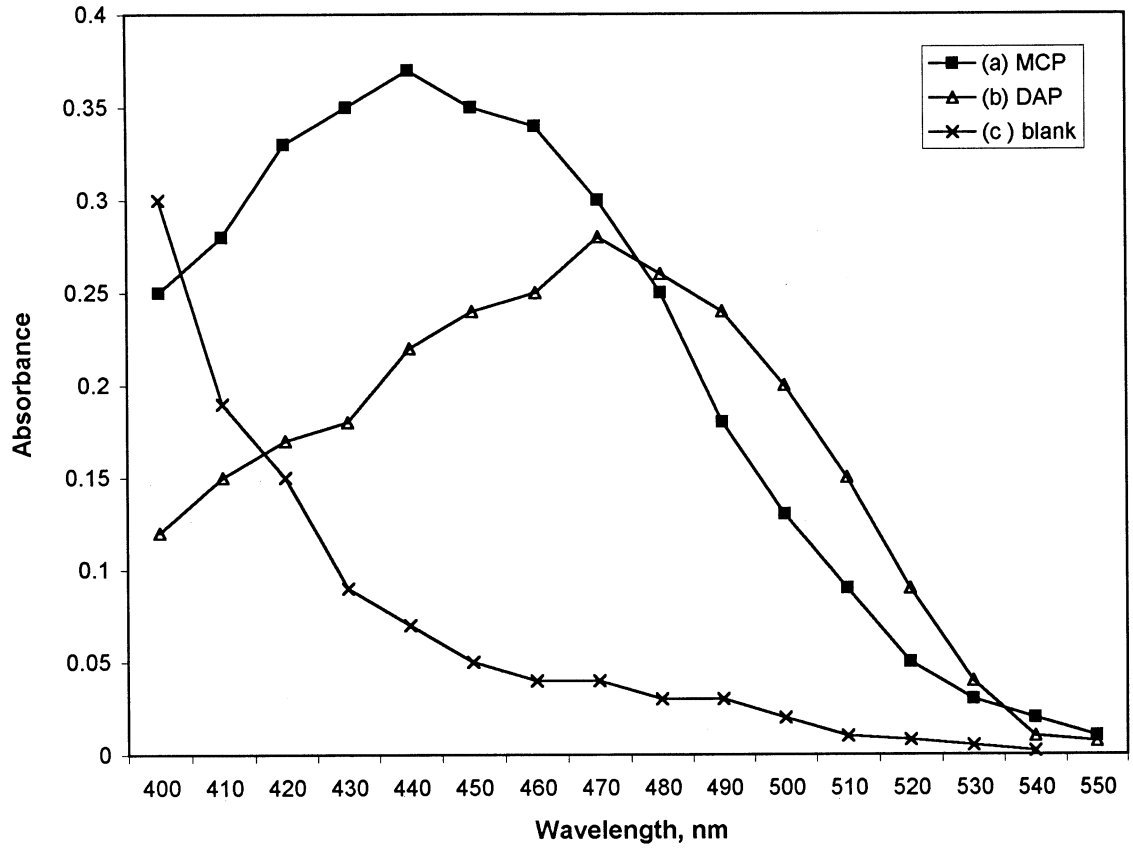


Fig. 1. Absorption spectra of the reaction products of DBM with (a) MCP [8 ppm]; (b) DAP [8 ppm]; (c) blank.

A volume of 2 ml of 1% solution in a total volume of 25 ml was found to be sufficient.

3.2. Effect of sodium nitrite

The optimum concentration of sodium nitrite solution was found to be 2 ml of 0.2% in a total volume of 25 ml of the reaction mixture. The excess of nitrite could be removed by the addition of 3 ml of 3% sulphamic acid.

3.3. Effect of acidity on diazotization

The hydrochloric acid concentration for diazotization was studied. A suitable acidity, as evident from the maximum absorbance and stability of the azo dye formed, was found to be 1 ml of 1 M hydrochloric acid per 25 ml of final volume. Diazotization was carried out at room temperature and cooling to 0–5°C was not necessary.

3.4. Effect of alkali

The optimum concentration of sodium hydroxide leading to a maximum intensity of colour was found to be 2 ml of 4 M in the final solution. The alkali concentration higher than 4 M may lead to partial decolourization of the coloured azo dye.

3.5. Effect of reaction time

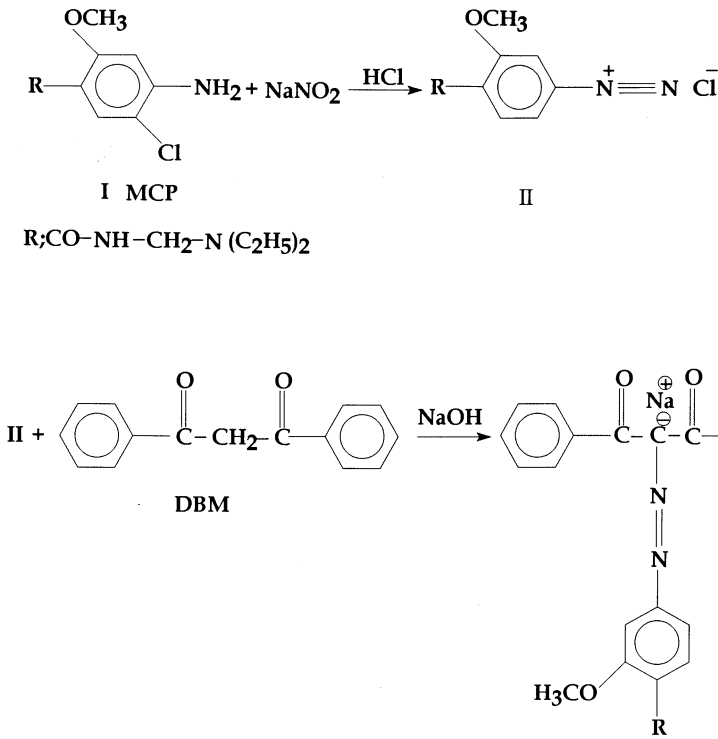
The coloured azo dyes developed rapidly after addition of the reagents and attained maximum intensity after about 10 min at room temperature. The colour was stable for a period of more than 2 h for both drugs.

3.6. Effect of solvents

The choice of diluent for the reaction mixture was also studied. Water, methanol, ethanol, acetone and isopropanol were tested as diluting solvents. Methanol was the best and thus selected for the experimental studies.

3.7. Effect of synthetic mixtures

To test the accuracy of the method, recovery experiments were performed on synthetic mixtures prepared in the laboratory. The usual tablet diluents and excipients were found not to interfere with the analysis by the proposed



Scheme 1. Proposed reaction mechanism of MCP with DBM.

Table 2
Analysis of MCP and DAP from various excipients by the proposed method

Name of the compound	Amount present (mg)	Excipients (mg)						%Recovery [a] ± SD
		Talc	Dextrose	Starch	Sodium algenate	Gelatin	Gum acacia	
MCP	100	250	350	250	100	50	100	99.9 ± 0.9
	120	150	250	180	75	75	50	100.1 ± 0.8
DAP	100	300	200	250	100	50	75	100.6 ± 1.1
	80	150	250	150	75	100	50	99.7 ± 0.8

[a] Average recovery from five experiments.

Table 3
Optical characteristics and precision data[b]

Parameter	MCP	DAP
Beer's law limit (μg ml^{-1})	1–12	1–14
Molar absorptivity (l mol^{-1} cm^{-1})	2.85×10^4	1.71×10^4
Sandell's sensitivity (μg cm^{-2}per 0.001 abs. unit)	0.0124	0.0145
Correlation co-efficient (r)	0.9999	1.000
Regression equation (Y*)[a]		
Slope (b)	0.0634	0.0695
Intercept (a)	0.0204	0.0042
% RSD ($n = 7$)	0.017	0.010
Detection limit, D_L (μg ml^{-1})	0.0333	0.0422
Quantitation limit, Q_L (μg/ml)	0.1009	0.1281

[a] $*Y = a + bx$, where x is the concentration in μg/ml.
[b] D_L; $3.3\sigma/S$; D_L = detection limit; Q_L; $10\sigma/S$; Q_L = quantitation limit; σ, standard deviation of blank; S, slope of calibration.

method. The results and composition are presented in Table 2.

3.8. Analytical data

The optical characteristics, such as Beer's law limit, molar extinction coefficient, correlation coefficient, slope, intercept, relative standard deviation, detection limit and quantitation limits are presented in Table 3.

3.9. Applications

The proposed method was applied to the quantitative determination of MCP and DAP in pharmaceutical formulations. The results of an assay of Perinorm, Reglon, Emenil, Dapsone tablets and injection solutions presented in Table 1, compare favourably with the reference methods [8,14].

Statistical analysis of the results by F and t-tests showed no significant difference in accuracy and precision between the proposed and reference methods. The precision of the proposed method was evaluated by replicate analyses of samples containing MCP and DAP at three different concentrations. The low values of the CVs at both the low and high concentration reflect the high precision of the proposed method.

4. Conclusion

First time dibenzoyl methane was used as a new coupling agent for the determination of MCP and DAP in both pure and dosage forms. The proposed method is simple, rapid, selective and offers the advantages of high sensitivity and a wide range of determination without the need for extraction or heating. The developed method does not involve any stringent reaction conditions and more sensitive than other spectrophotometric methods (Table 4). The method unaffected by slight variations in the experimental conditions such as basicity, reagent concentration and temperature. The wide applicability of the new method for routine quality control is well established by the analysis of MCP and DAP in pharmaceutical dosage forms.

Table 4
Comparison of the proposed method with other spectrophotometric methods

Reagents	Range (ppm)	Remarks	Reference
Catecol	10–40	Less sensitive than the proposed method	[15]
MBTH	–	Less sensitive	[14]
Bromothymol blue	1–10	Extractive	[11]
9-chloroacridine	20–200	Time consuming and less sensitive	[18]
Resorcinol	1–100	Less sensitive than the proposed method	[8]
Chloranil or Bromanil	40–160	Required heating at 80°C	[13]
$NaVO_3$	–	Less sensitive and required heating	[16]
Dibenzoyl methane	1–12 for MCP 1–14 for DAP	Most sensitive, rapid and a facile work	Proposed method

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