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Sensitive Spectrophotometric determination of Metoclopramide Hydrochloride And Dapsone in Bulk Sample And Dosage Forms

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ABSTRACT: A simple, sensitive and selective spectrophotometric method for the determination of metoclopramide hydrochloride (MCP) and dapsone (DAP) in both pure and dosage forms is described. The method is based on the diazo – coupling reaction of the studied drugs with a new coupling agent, imipramine hydrochloride, in an acid medium. The resulting violet – colored azo dyes exhibit maximum absorption at 570 nm for both MCP and DAP. All variables were studied in order to optimize the reaction conditions. The method is suitable for the determination of MCP and DAP in the presence of other ingredients that are usually present in dosage forms and the recoveries were obtained in the range of 99.5-100.5%. The results are reproducible with an accuracy of ±1%, and the validity of the method was tested against reference method.

KEYWORDS: Metoclopramide, dapsone, pharmaceutical analysis, spectrophotometry.

INTRODUCTION

Metoclopramide hydrochloride (MCP) and dapsone (DAP) are widely used as chemotherapeutics. MCP has been found to be remarkably useful in the treatment of drug induced nausea and vomiting, including cancer chemotherapy. DAP is a well known antileprotic drug. The importance of these drugs have prompted the development of few methods for their detection and quantification.

Several spectrophotometric methods have been reported for the determination of MCP and DAP based on diazotization and coupling with resorcinol or naphtha-2-ol[1], dibenzoyl methane[2], chromotropic acid[3], 3-aminophenol and salbutamol[4], NEDA[5], ion-association complex formation[6,7], an oxidative coupling reaction[8], charge-transfer complex formation[9] or through formation of the Schiff's base with p-dimethylaminocinnamaldehyde[10]. Other chromogenic reactions use sodium vanadate[11], ammonium meta vanadate[12], 3-methylbenzothiazolin-2-one hydrazone (MBTH)[3], nitrous acid-cresyl fast-violet acetate (CFVA)[13], 9-chloroacridine[14], catechol[15], sodium 3,4-dioxonaphthalene-1-sulphate[16] and Folin-ciocalteu reagent[17]. Some of these methods suffer from several disadvantages, such as use of heating step[11,12], low sensitivity[3,11,12,14], strong acid medium[11,12], low range of determination and critical working conditions[7,13] and poor selectivity. These deficiencies have encouraged the authors to develop a simple, rapid, accurate and inexpensive method for the analysis of the studied therapeutics. The present paper describes the application of imipramine hydrochloride (IPH) as an inexpensive new coupling agent for the determination of MCP and DAP in both pure and dosage forms.

MATERIALS AND METHODS

Apparatus: All absorbance measurements were made with an Elico Model SL–171 digital spectrophotometer with 1 cm matched cells.

Reagents : All chemicals used were of analytical – reagent grade. Aqueous solutions of imipramine hydrochloride (IPH, 0.5%), sodium nitrite (0.1%), sulfamic acid (2%) and hydrochloric acid (1 mol l^{-1}) were used.

Standard solution : Aqueous solutions of metoclopramide hydrochloride (MCP, IPCA Laboratories Ltd. India) and methanolic solutions of dapsone (DAP, Smithkline Beecham Ltd. India) were prepared daily by dissolving 100 mg of the sample in a 100 ml standard flask (1000 mg ml^{-1}). Solutions of lower concentrations were prepared by diluting the standard solutions.

Standard Procedure

Accurately measured volumes of drug solutions equivalent to 0.5-5.0 μg ml^{-1} and 0.5–4.0 μg ml^{-1} final solutions of MCP and DAP, respectively, were transferred into a series of 10 ml standard flasks. To each flask, 1 ml of 0.1% sodium nitrite and 0.5 ml of 1 mol l^{-1} hydrochloric acid were added. After 3 min, 1 ml of 2% sulfamic acid and 2 ml of 0.5% IPH solution were added and the contents were diluted to the mark with 6 M hydrochloric acid and mixed well. After 5 min, absorbance of the colored azo dye was measured at 570 nm for both MCP and DAP against the corresponding reagent blank. The amount of drugs was computed from the standard calibration graphs.

Procedure for Dosage Forms

In a 100 ml standard flask, an accurately weighed amount (from the mixed and powdered contents of 20 tablets), equivalent to 20 mg of the respective drug, was dissolved in 75 ml of distilled water and the contents were thoroughly shaken for about 30 min and brought up volume with distilled water for MCP or methanol for DAP, and then filtered. Appropriate aliquots of the drug solution were taken, and the above standard procedure was followed for analyzing the drug content.

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

Results and Discussion

Under the reaction conditions, MCP and DAP are treated with nitrite solution in acidic medium, which undergoes diazotization to give the diazonium chloride. The diazonium chloride couples with a new coupling agent, IPH, in an acidic medium to form an azo dye. The electron density in IPH is highest at the two and eight positions, which permits electrophilic substitution by the diazonium ion.

Under the proposed reaction conditions 1 ml of 0.1% sodium nitrite and 0.5 ml of 1 M hydrochloric acid were necessary for diazotiazation. The diazotization was carried out at room temperature (25 ± 5°C) and cooling to 0-5°C was not necessary. Two milliliters of 0.5 % IPH solution and addition of 6 M hydrochloric acid up to the final volume were found to be necessary for full color development, and the formed azo dye was stable up to 2 h in the acid medium.

The optical characteristics, the range over which

Table 1. Results of assay of metoclopramide and dapsone in dosage forms.

Samples		Proposed method[a]		% ReferenceMethod[3]	t-Value[b]	F-value[c]
	Amount taken(μg ml^{-1})	Amount found(μg ml^{-1})	% Recovery± SD	% Rec.± SD		
MCP						
Perinorm	1	0.99	99.60 ± 0.50	100.20 ± 0.40	2.30	2.10
tab (10 mg)	2	1.99	99.50 ± 0.30	99.80 ± 0.40	1.15	1.70
	3	2.99	99.60 ± 0.10	100.10 ± 0.10	1.80	1.17
Reglan	1	0.99	98.80 ± 0.30	99.90 ± 0.20	0.23	1.59
tab (10 mg)	2	1.99	99.50 ± 0.20	99.90 ± 0.30	1.89	2.25
	3	3.00	100.00 ± 0.90	100.30 ± 0.70	0.49	1.65
Emenil	1	1.00	100.00 ± 0.55	99.80 ± 0.50	1.26	1.21
tab (10 mg)	2	1.99	99.40 ± 0.56	99.80± 0.49	1.06	1.30
	3	2.99	99.60 ± 0.58	99.80 ± 0.50	1.47	1.29
Perinorm	1	0.99	99.50 ± 0.38	99.90 ± 0.19	0.23	3.20
Inj (5 mg ml^{-1})	2	1.99	99.50 ± 0.44	100.00± 0.34	0.24	1.67
	3	2.99	99.60 ± 0.53	99.80 ± 0.47	1.29	1.27
Reglan	1	0.99	99.70 ± 0.90	99.50 ± 0.50	0.78	2.25
Inj (5 mg ml^{-1})	2	1.99	99.50± 0.53	99.90± 0.47	1.29	1.27
	3	3.00	100.00 ± 0.61	99.90 ± 0.48	1.25	1.61
DAP						
Dapsone	1	1.00	100.00 ± 0.55	99.80 ± 0.50	1.26	1.21
tab (25 mg)	2	1.99	99.50 ± 0.40	100.20 ± 0.58	2.30	2.10
	3	2.99	99.60± 0.13	100.10 ± 0.12	1.80	1.10
Dapsone	1	0.99	99.90± 0.60	99.80 ± 0.48	1.25	1.61
tab (100 mg)	2	1.99	99.90 ± 0.58	99.80 ± 0.51	1.47	1.29
	3	3.00	100.00 ± 0.54	99.70 ± 0.46	1.75	1.37

[a]Average of five determinations;
[b]Tabulated t - value 2.78;
[c]Tabulated F value 6.39.

Beer's law applies, molar extinction coefficient and correlation coefficient (r) of the standard curve for MCP, were found to be 0.5-5 $\mu g\ mL^{-1}$, $4.5\times10^4\ l\ mol^{-1}cm^{-1}$ and 0.999, respectively and for DAP 0.5-4 $\mu g\ mL^{-1}$, $2.96\times10^4\ l\ mol^{-1}cm^{-1}$ and 0.9999, respectively. The detection limit (DL=3.3Ã/s) and quantitation limit (QL=10Ã/s) [where 'Ã' the standard deviation of reagent blank and 's' is the slope of calibration curve] of the method were found to be 0.0144 and 0.0437 $\mu g\ ml^{-1}$ for MCP, and 0.0132 and 0.0402 $\mu g\ ml^{-1}$ for DAP, respectively.

As shown in Table 1, the method could be used to quantify MCP and DAP in various drug dosage formulations with 99.5-100% recovery.

Conclusions

The developed method is simple, rapid, selective, inexpensive and exhibits a fair degree of precision and accuracy. The method does not involve any critical reaction conditions and can be compared favourably with other existing methods [1-17]. The proposed method can serve as an alternative method for the routine analysis of MCP and DAP in pure drugs and in pharmaceutical formulations.

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