Journal of Analytical Chemistry, Vol. 60, No. 7, 2005, pp. 633–635. From Zhurnal Analiticheskoi Khimii, Vol. 60, No. 7, 2005, pp. 711–714.

ARTICLES

Spectrophotometric Determination of Metoclopramide in Pharmaceutical Preparations[1]

J. Shah, M. Rasul Jan, M. Azam Khan, and S. Amin

Department of Chemistry, University of Peshawar, N.W.F.P., 25120 Pakistan

e-mail: jasminshah2001@yahoo.com

Received September 30, 2003; in final form, May 6, 2004

Abstract—A simple and rapid spectrophotometric method for the determination of metoclopramide is described. The method is based upon simple diazotization reactions with nitrite and aniline as the coupling reagent. The absorbance was measured at 410 nm. The method was optimized for acidity, the amount of reagents required, and the amount of sodium hydroxide. The range of linearity was 0.5–12.0 μg/mL. The method was successfully applied to the determination of metoclopramide in pharmaceutical preparations without any interference from common excipients.

INTRODUCTION

Metoclopramide [monohydrate of 4-amino-5-chloro-*N*-(2-diethylaminoethyl)-2-methoxy benzamide hydrochloride (MCP)] is the active ingredient of many pharmaceutical preparations concerned with gastroenterology, surgery, gynecology, and cardiology. A number of the analytical techniques available in the literature for the quantification of MCP involve HPLC [1–3], gas chromatography–mass spectrometry (GC–MS) [4], ion-selective electrodes [5–12], anodic stripping voltammetry [13], and differential scanning calorimetry [14].

Official methods used for the determination of these drugs in pharmaceutical preparations are usually based on the extraction of a freebase and subsequent determination by UV-spectrophotometry [15, 16]. Many organic compounds, drug excipients, and diluents (as well as various organic bases) strongly interfere with metoclopramide determination using UV spectrophotometry. A number of spectrophotometric methods are available in the literature for metoclopramide. Some of the spectrophotometric methods are based upon charge-transfer complexes [17], ion pair complexes [18], complexes after oxidation of metoclopramide with metal [19], the production of Schiff base with *p*-dimethylaminocinnamaldehyde [20], and diazotization [21–24]. The spectrophotometric methods for the determination of metoclopramide in pharmaceutical preparations are summarized in Table 1. The development of a simple, rapid, and sensitive spectrophotometric method is highly desirable for routine quality control. The aim of the present work is to provide a simple, accurate, and inexpensive method for the analysis of metoclopramide in pharmaceutical preparations, employing aniline as a coupling reagent.

EXPERIMENTAL

Instrument. A UNICO UV-2100 spectrophotometer (United States) was used during this study.

Reagents. All chemicals used were of analytical reagent grade purity. Standard reference metoclopramide was obtained from Nafar Pharmaceutical (Pakistan). Pharmaceutical preparations containing metoclopramide were purchased on the commercial market.

Solutions. *Standard nitrite solution (0.1%).* Prepared by dissolving 0.15 g of sodium nitrite in water and diluting to 100 mL.

Aniline reagent (10%). Prepared by diluting 10 g of aniline to 100 mL volume using methanol/ethanol as a solvent.

Sodium hydroxide solution (6 M). Prepared by dissolving 240 g of sodium hydroxide pellets in distilled water and diluting to 1 L.

Standard drug solution (1000 μg/mL). Prepared by dissolving 0.1 g of pure metoclopramide in water diluting to 100 mL.

Concentrated hydrochloric acid. Molarity of solutions in the range of 3–7 M was adjusted by using concentrated hydrochloric acid of 11.8 M.

Procedure. First, 0.6 mL of 0.1% solution of nitrite was added to an aliquot of solutions containing 2–12 μg/mL of metoclopramide, and the acidity of the solutions for diazotization was adjusted to 3 M with the addition of concentrated hydrochloric acid. The solutions were shaken thoroughly for 1 min to allow the diazotization reaction to be completed. Next, 4 mL of 10% aniline was added to each solution and heated on a boil-

[1] The text was submitted by the authors in English.

1061-9348/05/6007-0633 © 2005 Pleiades Publishing, Inc.

Table 1. Published methods for the spectrophotometric determination of metoclopramide in pharmaceutical dosage

Sample no.	λ_{max}, nm	Range, μg/mL	Detection limit, μg/mL	Reference
1	440	1–12	0.0333	[24]
2	548	5–30	5.0	[20]
3	576	5–25	5.0	[20]
4	539	0.5–85	0.5	[26]
5	410	0.5–12	0.047	Proposed method

Table 2. Analytical results obtained for the determination of metoclopramide in various pharmaceutical preparations

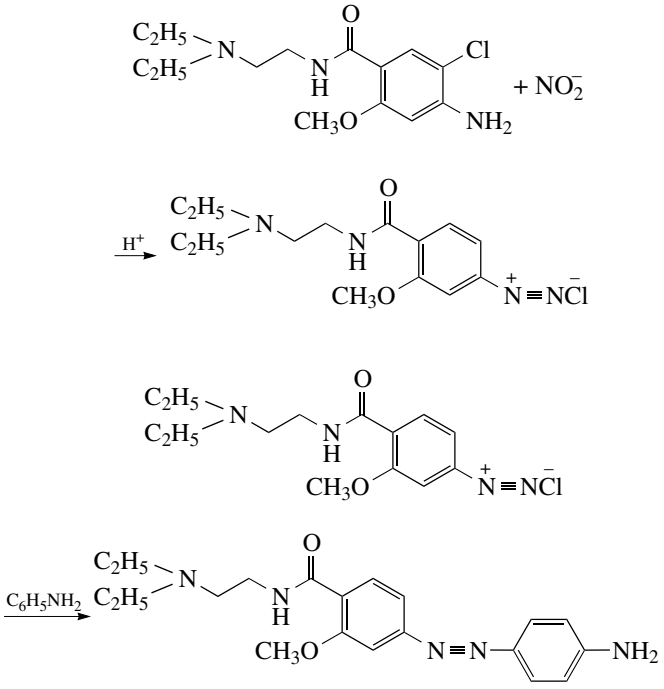
Sample	Label value	Proposed method	Literature method [15]
Maxalon syrup	5.0 mg/5 mL	5.5 ± 0.33 mg/5 mL	5.4 ± 0.42 mg/5 mL
Metomide injection	10.0 mg/2 mL	10.8 ± 0.4 mg/2 mL	10.03 ± 0.020 mg/2 mL
Metocolon injection	10.0 mg/2 mL	9.88 ± 0.26 mg/2 mL	10.3 ± 0.141 mg/2 mL
Maxolon tablets	10.0 mg/tab	10.21 ± 0.32 mg/tab	10.54 ± 0.023 mg/tab

ing water bath for 4 min. After cooling, 14 mL of 6 M sodium hydroxide solution was added and the contents were diluted to 100 mL using double-distilled water. The absorbance of the colored azo dye was then measured at 410 nm against a reagent blank.

RESULTS AND DISCUSSION

The drug (metoclopramide) has a primary aromatic amine group. When primary aromatic amines are treated with nitrous acid, diazonium compounds are formed. The diazonium compounds, by coupling with a phenolic or other amino compounds, form azo compounds. The coupling takes place in the *para* position on the amine or phenol. The coupling procedures vary somewhat, depending on the reactivity of the compounds involved. Some compounds will couple in a solution at pH 5; other will couple in a very alkaline solution. The more alkaline the solution, the faster the coupling reaction of diazonium compounds [25].

The same reaction is applied for analytical determination of metoclopramide in pharmaceutical preparations. The present method involves the diazotization between metoclopramide and nitrite, followed by the coupling with aniline in an alkaline medium to yield a colored azo dye (reaction scheme). The absorption spectrum of the azo dye formed has an absorption maximum at 410 nm against the reagent blank.



Effect of acidity on diazotization. Constant absorbance was obtained in the range of 3–7 M of hydrochloric acid. Above this range, a decrease in absorbance was observed. The acidity for the formation of diazonium chloride was fixed at 3 M.

The diazotization time was studied at room temperature. The maximum time for the diazotization reaction was found to be 0–2 min. This indicates that the diazotization reaction is rapid at room temperature.

Effect of reagent concentration. It was found that 0.6 mL of 0.1% solution of nitrite was sufficient for complete diazotization. There was no change in absorbance from 0.4–1.0 mL of 0.1% of nitrite solution. We used 10% aniline solution as a coupling reagent. It was found that the absorbance was constant with 2–4 mL of aniline solution. Hence, 4 mL of aniline solution was fixed as the coupling reagent. The coupling reaction of the diazotized compound with aniline was slow at room temperature. Coupling was carried out in a boiling water bath, and 4 min of heating was found the maximum required for azo dye formation.

Sodium hydroxide. The effect of sodium hydroxide concentration on the maximum color intensity and stability of the azo dye was studied. Volumes from 5 to 18 mL of 6 M sodium hydroxide solutions were examined; 14 mL of sodium hydroxide yielded the maximum absorbance and stability of the azo dye.

Analytical data. Beer's law was obeyed in the range 0.5–12 μg/mL of metoclopramide. The molar absorptivity for the azo dye was found to be 3.53×10^4 L/(mol cm). The limit of detection, quantification, standard deviation and relative standard deviation, slope, and intercept of the regression equation were 0.047 μg/mL, 0.156 μg/mL, 0.014 μg/mL, and 0.009, respectively.

Applications. The proposed method was applied to the determination of metoclopramide in different pharmaceutical preparations. The results are given in Table 2. The amount of active ingredient found in the samples agrees closely with the amount given on the label and is comparable to that in the reference methods [15, 16]. The close agreement of the results indicates the applicability of the method to actual samples.

REFERENCES

1. Lamarezyk, H., Chmielewska, A., Konicznal, L., *et al.*, *Biomed. Chromatogr.*, 2001, vol. 15, no. 8, p. 513.
2. Venkatashwaran, T.G., Kimng, D.T., and Stewart, J.T., *J. Liq. Chromatogr.*, 1995, vol. 18, no. 1, p. 117.
3. El-Gindy, A., *J. Pharm. Biomed. Anal.*, 2003, vol. 32, no. 2, p. 277.
4. Riggas, K.W., Szeitz, A., Rurak, D.W., *et al.*, *J. Chromatogr. B: Biomed. Appl.*, 1994, vol. 660, no. 2, p. 315.
5. Malinowska, E., Manzonia, A., and Meyerhoff, M.E., *Anal. Chim. Acta*, 1999, vol. 382, no. 3, p. 265.
6. Baniwal, S., Cfhandra, S., Panwar, A., and Singh, A.K., *Talanta*, 1999, vol. 50, no. 3, p. 499.
7. Hassan, S.S.M., Saleh, M.B., Abdel, GaberA.A., *et al.*, *Talanta,* 2000, vol. 53, no. 2, p. 285.
8. Abbas, M.N., Mostafa, G.A.E., and Homoda A.M.A., *Talanta*, 2000, vol. 53, no. 2, p. 425.
9. Abbas, M.N., Mostafa, G.A.E., and Homoda, A.M.A., *Talanta,* 2001, vol. 647, no. 3, p. 55.
10. Durust, N., Meyerhoff, M.E., *Anal. Chim. Acta,* 2001, vol. 432, no. 2, p. 253.
11. Shamsipur, M., Jalai, F., and Haghgoo, S., *J. Pharm. Biomed. Anal.*, 2002, vol. 27, no. 6, p. 867.
12. Mostafa, G.A.E., *J. Pharm. Biomed. Anal.*, 2003, vol. 31, no. 3, p. 515.
13. Wang, Z., Zhang, H., Zhou, S., and Dong, W., *Talanta*, 2001, vol. 53, no. 6, p. 1133.
14. Poban, C.V., Frutos, P., Lastres, J.L., and Frutos, G., *J. Pharm. Biomed. Anal.*, 1996, vol. 15, no. 1, p. 131.
15. *British Pharmacopoeia*, 1993, vol. 1.
16. *United State Pharmacopoeia*, 1980, vol. 20.
17. El-Gendy, A.E., *Spectrosc. Lett.*, 1992, vol. 25, no. 8, p. 1297.
18. Abdel-Gawad, F.M. and El-Guindi, N.M., *Anal. Lett.*, 1995, vol. 28, no. 8, p. 1437.
19. Amin, A.S. and Ragab, G.H., *Anal. Sci.,* 2003, vol. 19, no. 5, p. 747.
20. Moussa, B.A., *J. Pharm. Biomed. Anal.,* 2000, vol. 23, no. 6, p. 1045.
21. Zarapker, S.S., Vaidya, S.J., and Lele, R.V., *Indian Drugs*, 1988, vol. 26, no. 3, p. 115.
22. Zarapker, S.S. and Mehra, S.R., *Indian Drugs*, 1989, vol. 26, no. 7, p. 357.
23. Singh, S. and Shukla, S., *J. Inst. Chem. (India),* 1990, vol. 62, no. 3, p. 126.
24. Revanasiddappa, H.D. and Manju, B., *J. Pharm. Biomed. Anal.,* 2001, vol. 25, nos. 3–4, p. 631.
25. Siggia, S., *Quantitative Organic Analysis,* 3rd ed., New York: Wiley, 1963.
26. Herrero, M.R., Romero, A.M., and Calatayud, J.M., *Talanta*, 1998, vol. 47, p. 223.