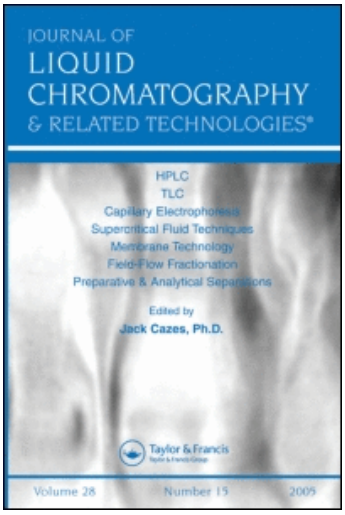

Journal of Liquid Chromatography & Related Technologies

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

HPLC Analysis for Simultaneous Determination of Rabeprazole and Domperidone in Pharmaceutical Formulation

Bhavesh H. Patel[a]; Madhabhai M. Patel[a]; Jignesh R. Patel[a]; Bhanubhai N. Suhagia[b]
[a] Department of Pharmaceutical Chemistry, Shree S.K. Patel College of Pharmaceutical Education and Research, Mehsana, Gujarat, India [b] Department of Pharmaceutical Chemistry, L. M. College of Pharmacy, Ahmedabad, Gujarat, India

To cite this Article Patel, Bhavesh H. , Patel, Madhabhai M. , Patel, Jignesh R. and Suhagia, Bhanubhai N.(2007) 'HPLC Analysis for Simultaneous Determination of Rabeprazole and Domperidone in Pharmaceutical Formulation', Journal of Liquid Chromatography & Related Technologies, 30: 3, 439 — 445
To link to this Article: DOI: 10.1080/10826070601084928
URL: http://dx.doi.org/10.1080/10826070601084928

Journal of Liquid Chromatography & Related Technologies®, 30: 439–445, 2007

ISSN 1082-6076 print/1520-572X online
DOI: 10.1080/10826070601084928

HPLC Analysis for Simultaneous Determination of Rabeprazole and Domperidone in Pharmaceutical Formulation

Bhavesh H. Patel, Madhabhai M. Patel, and Jignesh R. Patel
Department of Pharmaceutical Chemistry, Shree S.K. Patel College of Pharmaceutical Education and Research, Mehsana, Gujarat, India

Bhanubhai N. Suhagia
Department of Pharmaceutical Chemistry, L. M. College of Pharmacy, Ahmedabad, Gujarat, India

Abstract: A simple and sensitive reversed phase high performance liquid chromatographic (RP-HPLC) method has been developed for the quantitative estimation of rabeprazole and domperidone in their combined dosage forms. Rabeprazole and domperidone were chromatographed using 0.01 M, pH 6.5 ammonium acetate buffer: methanol:acetonitrile (40:30:30 v/v, pH 7.44) as the mobile phase at a flow rate of 1.0 mL min^{-1} at ambient temperature and detected at 287 nm. The retention time (RT) of rabeprazole and domperidone were found to be 6.13 ± 0.01 and 8.38 ± 0.02, respectively. The linearities of rabeprazole and domperidone were in the range of 200–2000 ng/mL and 300–3000 ng/mL, respectively. The limit of detection was found to be 65.67 ng/mL for rabeprazole and 98.33 ng/mL for domperidone. The proposed method was applied for the determination of rabeprazole and domperidone in combined dosage forms.

Keywords: RP-HPLC, Rabeprazole and domperidone, Validation, Capsule

Address correspondence to Bhavesh H. Patel, Department of Pharmaceutical Chemistry, Shree S.K. Patel College of Pharmaceutical Education and Research, Ganpat Vidyanagar, Kherva, Mehsana, Gujarat 382711, India. E-mail: bhpmph@yahoo.co.in

INTRODUCTION

Rabeprazole, 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]-1H-benzimidazole, is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the gastric H^+, K^+ ATPase enzyme system at the secretory surfaces of the gastric parietal cells.

The chemical name of Domperidone is 5-chloro-1-[1-[3-(2,3-dihydro-2-oxo-1H-benzimidazole-1-yl)-propyl]-4-piperidinyl]-1-3-dihydro-2H-benzimi dazole-2-one. It is a peripheral dopamine−2-receptor antagonist. It is a unique gastrokinetic and antiemetic drug.[1,2]

Literature review reveals that spectrophotometric,[3,4] LC-MS/MS,[5] HPTLC,[6] and HPLC[7] methods have been reported for the estimation of rabeprazole in dosage forms and from human plasma. As far as domperidone is concerned, many reports are available for its estimation in pure powder and formulation using high performance liquid chromatography (HPLC), spectrophotometry, and high performance thin layer chromatography (HPTLC) in combination with pantoprazole, cinnarazine and ranitidine.[8–13] Hence, no official method is available for estimating rabeprazole and domperidone together in formulations by HPLC. Therefore, the aim of this work was to develop an HPLC method for determination of rabeprazole and domperidone.

EXPERIMENTAL

Reagents

Rabeprazole and domperidone working standards were procured as a gift sample from Torrent Pharmaceutical Ltd., Ahmedabad, India. Acetonitrile, ammonium acetate and methanol (HPLC grade, S.D.fine chemicals, Ahmedabad, India) were used for mobile phase preparation and as solvents. A commercially available combined capsule formulation of rabeprazole and domperidone was procured from a local market.

Apparatus

A Shimadzu HPLC instrument (LC-10AT vp) equipped with UV-Visible detector, manual injector of 20 μL loop and column Phenomenex C_{18} (250 mm × 4.6 mm i.d., 5 μm particle size) was used; a weighing balance (Sartorious CP 225 D, Mumbai, India) and a sonicator (Frontline FS-4, Mumbai, India) were used during the study.

Chromatographic Conditions

Chromatographic estimations were performed under the following conditions: Phenomenex C_{18} (2) column (250 mm × 4.6 mm i.d., 5 μm) was used at ambient temperature. The mobile phase comprised 0.01 M pH 6.5 ammonium acetate buffer:methanol:acetonitrile (40:30:30, v/v/v) and final pH adjusted to 7.44 ± 0.02 with acetic acid/ammonia was pumped at a flow rate of 1 mL/min. The mobile phase was filtered through Nylon 0.45 μm, 47 mm membrane filter and was degassed before use. The elution was monitored at 287 nm. The injection volume was 20 μL.

Preparation of Combined Standard Solution of Rabeprazole and Domperidone

Rabeprazole (20 mg) and domperidone (30 mg) were weighed accurately and transferred into a 100 mL volumetric flask. Methanol (50 mL) was added and the flask was sonicated for 20 min., and then diluted up to the mark with methanol. An aliquot (1.0 mL) was further diluted to 100 mL with the same solvent. The final solution contained 2000 ng of rabeprazole and 3000 ng of domperidone per mL of solution.

Preparation of Calibration Curve

Calibration curves were constructed by plotting peak areas versus concentrations of rabeprazole and domperidone and the regression equations were calculated. The calibration curves were plotted over a concentration range 200–2000 ng/mL and 300–3000 ng/mL for rabeprazole and domperidone, respectively. Accurately measured standard working solutions of rabeprazole and domperidone (0.5, 1.0, 2.0, 3.0, 4.0, and 5.0 mL) were transferred into a series of 5.0 mL of volumetric flasks and diluted to the mark with mobile phase. 20 μL of each solution was injected under operating chromatographic conditions described above.

Procedure for Pharmaceutical Formulation

Pellets of each of 20 capsules were accurately weighed and analyzed as follows. The mass of pellets (powder) equivalent to rabeprazole (20 mg) and domperidone (30 mg) was accurately weighed and transferred into a 100 mL volumetric flask, mixed with methanol (50 mL), and sonicated for 20 min. The solution was filtered through Whatman filter paper No. 41. The residue was thoroughly washed with methanol. The filterate and washings were combined in a 100 mL volumetric flask and diluted to mark with

methanol. The filtrate (1.0 mL) was further diluted to 100 mL with the same solvent. The final test solution contained 2000 ng of rabeprazole and 3000 ng of domperidone per mL of solution. Accurately measured standard working solutions of rabeprazole and domperidone (1.0, 2.0, and 5.0 mL) were transferred into a series of 5 mL volumetric flasks and diluted to the mark with mobile phase. Sample solution (20 μL) was injected into the instrument and chromatographed. The amount of rabeprazole and domperidone present in the sample solutions were determined by fitting area values of peaks corresponding to rabeprazole and domperidone to the equation of the line representing the calibration curve of rabeprazole and domperidone. All determinations were performed in triplicate.

RESULTS AND DISCUSSION

Rabeprazole and domperidone are soluble in methanol; therefore, methanol was selected as the solvent. The formulation was dissolved in methanol with sonication for 20 min to ensure complete release of drug from the formulation matrix. The mixture of ammonium acetate buffer:methanol:acetonitrile (40:30:30, v/v/v) could resolve rabeprazole and domperidone with a better peak shape. The combination of this mobile phase offered optimum separation (6.13 ± 0.01 for rabeprazole and 8.38 ± 0.02 min for domperidone) and resolution. (Fig. 1)

The linearity of rabeprazole and domperidone were in the range of 200–2000 ng/mL and 300–3000 ng/mL, respectively, with correlation coefficients of more than 0.9998. The average linear regression equation was represented as $Y = 252.44X - 1482.43$ for rabeprazole and $Y = 186.55X - 7869.0$ for domperidone, where X is the concentration of drug

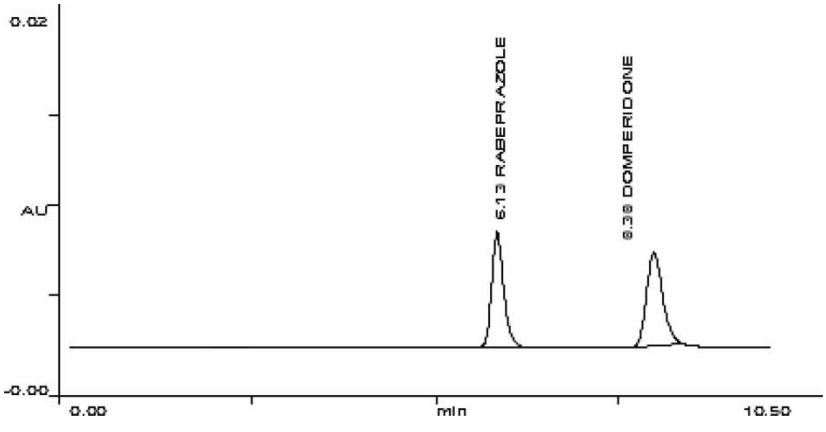

Figure 1. Chromatogram of rabeprazole and domperidone from a capsule formulation.

and Y is the peak area. The limit of detection was found to be 65.67 ng/mL for rabeprazole and 98.33 ng/mL for domperidone. The limit of quantification was found to be 198.69 ng/mL for rabeprazole and 297.98 ng/mL for domperidone.

The intra-day precision (RSD) was determined for standard rabeprazole and domperidone 3 times on the same day and inter-day precision (RSD) was calculated for standard rabeprazole and domperidone, 5 times over a period of one week. The intra-day and inter-day coefficients of variation for both drugs were found to be in the range of 0.32–1.71% and 0.19–0.92%, respectively. These values indicate that the method is precise.

The precision of the instrument was checked by repeated scanning of the same spot (1200 ng/mL for rabeprazole and 1800 ng/mL for domperidone) of both drugs seven times without changing the condition of the instrument; the RSD for measuring the peak area was found to be 0.278% for rabeprazole and 0.155% for domperidone. The %RSD for measuring the peak area (less than 2%), ensured proper functioning of HPLC system.

The accuracy of the method was evaluated by calculating the recovery of rabeprazole and domperidone by a standard addition method at 5 levels of the calibration curve (n = 3) The percentage recovery was found to be 98.87–100.08% for rabeprazole and 99.09–99.55% for domperidone, ensuring that the method is accurate.

Various validation parameters for the proposed HPLC method for determining the rabeprazole and domperidone content are summarized in Table 1. This method was applied to determine the contents of rabeprazole and

Table 1. Summary of the validation parameters of the proposed HPLC method

	HPLC method	
Parameters	Rabeprazole	Domperidone
Linearity range (ng/mL)	200–2000	300–3000
Correlation co-efficient	0.9937	0.9996
LOD[a] (ng/mL)	65.67	98.33
LOQ[b] (ng/mL)	198.69	297.98
Accuracy (%)	98.87–100.08	99.09–99.55
Precision (%RSD)[c]		
Intra day (n[d] = 3)	0.32–0.42	0.49–0.92
Inter day (n = 5)	0.63–1.71	0.19–0.80
Repeatability (n = 7)	0.278	0.155

[a]LOD = Limit of detection.
[b]LOQ = Limit of quantification.
[c]RSD = Relative standard deviation.
[d]n = number of determination.

Table 2. Analysis of marketed capsule formulations contains rabeprazole and domperidone by the proposed HPLC method

Formulation	Drugs	Amount found ± SD[a] (%)
A	Rabeprazole	99.29% ± 0.54
	Domperidone	99.24% ± 0.61
B	Rabeprazole	100.16% ± 1.05
	Domperidone	100.49% ± 0.83

[a]SD = Standard deviation.

domperidone in two combined market samples of rabeprazole and domperidone capsules. The result indicates that the proposed HPLC method is simple, rapid, precise, and accurate for the simultaneous estimation of rabeprazole and domperidone in its combined formulations (Table 2).

REFERENCES

1. Langtry, H.D.; Wilde, M.I. Proton pump inhibitors. Drugs **1998**, *56*, 447–486.
2. Budavari, S. Ed. *The Merck Index*, 13th ed.; Merck and Co. Inc.: Whitehouse Station, New Jersey, 2001, 6306, 3476.
3. Macek, J.; Ptáek, P.; Klíma, J. Spectrophotometric determination of rabeprazole, lansoprazole and pantoprazole sodium via their metal chelates. J. Chromatogr. B **1997**, *689*, 239–243.
4. El-Gindy, A.; El-Gindy, F.; Maher, M.M. Spectrophotometric and chromatographic determination of rabeprazole in presence of its degradation products. J. Pharm. Biomed. Anal. **2001**, *24*, 715–719.
5. Haung, J.; Xu, Y.; Guo, Q. Development of a liquid chromatography/tandem mass spectrometry assay for quantification of rabeprazole in human plasma. Rapid Comm. Mass Spectrom. **2005**, *19* (16), 2321–2324.
6. Presannakumaran, P.N.; Tharuz, T. Estimation of rabeprazole by HPTLC. *Indian Pharm. Congr*; Hyderabad, India Dec. 3–5, 2004, 274.
7. Miura, M.; Sathos, S.; Tada, H.; Suzuki, T. Determination of rabeprazole enantiomers and their metabolite by HPLC with SPE. J. Pharm. Biomed. Anal. **2006**, *18*, 415–449.
8. Kanyavar, N.S.; Zarapkar, S.S. Spectrophotometric determination domperidone in pharmaceutical formulations. Indian Drugs **2002**, *39*, 217–220.
9. Smit, M.J.; Sutherland, F.C.W.; Hundt, H.K.L. Rapid and sensitive liquid chromatography-tandem spectrometry method for quantification of domperidone in human plasma. J. Chromatogr. B **2002**, *949*, 65–70.
10. Vinodhini, C.; Ajithdas, A.A.; Shantha, A. Simultaneous estimation of domperidone and cinnarazine by HPLC. Indian Drugs **2002**, *39*, 491–493.
11. Kobylinka, M.; Kobylinka, K. High performance liquid chromatographic determination of domperidone in human plasma. J. Chromatogr. B **2000**, *744*, 207–212.

12. Kakde, R.B.; Gedam, S.N.; Kasture, A.V. Spectrophotometric and densitometric HPTLC determination of pantoprazole and domperidone in pharmaceutical formulation. Asian J. Chem. **2006**, *18* (2), 1347–1351.
13. Havaldar, F.; Chaudhari, V. Simultaneous estimation of omeprazole and domperidone by HPLC method. Indian Drugs **2004**, *41*, 604–608.

Received October 10, 2006
Accepted November 14, 2006
Manuscript 6963