Journal of Pharmaceutical Research Vol. 8, No. 1, January 2009 : 52-55.

SIMULTANEOUS QUANTITATION OF LANSOPRAZOLE AND DOMPERIDONE IN PHARMACEUTICAL DOSAGE BY LIQUID CHROMATOGRAPHY

Sherje AP[1]* and Kasture AV[2]
STES's Sinhgad Institute of Pharmacy, S. No. 49/1, Off Westerly Bypass, Pune-Mumbai Expressway, Narhe, Pune-411 041 (M.S.) India.
Institute of Pharmaceutical Education and Research, Borgaon (Meghe), Wardha- 442 001 (M.S.) India

Received on : 17.12.2007 Revised : 15.12.08 Accepted : 29.01.09

ABSTRACT
A simple and precise HPLC method has been developed for simultaneous quantitation of lansoprazole and domperidone in pharmaceutical formulations. The chromatographic separation was achieved at ambient temperature using an Intersil C_{18} (4.6x 250 mm, 10 □m) column using a mobile phase comprising of 0.1 M sodium acetate and acetonitrile (55: 45 v/v), pH adjusted to 7.0 with orthophosphoric acid. The retention times for lansoprazole and domperidone were 5.78 min and 3.77 min respectively. The mean recoveries from the capsule formulations were between 99-101%. The detector response was found to be linear in the concentration range of 24–36 □g/mL for lansoprazole and 8-12 □g/mL for domperidone. The developed method herein described can be employed for quality control and routine analysis of drugs in capsule formulation.

Key words: *Lansoprazole; Domperidone; Quantitation; RP-HPLC*.

INTRODUCTION

Lansoprazole {2-(((3-methyl-4-[2,2,2-trifluoroethoxy]-2-pyridinyl)methyl)sulfinyl)-1*H*-benzimidazole} is a proton pump inhibitor and has been demonstrated to be effective in treatment of peptic ulcers, gastroesophageal reflux diseases and Zollinger-Ellison syndrome[1-3]. It has been determined in biological samples and in pharmaceutical formulations by different methods, like UV-Visible spectrophotometry[4-5], high performance liquid chromatography (HPLC)[6-7], high performance thin layer chromatography (HPTLC)[8] and liquid chromatography electrospray tandem mass spectrometry (LC-MS-MS)[9]. It is official in United States Pharmacopoeia where the method of assay involves liquid chromatography[2].

Domperidone is a peripheral dopamine receptor antagonist and indicated as antiemetic and antinauseant. It is a prokinetic agent and thus stimulates gastrointestinal motility[10]. Chemically, it is 5-chloro-1-[1-[3-(2-oxo-1-benzimidazolinyl)propyl]-4-piperidyl]-2- benzimidazolinone[11]. It is official in British Pharmacopoeia[12] and European Pharmacopoeia[13]. Non-aqueous titration is the official method for assay of domperidone in latest edition of British Pharmacopoeia[14] and European Pharmacopoeia[15]. Many reports are available in the literature for analysis of the drug individually or in combination with other drugs from dosage forms and in biological samples. The techniques include spectrophotometry[16], HPLC[17-18] and LC-MS-MS[19].

A fixed-dose combination containing lansoprazole and domperidone is available commercially in the market as capsule dosage form and is indicated in acid related disorders. To date, there is no known HPLC method that is capable of resolving lansoprazole and domperidone in the combination. The purpose of the present investigation was to develop a simple, accurate and precise HPLC method, capable of quantifying both the drugs simultaneously.

MATERIALS AND METHODS

An isocratic HPLC system from Jasco, India equipped with Intersil C18 column (4.6 x 250 mm, i.d. and 10 □m particle size), PU 1580 pump, UV- Visible detector and a 20□l injecting loop was used for the study. All the reagents and chemicals were either Analytical Reagent (AR) grade or HPLC grade. Reference standard of lansoprazole was obtained from Dr. Reddy's Laboratories Ltd., Hyderabad, India and domperidone was obtained from Aurobindo Pharma Ltd., Hyderabad, India. Their authenticity and purity (lansoprazole 100.0 % pure and domperidone 99.81 % pure) were certified by respective laboratories. Sodium acetate (AR grade), orthophosphoric acid (AR grade), acetonitrile (HPLC grade), and purified water (HPLC grade) were purchased from E-Merck, India Ltd. A commercial capsule formulation containing lansoprazole (30 mg) and domperidone (10mg) were purchased from the local market.

***Correspondence :** atulsatul@rediffmail.com

Standard preparation

The standard stock solution of lansoprazole and domperidone was prepared by weighing about 50 mg of each compound in a 100 ml volumetric flask. The compounds were dissolved and diluted up to the mark with the mobile phase. The stock solutions were further diluted with the mobile phase to obtain a working standard containing a concentration of 30 □g/ml of lansoprazole and 10 □g/ml of domperidone.

Sample preparation

Twenty capsules were weighed, contents removed and crushed to a fine powder. The powder equivalent to 30 mg of lansoprazole and 10 mg of domperidone was taken in a 100 ml volumetric flask. The compounds were dissolved and sonicated for 10 minutes. The solution was filtered through 0.45ì membrane filter paper and the filtrate was further diluted with mobile phase to obtain a solution containing 30 µg/ml of lansoprazole and 10 µg/ml of domperidone.

Mobile phase preparation

8.203g of sodium acetate was dissolved in 100ml water to yield 0.1N sodium acetate solution. The mobile phase was prepared by mixing 45 volumes of acetonitrile and 55 volumes of 0.1 N sodium acetate and pH was adjusted to 7.0 with orthophosphoric acid. The prepared mobile phase was then filtered through 0.45ì membrane filter and degassed.

System suitability tests

An aliquot (20 ìL) of standard preparation of each drug was injected into HPLC column operating at ambient temperature. The compounds were eluted by pumping the mobile phase at a flow rate of 1.5 mL/minute. The eluent was monitored at 284 nm. The system suitability was evaluated by making replicate injections of standard preparations of both the drugs under above optimized chromatographic conditions. The results of system suitability study are presented in Table 1.

Table 1. *Results of system suitability studies*

Sr. No.	Parameters	Lansoprazole	Domperidone
1	Calibration range (µg/ml)	5- 50	5- 50
2	Theoretical plates	12079.27	79992.6
3	Asymmetry factor	1.168	1.120
4	Capacity factor	7.21	4.71
5	Selectivity	1.52	
6	Resolution	4.40	

Linearity and calibration

An aliquot (20 ìl) of standard preparation of each drug was diluted with the mobile phase so that the final concentration of lansoprazole and domperidone was in the range of 5-50 µg/mL. The resulting solutions were injected, and eluent was monitored at 284 nm. The peak area responses were recorded for all the peaks. The calibration curve was obtained by plots of peak area response versus concentration of respective drugs.

Assay

Five injections of mixed working standards and sample preparation were chromatographed using an injection volume of 20ìl after equilibrium of stationary phase with the mobile phase. The content of lansoprazole and domperidone in commercial formulation was calculated using the following formula-

$$LC = \frac{At}{As} X \frac{Ds}{Dt} X \frac{Ws}{Wt} X \frac{A}{LC} X 100$$

Where, At = average peak area response for each drug sample, As = average peak area response respective to standard drug, Ds = dilution factor for standard drug, Dt = dilution factor for sample drug, Ws = weight of standard drug in mg, Wt = weight of sample drug in mg, LC = label claim, A = average weight of capsule in mg.

Method validation

The analytical method was validated as per the guidelines of International Conference on Harmonization (ICH) and USP for parameters like accuracy, precision, specificity, ruggedness, linearity and range[20]. To ensure the reliability and accuracy of the proposed method, recovery studies were carried out by mixing a known quantity of standard drug at three different levels (above and below the normal level) with pre-analyzed sample and contents were reanalyzed by the proposed method. Precision of analytical method was assessed in terms of repeatability which was checked by analyzing five independent samples of lansoprazole and domperidone at 100 % concentration level and calculating their percent relative standard deviation (% RSD). The ruggedness (degree of reproducibility of the test results under a variety of conditions) of analytical method was studied by analyzing the sample at different conditions, like inter-day, different days, different analyst, etc. In addition, the drug solutions were tested for drug stability during experimental time period. The results of formulation analysis and recovery studies are summarized in Table 2 and results of method validation studies are given in Table 3.

Table 2. *Capsule formulation analysis and recovery studies*

Sr. No.	Formulation	Drug	Label claim (mg/ capsule)	Drug found* % (±S.D.)	Recovery* % (±S.D.)
1	Market formulations	Lansoprazole	30	29.98 (0.49)	99.93 (0.19)
		Domperidone	10	10.14 (0.54)	99.96 (0.43)

** Mean (± standard deviation), n = 5.*

RESULTS AND DISCUSSION

A typical chromatogram of lansoprazole and domperidone in commercial formulation is depicted in Figure 1. The mobile phase containing 55 volumes of 0.1 N sodium acetate and 45 volumes of acetonitrile (pH 7.0) was found suitable for both the drugs giving reproducible and stable peak. The retention times for lansoprazole and domperidone were 5.78 min and 3.77

min respectively. During analysis of drugs in combination, the drug peaks were well resolved and eluted at same retention time as when analyzed alone. Thus the method was capable of analyzing both the drugs alone or in combination. The system suitability was evaluated by making five replicate injections of mixed working standards and standard preparation, and peak responses were recorded at optimized chromatographic conditions. The results are presented in Table 1. There was good repeatability of proposed method as the precision (%RSD) of the method was less than 2% for both the drugs. The mean recovery observed was 99.93 % (±0.1944) for lansoprazole and 99.96 % (±0.4370) for domperidone which indicated that method was accurate. The content of the drug in the commercial formulation was in good agreement with the labeled claim. The lansoprazole and domperidone marketed formulation was found to be linear in the range of ±20% of the test concentration. The linearity range was found to be 24-36 □g/mL and 8-12 □g/mL for lansoprazole and domperidone respectively. Specificity studies indicated no significant matrix effect on the result of analysis as retention time for both drug in the marketed formulation was same as that of the pure sample of the drugs.

Table 3. *Results of method validation studies for lansoprazole and domperidone*

Sr. No.	Parameters	Results	
		LAN	DOM
1	Accuracy*	99.9 (0.1944)	99.96 (0.4370)
2	Precision	0.4914	0.5469
3	Linearity and range (µg/m l)	24-36	8- 12
4	Ruggedness **		
	Intra-day	100.11 (0.23)	99.97 (0.41)
	Inter-day	99.73 (0.66)	99.89 (0.54)
	Different analyst	99.99 (0.34)	100.47 (0.28)
5	Correlation coefficient	0.9997	0.9998
6	Specificity	Specific	Specific

** Mean % recovery (± standard deviation), n=3 and ** % estimation of drugs in marketed formulation (± standard deviation), n=3.*

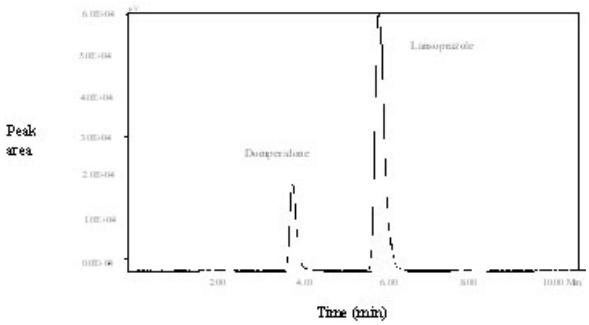

Fig. 1: A typical chromatogram of lansoprazole and domperidone.
Retention time for domperidone (3.77 min.) and lansoprazole (5.78 min.)

CONCLUSION

The proposed reverse phase HPLC method provides a convenient and efficient method for separation and estimation of lansoprazole and domperidone in combined dosage form. There was no interference from the expicient used in capsule formulation and hence the method was suitable for analysis of capsule formulation. The result of validation showed that the proposed method was simple, precise, accurate, linear and selective. Therefore the method herein described can be employed for quality control and routine analysis of both drugs in their combined pharmaceutical dosage form.

ACKNOWLEDGEMENTS

The authors are thankful to Dr. Reddy's Laboratories Ltd., Hyderabad, India and Aurobindo Pharma Ltd., Hyderabad, India for providing the gift samples of lansoprazole and domperidone, respectively.

REFERENCES

1. Sweetman SC. In *Martindale - The complete drug reference.* London: Pharmaceutical Press, 2002, p 1224.
2. The United States Pharmacopeia 27 National Formulary 22, Rockville MD: The United States Pharmacopeial Convention Inc, 2004, p 1068.
3. Tolman KG. In *Remington: The Science and Practice of Pharmacy.* Gennaro AR, eds. Maryland: Lippincott Williams Wilkins, 2000, p 1226.
4. Wahbi AA, *et al.* J Pharm Biomed Anal. 2002; 30: 1133.
5. Moustafa AAM, *et al.* J Pharm Biomed Anal. 2000; 22: 45.
6. Miura M, *et al.* J. Chromatogr Analyt Technol Biomed Life Sci. 2004; 804: 389.
7. Unoa T, *et al.* J. Chromatogr B Analyt Technol Biomed Life Sci. 2005; 816: 309.
8. Pandya KK, *et al.* J Chromotogr B Biomed Sci Appl. 1997; 693: 199.
9. Celso H, *et al.* J Chromatogr B. 2003; 783: 453.
10. McQuaid KR. In *Basic and clinical Pharmacology.* Katzung BG, eds. Delhi: Mc-Graw Hill Publishing Division, 2001, p 1067.
11. Merck Index. 13th Edn., NJ USA: Merck and Company, 2001, p 602.
12. British Pharmacopoeia. London: The Stationary Office, 2001, p 690.
13. European Pharmacopoeia. Strasbourg: Council of Europe, 2005, p 1473.
14. British Pharmacopoeia. London: The Stationary Office, 2004, p 690.

15. European Pharmacopoeia. Strasbourg: Council of Europe, 2005, p 1473.

16. Amin AS, *et al.* Anal. Sci. 2003; 19: 747.

17. Maria K, *et al.* J Chromatogr B Biomed Sci Appl. 2000; 744: 207.

18. Zarapkar SS, *et al*. Indian Drugs. 2001; 39: 217.

19. Smit MJ, *et al.* J Chromatogr A. 2002; 949: 65.

20. The United States Pharmacopeia 27 National Formulary 22. Rockville MD: The U. S. Pharmacopeial Convention Inc, 2004, p 2622.