Asian Journal of Chemistry; Vol. 25, No. 7 (2013), 3989-3992

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2013.13865

Determination of Ilaprazole and Domperidone in Individual Dosage form Tablets by RP-HPLC

G. SUNEETHA[1], P. VENKATESWARLU[1,*], P.S.S. PRASAD[2] and P. MURALI KRISHNA[1]

[1]Department of Chemistry, Sri Venkateswara University, Tirupati-517 502, India
[2]Department of Drugs Control Administration, Hyderabad-500 038, India

*Corresponding author: E-mail: sunithareddy04@gmail.com

(*Received*: 9 April 2012; *Accepted*: 21 January 2013) AJC-12737

A simple, sensitive and precise high performance liquid chromatographic method for the analysis of ilaprazole and domperidone has been developed, validated and used for the determination of compounds in commercial pharmaceutical products. The compounds were well separated an isocratically on a C_{18} column inertisil C_{18}, 5 µm, [250 mm × 4.6 mm] utilizing a mobile phase consisting of acetonitrile: phosphate buffer (60:40, v/v, pH 7.0) at a flow rate of 1.0 mL/min with UV detection at 243 nm. The retention time of ilaprazole and domperidone was found to be 2.543 min and 7.245 min, respectively. The method was found selective and peaks of ilaprazole and domperidone were well separated. The proposed method is linear (r^2 = 0.999 for ilaprazole and domperidone), accurate with 99.5 % recovery for ilaprazole and 99.4 % recovery for domperidone and precise (% RSD < 1 %). The method has been used to determine potency of commercial product and potency was found within limit. The method can be used for the analysis of ilaprazole and domperidone in tablet dosage form.

Key Words: Domperidone, Ilaprazole, Validation, RP-HPLC.

INTRODUCTION

Ilaprazole (Fig. 1) is a new proton-pump inhibitor not previously studied in human patients with ulcer disease. This study evaluated and compared it with a reference proton-pump inhibitor omeprazole in the treatment of gastric and duodenal ulcers. Proton-pump inhibitors have been used therapeutically for many years and show great efficacy in accelerating ulcer healing. Currently researches are focused on more potent proton-pump inhibitors. Some preclinical studies have shown that ilaprazole might be such a new substitute. The chemical structures of enantiomers is ilaprazole [-[(4-methoxy-3-methyl-pyridin-2-yl) methylsulfinyl]-6-pyrrol-1-yl-1H.

Benzoimidazole and a substituted benzimidazole, is a new candidate drug that is an H^+/K^+-ATP ase inhibitor designed for the treatment of gastric ulcers[1,2]. Ilaprazole was under development by IIYang Pharmacy Co. (Seoul, Korea) and has been proven by a series of animal studies to be a potent and safety antiulcer agent and the major one being ilaprazole sulfone. Recently, a new metabolite of ilaprazole, ilaprazole thiol ether, was identified an improved LC-MS/MS method for quantitative determination of ilaprazole and its metabolites in human plasma[3,4]. A validated method was performed in accordance with current guidelines[5,6], 212 gastric ulcer patients (median age 53.3 years) and 306 duodenal ulcer patients (median age 49.7 years) were recruited.

Domperidone, 5-chloro-1-[1-[3-(2, 3-dihydro-2-oxo-1H-benzimidazol-1-yl)propyl]-4-piperidinyl]-1,3-dihydro-2H-benzimidazol-2-one (Fig. 1), is a potent dopamine antagonist used for treatment of nausea and vomiting. Domperidone does not cross the blood-brain barrier and therefore has fewer adverse CNS effects than other dopamine antagonists[7,8]. Domperidone has been determined in human plasma[9], human serum and human milk[10] and rat plasma[11], has been evaluated in coevaporates by HPLC[12] and has been determined, with cinnarizine, in tablets, by HPLC[13].

To our best of knowledge simple and economical analytical method for simultaneous determination of ilaprazole and domperidone has not been reported so far. So attempt was taken to develop and validate an economic, rapid reversed-phase high performance liquid chromatographic method for the quality control of ilaprazole and domperidone in pharmaceutical preparations with lower solvent consumption along with the short analytical run time that leads to an environmentally friendly chromatographic procedure and will allow the analysis of a large number of samples in a short period of time. The method was validated and found to be accurate, precise and reproducible.

EXPERIMENTAL

Ilaprazole and domperidone were kind gift from Emanthi Pharmaceuticals, Hyderabad. HPLC grade acetonitrile was

TABLE-1
RESULT OF SYSTEM SUITABILITY TESTS OF ILAPRAZOLE AND DOMPERIDONE

Parameters	Ilaprazole			Domperidone		
	Average	SD	% RSD	Average	SD	% RSD
Retention time	3.168	0.001	0.041	5.424	0.004	0.076
Area	125978.00	1249.903	0.992	1622441.5	376.285	0.023
Theoretical plates	4561.153	18.79	0.412	8739.667	5.750	0.066
Tailing factor	1.357	0.004	0.287	1.355	0.015	1.090

obtained from Rankem, Ranbaxy Fine Chemical Limited, New Delhi, India. All the other chemicals of analytical grade were procured from local sources unless specified.

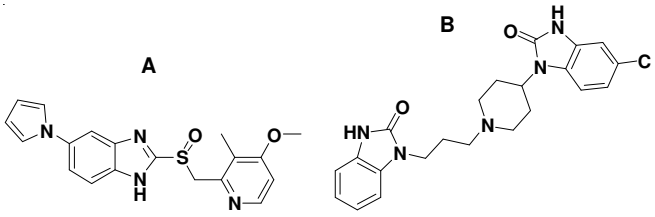

Fig. 1. Chemical structures of A) ilaprazole; B) domperidone

Chromatographic conditions: The instrument used was a waters model alliance 2695 separation module equipped with auto sampler, waters 2998 PDA detector and the data recorded using empower software. Inertisil C_{18}, 5 µm, 250 mm × 4.6 mm was used at ambient temperature and utilizing a mobile phase consisting of acetonitrile: phosphate buffer (60:40, v/v, pH 7.0) at a flow rate of 1.0 mL/min with UV detection at 243 nm.

Preparation of standard stock solution: 20 mg ilaprazole was dissolved in 100 mL mobile phase and 25 mg domperidone was dissolve in 25 mL mobile phase separately to get stock solutions of ilaprazole (200 mcg/mL) and ilaprazole (1000 mcg/mL). Several aliquots of standard solutions of ilaprazole and domperidone were taken in different 100 mL volumetric flasks and diluted up to the mark with mobile phase to get five different concentrations (80, 90, 100, 110 and 120 % of target concentration). Solution containing mixture of ilaprazole and domperidone of five different concentrations (80, 90, 100, 110 and 120 % of target concentration) were prepared in the same way.

Preparation of sample solution: Sample solution containing both the drugs was prepared by dissolving tablet powder into mobile phase. Twenty ilaprazole and domperidone tablets were weighed separately. Their average weights were determined. Powder of tablets equivalent to 5 mg of ilaprazole and 125 mg of domperidone were weighed and taken in a 100 mL volumetric flask, dissolved in mobile phase and shaken for about 10 min then filtered through filter paper. The filtered solution was further diluted in the mobile phase to make the final concentration of working sample equivalent to 100 % of target concentration.

Development and validation of HPLC method: Present study was conducted to obtain a new, affordable, cost-effective and convenient method for HPLC determination of ilaprazole and domperidone in tablet dosage form. The experiment was carried out according to the official specifications of USP-30, ICH-1996 and global quality guidelines-2002.The method was validated for the parameters like system suitability, selectivity, linearity, accuracy, precision and robustness.

System suitability: System suitability study of the method was carried out by six replicate analysis of solution containing 100 % target concentration of ilaprazole and domperidone. Various chromatographic parameters such as retention time, peak area tailing factor, theoretical plates (Tangent) of the column and resolution between the peaks were determined and the method was evaluated by analyzing these parameters.

Selectivity: Selectivity test determines the effect of excipients on the assay result. To determine the selectivity of the method, standard sample of ilaprazole and domperidone were injected first. Then commercial product, blank and excipients solution were run in the instrument one after another.

Linearity: Linearity of the method was determined by constructing calibration curves. Standard solutions of ilaprazole and domperidone of different concentrations level (80, 90, 100, 110 and 120 %) were used for this purpose. Each measurement was carried out in six replicates and the peak areas of the chromatograms were plotted against the concentrations to obtain the calibration curves and correlation coefficients.

Accuracy: Spike and recovery method was used to determine the accuracy of the method. Both the drugs at different level were added to placebo formulations. The accuracy was calculated as the percentage of the dug recovered by the assay.

Precision: Intra-day precision (repeatability) was determined by performing four repeated analysis of the three standard solutions (90, 100 and 110 % of target concentration) on the same day. On the other hand inter-day precision (intermediate) of the method was assessed by carrying out the analysis of standard solutions (90, 100 and 110 % of target concentration) on three different days in the same laboratory. The relative standard deviation (% RSD) was calculated in order to assess the precision of the method.

Robustness: Robustness of the method was determined by the analysis of the samples under a variety of conditions. Small changes were made in the buffer pH (6.8 and 7.0), mobile phase composition, flow rate (0.9 and 1.1/min) and in temperature (30 ºC and 28 ºC). Percent recovery was calculated to find out the robustness of the method.

RESULTS AND DISCUSSION

Results of system suitability study are summarized in Table-1. Six consecutive injections of the standard solution showed uniform retention time, theoretical plate count, tailing factor and resolution for both the drugs which indicate a good system for analysis.

Chromatograms shown in Fig. 2 explain that retention time for standard sample and commercial product of ilaprazole and domperidone are same. This proves that, excipients have no effect on the analytical method. On the other hand, blank

peak did not overlap drug peak. So the method is highly selective. A linear relationship between peak areas (average peak areas of six replicates) *versus* concentrations was observed for ilaprazole and domperidone in the range of 80 % to 120 % of nominal concentration. Correlation coefficient was 0.999 for both the drugs which prove that the method is linear. Calibration curve of ilaprazole and domperidone are shown in Figs. 3 and 4.

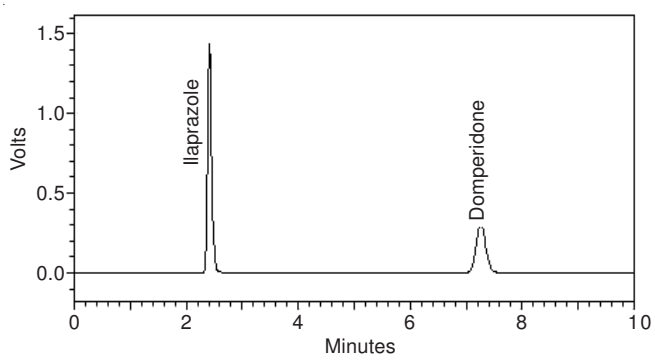

Fig. 2. Chromatogram of ilaprazole and domperidone

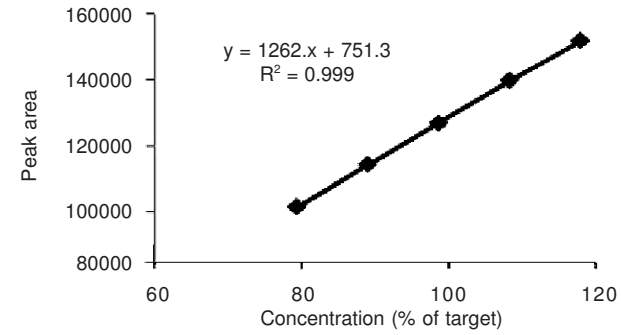

Fig. 3. Calibration curve of ilaprazole

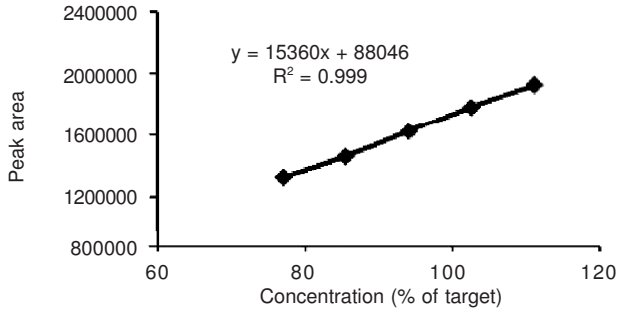

Fig. 4. Calibration curve of domperidone

Results of accuracy study are presented in Table-2. The measured value was obtained by recovery test. Spiked amount of both the drug were compared against the recovery amount. % Recovery was 99.50 % for domperidone and 99.39 % for ilaprazole. All the results indicate that the method is highly accurate. Results of intra-day and inter day variability were summarized in Table-3. Intra-day variability was done from 9.00 am to 6.00 pm on the same day. % RSD of peak areas was calculated for various run. The method is highly precise as % RSD of peak area was less than 1 % in all tests.

The results of robustness of the present method showed that small changes were made in the buffer pH, mobile phase composition, flow rate and temperature did not produce significant changes in analytical results which are presented in Table-4. As the changes are not significant we can say that the method is robust.

TABLE-2
ACCURACY (% RECOVERY) RESULTS OF ILAPRAZOLE AND DOMPERIDONE

Sample no.	Ilaprazole			
	Spiked amount (mg)	Recovered amount (mg)	Recovered (%)	Average recovery (%)
1	10	9.79	97.90	
2	15	14.85	99.00	99.50
3	20	20.32	101.60	
	Domperidone			
1	15	14.31	95.40	
2	22.5	22.87	101.64	99.39
3	30	30.34	101.13	

TABLE-3
INTRADAY AND INTER DAY PRECISION RESULT OF ILAPRAZOLE AND DOMPERIDONE

Drug	% RSD (intraday)	% RSD (inter day)
Ilaprazole	0.929	0.824
Domperidone	0.054	0.374

TABLE-4
RESULTS FOR ROBUSTNESS TEST OF ILAPRAZOLE AND DOMPERIDONE

Parameters	Changes	% Recovery of Ilaprazole	% Recovery of Domperidone
Flow rate (mL/min)	0.9	98.89	98.71
	1.1	99.19	99.14
Column temperature	28	99.27	99.64
(ºC)	30	99.13	99.59
pH	7.0	99.12	99.74
	6.8	98.87	99.62

Conclusion

The proposed high-performance liquid chromatographic method has been evaluated for the accuracy, precision and linearity. The measured signals were shown to be precise, accurate and linear over the concentration range tested (80-120 % of target concentration) with a correlation coefficient of 0.999. In this method, there was no interference from matrix sources. Moreover, the lower solvent consumption along with the short analytical run time of 10 min leads to an environmentally friendly chromatographic procedure that allows the analysis of a large number of samples in a short period of time. Therefore, this HPLC method can be used as a routine sample analysis.

ACKNOWLEDGEMENTS

The authors are thankful to Sri Venkateswara University, Tirupati for providing the laboratory facilities.

REFERENCES

1. E.J. Kim, S.M. Lee and D.Y. Kim, *Arzneimittelforschung,* **51**, 51 (2001).
2. A.P. Periclou, R. Goldwater, S.M. Lee, D.W. Park, D.Y. Kim and K.D. Cho, *Clin. Pharmacol. Ther.*, **68**, 304 (2000).
3. S.W. Myung, H.K. Min, C. Jin, M. Kim, S.M. Lee and G.J. Chung, *Arch. Pharm. Res.*, **22**, 189 (1999).
4. Y. Li, W. Zhang, D. Guo, G. Zhou, H. Zhou and Z. Xiao, *Clin. Chim. Acta*, **39**, 60 (2008).
5. A.M. Rulis and L.A. Suydam, *Federal Register*, **66**, 28526 (2001).
6. V.P. Shah, K.K. Midha, J.W. Findlay, H.M. Hill, J.D. Hulse and I.J. McGilveray, *Pharm. Res.*, **17**, 1551 (2000).
7. P.M. Laduron and J.E. Leysen, *Biochem. Pharmacol.*, **28**, 2161 (1979).
8. R.N. Brogden, A.A. Carmine, R.C. Heel, T.M. Speight and G.S. Avery, *Drugs*, **24**, 85 (1982).
9. M. Kobylinska and K. Kobylinska, *J. Chromatogr. B.*, **744**, 207 (2000).
10. A.P. Zavitsanos, C. MacDonald, E. Bassoo and D. Gopaul, *J. Chromatogr. B.*, **730**, 9 (1999).
11. K. Yamamoto, M. Hagino, H. Kotaki and T. Iga, *J. Chromatogr. B.*, **720**, 251 (1998).
12. M.S. Nagarsenker, S.D. Garad and G. Ramprakash, *J. Control. Rel.*. **63**, 31 (2000).
13. A.P. Argekar and S.J. Shah, *J. Pharm. Biomed. Anal.*, **19**, 813 (1999).