Asian Journal of Chemistry; Vol. 24, No. 11 (2012), 5409-5410

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

NOTE

Simultaneous Determination of Paracetamol, Phenylephrine Hydrochloride and Loratadine

NITIN DUBEY*, RIZWANA SIDDIQUI and DINESH K. JAIN

College of Pharmacy, IPS Academy, Indore-452 012, India

*Corresponding author: E-mail: nitindubeympharm@yahoo.com

(*Received*: 20 October 2011; *Accepted*: 21 June 2012) AJC-11653

A simple, selective, accurate RP-HPLC method was developed and validated for the analysis of paracetamol, phenylephrine hydrochloride and loratadine in commercially available tablet formulations. Chromatographic separation achieved isocratically using methanol:acetonitrile: water: THF (50:40:10:2.5 % v/v/v/v) as mobile phase at a flow rate of 0.8 mL/min. The retention time of phenylephrine, paracetamol and loratadine were found to be 2.563, 3.643, 5.779 min. respectively. The developed method was validated in terms of accuracy, precision, linearity, limit of detection, limit of quantitation. It may be used for the estimation of these drugs in combined tablet dosage forms.

Key Words: Paracetamol, Phenylephrine hydrochloride, Loratadine, RP-HPLC, Validation.

Paracetamol ($C_8H_9NO_2$) is chemically *N*-(4-hydroxyphe-nyl) acetamide. It is a centrally and peripherally acting non-opioid analgesic and antipyretic. The main mechanism of action of paracetamol is considered to be the inhibition of cyclooxygenase (COX) and it is highly selective for cyclooxygenase-2. It has analgesic and antipyretic properties comparable to those of aspirin or other NSAIDs, its peripheral antiinflammatory activity is usually limited by several factors, one of which is high level of peroxides present in inflammatory lesions[1].

Phenylephrine ($C_9H_{13}NO_2$) is chemically (R)-3-[-1-hydroxy-2-(methylamino)ethyl] phenol. It is used as a decongestant. It is a direct selective α-adrenergic receptor agonist[2,3].

Loratadine ($C_{22}H_{23}N_2O_2Cl$) is chemically ethyl-4-(8-chloro-5,6-dihydro-11H-benzo5,6]ohepta[1,2-b]yridin-11-ylidine)-1-piperidinecarboxylate. It is a tricyclic antihistamine, which acts as selective inverse agonists of peripheral histamine H_1-receptors[4,5]. The structure of these drugs are shown in the Fig. 1.

Literature survey revealed that chromatographic estimation has been performed on these drugs in single or in combination with other drugs[6-10]. But so far no chromatographic method was reported for simultaneous quantitative estimation of all the three drugs in combine dosage form. Fixed dose combination SNIZID PLUS containing Paracetamol (500 mg), phenylephrine (7.5 mg) and loratadine (5 mg) available in the tablet form in the market. The aim of this work was to develop an RP-HPLC method for the simultaneous determination of paracetamol, phenylephrine and loratadine in pharmaceutical dosage forms. The present RP-HPLC method was validated following ICH guidelines[11].

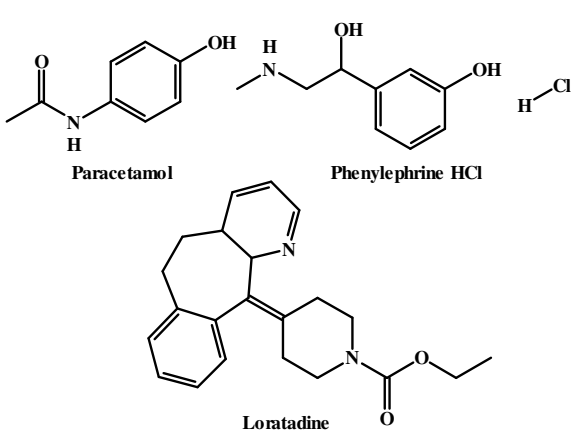

Fig. 1. Chemical structures of paracetamol, phenylephrine and loratadine

The gratis sample of the paracetamol, phenylephrine and loratadine were obtained from Schon Pharmaceutical Ltd. Indore (M.P.), Apco Pharma Ltd. (Haridwar) and Tonira Pharma Ltd. Vadodara (Gujrat) respectively. All the chemicals and reagents used were of HPLC grade and purchased from Merck Ltd. (Mumbai, India). The percent purity of paracetamol, phenylephrine and loratadine were found to be 99.79, 100 and 99.31 % respectively.

Chromatographic system and condition: The LC system consists of (Shimadzu LC $10AT_{VP}$) gradient pump with universal loop injector (Rheodyne 7725i) of 20 µL injection capacity, photodiode array detector (PDA) SPD-10 A_{VP} and Luna C_8 (25 cm × 5 mm × 4.6 mm i.d.) column at 1.0 mL/min flow rate

controlled by a PC work station equipped with software CLASS-VP (software M 10 version 1.6) (Shimadzu, Japan).

The mobile phase consisted of a mixture of methanol: acetonitrile:water:THF (50:40:10:2.5 % v/v/v/v). Mobile phase prior to use was filtered through a 0.45 µm membrane filter. The mobile phase was prepared daily, sonicated before use and delivered at a flow rate of 0.8 mL/min.

Standard stock solutions: The equivalent of 10 mg each of paracetamol, phenylephrine and loratadine were accurately weighed in 10 mL volumetric flask and dissolve to produce 10 mL solution in mobile phase. These standard stock solutions were observed to contain 1000 µg/mL for paracetamol, phenylephrine and loratadine and from this 100 µg/mL stock solution were prepared for paracetamol and loratadine. From the standard stock solutions of 1000 µg/mL and 100 µg/mL, different dilutions were prepared for each drug having concentration from 60, 80, 100, 120, 140 µg/mL for phenylephrine and 6, 8, 10, 12, 14 µg/mL for paracetamol and loratadine with mobile phase. Then 20 µL of these solutions were injected into the LC system with the help of Hamilton syringe. Then the chromatograms were recorded at λ_{max} of 273 nm, 247 nm and 246 nm for phenylephrine, paracetamol and loratadine respectively. From the chromatogram their area was noted and calibration curve were plotted between the peak areas against their respective concentrations.

Analysis of tablets: Twenty tablets (Snizid Plus, Profic organic Ltd. Delhi) each containing 500 mg paracetamol, 7.5 mg phenylephrine and 5 mg loratadine were weighed and powder equivalent to 25 mg of paracetamol was weighed accurately and taken into 25 mL volumetric flask. The drugs were extracted into acetonitrile, volume was adjusted to 25 mL, vortexed and then filtered through 0.45 µ membrane filter. From this solution, further dilutions were made using mobile phase to get a final concentration of 12 µg/mL of phenylephrine and 60 µg/mL of paracetamol and 12 µg/mL of loratadine. Twenty microliters of solution was injected into HPLC system to obtain chromatogram for standard drug solution (three replicates) and sample solution (three replicates). Concentrations of phenylephrine, paracetamol and loratadine in the formulation were calculated by comparing AUC of sample with that of standard. To check the accuracy of the developed method recovery study was carried out in triplicate as per ICH norms. Where to a preanalyzed sample solution, standard solutions of all the three drugs were added equivalent to 80, 100 and 120 % of target drug concentration. Precision of the method was checked by three replicate over three concentration levels of within range expressed as % RSD values (Tables 1, 2).

For the RP-HPLC method, chromatographic conditions were optimized to achieve the best resolution and peak shape for phenylephrine, paracetamol and loratadine. Mobile phase consist methanol: acetonitrile: water: THF (50:40:10:2.5 % v/v/v/v) was selected as optimal for obtaining well-defined and resolved peaks. The quantitation was carried out at λ_{max} of 273, 247 and 246 nm for phenylephrine, paracetamol and loratidine at which the best detector response for all the substances were obtained. Straight line calibration curves were obtained for phenylephrine, paracetamol and loratadine in the RP-HPLC methods. Table-1 summarizes linear regression equation, correlation coefficient, limit of detection, limit of quantitation and λ_{max} values for all three drugs.

TABLE-1
VALIDATION AND SYSTEM SUITABILITY PARAMETERS FOR RP-HPLC METHOD

Parameters	PHE	PCM	LOR
Linearity range (µg/mL)	20-140	2-400	3-200
$\lambda_{max.}$ (nm)	253	247	246
Limit of detection (µg/mL)	5.48	0.52	0.58
Limit of quantitation (µg/mL)	16.61	1.56	1.75
Theoretical plate number	2421	3365	2875
Retention time (min)	2.563	3.643	5.779
Tailing factor	1.74	1.77	1.65
Capacity factor (k')	-	2.48	3.25
Resolution	-	4.64	5.64

PHE: Phenylephrine; PCM: Paracetamol; LOR: Loratadine

TABLE-2
RESULTS OF STATISTICAL VALIDATION OF RECOVERY STUDY

Particulars	Conc. of drug added (%)	PHE conc. found (%)	PCM conc. found (%)	LOR conc. found (%)
Recovery Study	80	100.35 ± 2.04	99.74 ± 0.476	100.01 ± 1.95
	100	100.13 ± 2.35	99.48 ± 0.882	101.08 ± 1.64
	120	99.39 ± 0.735	99.4 ± 0.615	99.21 ± 2.29
Commercial Tablet Analysis		100.76 ± 1.00*	99.30 ± 0.50*	100.33 ± 0.90*

*12 µg/mL for PHE, 60 µg/mL for PCM and 12 µg/mL for LOR respectively (% RSD, n = 3)

The proposed methods were also evaluated in the assay of commercially available tablets containing phenylephrine, paracetamol and loratadine. Three replicates determination were performed on the accurately weighed amounts of tablets. Linearity were found to be in the range of 20-140, 2-400 and 3-200 µg/mL with LOQ of 16.61, 1.56 and 1.75 µg/mL for phenylephrine, paracetamol and loratadine respectively, the recovery study showed an acceptable range of variation below RSD of 2.

REFERENCES

1. Indian Pharmacopoeia, The Controller of Publication, Government of India, Delhi, India, edn. 5, pp. 900-902 (2007).
2. Martindale, The Complete Drug Reference Pharmaceutical Press: London, edn 33, pp. 1585-86 (2002).
3. British Pharmacopoeia, The Stationary Office London, edn. 2, p. 1534 (2002).
4. A.C. Moffat, M.D. Osselton, B.Widdop and E.G.C. Clarke, Clarke's Analysis of Drugs and Poison University of Michigan: Pharmaceutical Press, pp. 1886-87 (2004).
5. L.S. Goodman, J.G. Hardman, L.E. Limbird and A.G. Gilman, The Pharmacological Basis of Therapeutics, New York, McGraw Hill Book, edn. 10, pp. 653-54 (2001).
6. S.R. Pattan, S.G. Jamdar and R.K. Godge, *J. Chem. Pharm. Res.*, **1**, 329 (2009).
7. F.L. Rimawi, *Saudi Pharm. J.*, **18**, 103 (2010).
8. T. Radhakrishna, A. Narasaraju, M. Ramakrishna and A. Satyanarayana, *J. Pharm. Biomed. Anal.*, **31**, 359 (2003).
9. K.V. Nagappan, S.N. Meyyanathan, B.R. Rajinikanth and S. Reddy, *Res. J. Pharm. Tech.*, **1**, 366 (2008).
10. I. Singhvi and N. Bhatiya, *Indian J. Pharm. Sci.*, **68**, 72 (2006).
11. ICH Q2A and Q2B Guideline, Validation of Analytical Procedures: Definition and Terminology (CPMP III/ 5626/94), ICH, Geneva, Switzerland (1995).