http://www.e-journals.net

ISSN: 0973-4945; CODEN ECJHAO
E-Journal of Chemistry
2011, **8(3),** 1275-1279

Simultaneous Determination of Paracetamol, Phenylephrine Hydrochloride, Oxolamine Citrate and Chlorpheniramine Maleate by HPLC in Pharmaceutical Dosage Forms

OZAN PIROL, MURAT SUKUROGLU and TUNCEL OZDEN

Gazi University, Faculty of Pharmacy
Department of Pharmaceutical Chemistry, 06330, Turkey
tozden@gazi.edu.tr

Received 27 November 2010; Accepted 22 January 2011

Abstract: A new high performance liquid chromatographic (HPLC) method was developed for the determination of paracetamol, phenylephrine hydrochloride, oxolamine citrate and chlorpheniramine maleate in combined pharmaceutical formulations and dosage forms. The separation was performed on an Agilent Zorbax SB-CN column with the mobile phase consisting of 0.02 M phosphate buffer (pH:4) and acetonitrile (85:15,v/v) in flow rate 1.5 mL at 22 °C. The overall retention time of the analytes was 3.5 min. The method was validated with respect to linearity, precision, accuracy and recovery. The relative standard deviation for 10 replicate measurements of paracetamol, phenylephrine HCl, oxolamine citrate and chlorpheniramine maleate were 0.12, 0.36 0.18 and 0.59%, respectively. Total recoveries of analytes were 99.99, 100.56, 100.20 and 99.60%, respectively. No chromatographic interference from the tablet excipients was found. The linearity of paracetamol, phenylephrine HCl, oxolamine citrate and chlorpheniramine maleate were in the range of 20-120 µg/mL, 0.4-2.4 µg/mL, 8-48 µg/mL and 0.16-0.96 µg/mL, respectively. This simple, fast, economical and precise high performance liquid chromatographic method can be adopted for routine quality control analysis.

Keywords: Paracetamol, Phenylephrine hydrochloride, Oxolamine citrate, Chlorpheniramine maleate, HPLC determination

Introduction

Against the common cold, new cough-cold formulations are usually given with some combination of an analgesic (*e.g.,* acetaminophen), an antitussive (*e.g.,* oxolamine citrate), an antihistamine (*e.g.,* chlorpheniramine maleate) and a nasal decongestant (*e.g.,* phenylephrine hydrochloride). In many cases, pharmaceutical formulations for the relief common cold symptoms

usually contain a high proportion of acetaminophen and small amounts of phenylephrine hydrochloride, oxolamine citrate and chlorpheniramine maleate. All these compounds with very different properties and proportions have to be separated in a HPLC method developed as stability-indicating method.

Several methods in the literature report the simultaneous quantification of acetaminophen, chlorpheniramine and phenylephrine[1-3]. Senyuva *et al.*[4] studied the rapid determination of three active compounds in combined pharmaceutical dosage forms using a Bondapak CN column. Gupta *et.al*.[5] has described three different analyses with three different mobile phases. Kanumula *et al*.[6] studied the use of wavelength programming and pseudoephedrine hydrchloride as internal standard and the method was developed by Krieger[7] for the separation of acetaminophen in analgesic preparations containing chlorpheniramine and phenylephrine hydrochloride. A gradient method has been developed to determine acetaminophen, phenylephrine and chloramine by Barbas *et al*.[8]. Gradient elution is not suitable because it increases the column re-equilibration time and baseline disturbances. On the other hand, in the literature, no HPLC method applied to medications containing a combination of these four drugs (acetaminophen, oxolamine citrate, chlorpheniramine maleate and phenylephrine hydrochloride) has been reported.

The aim of the present study was to develop a HPLC method for the simultaneous determination of acetaminophen, oxolamine citrate, chlorpheniramine maleate and phenylephrine hydrochloride in pharmaceutical tablets.

Experimental

HPLC grade acetonitrile (Merck) and methanol (Merck), ASC grade triethylamine (Merck) and *o*-phosphoric acid (Sigma) were used in the study. Working reference standards (pure drug) of acetaminophen, oxolamine citrate, chlorpheniramin maleat and phenylephrine hydrochloride were purchased from Tyco Healthcare Group (Istanbul-Turkey), Sandoz A.Ş. (Istanbul-Turkey), Chemopharma (Istanbul-Turkey) and Boehringer-Ingelheim (Istanbul-Turkey) respectively. Tablet formulation of Forza® (ARİS Istanbul Turkey) and Oledro (Drogsan, Ankara Turkey) were purchased from local pharmacies in Ankara-Turkey. Ultra pure water obtained from Ultrapure water system (Simplicity®185, Millipore) was used to prepare all solutions for the method. 0.45 µm nylon membrane filter (Millipore) were used during analyses.

Chromatographic condition

The HPLC was Thermo Finnigan Surveyor (USA) equipped with an automatic injector, a diode-array detector and a column oven. Chromatographic separation was carried out on Agilent zorbax SB-CN (150x4.6 mm, 5 µ) column using the mobile phase consisting of 0.02 M phosphate buffer (pH 4.0) and acetonitrile in the ratio 15:85 v/v, respectively. Phosphate buffer was prepared from orthophosphoric acid and triethylamine. The flow rate was 1.5 mL/min and injection volume was 10 µL. UV detection was performed at 365 nm.

Preparation of the standard solutions

Stock standard solutions of pure drugs were prepared by dissolving drugs in the methanol to give final concentrations of 0.8 mg/mL paracetamol, 0.32 mg/mL oxolamine citrate, 0.016 mg/mL phenylephrine hydrochloride and 0.0064 mg/mL chlorpheniramine maleate. Standard solutions of paracetamol (20, 40, 60, 80, 100 and 120 µg/mL), oxolamine citrate (8, 16, 24, 32, 40 and 48 µg/mL), phenylephrine hydrochloride (0.4, 0.8, 1.2, 1.6, 2 and 2.4 µg/mL) and chlorpheniramine maleate (0.16, 0.32, 0.48, 0.64, 0.8 and 0.96 µg/mL) were prepared by subsequent dilution with mobile phase.

Preparation of sample solutions

Twenty tablets were weighed and powdered. A portion of the powder equivalent to about one tablet was weighed accurately and transferred to a 25 mL volumetric flask and stirred with 10 mL methanol on a magnetic stirrer for 15 minutes. The solution was filtered through 0.45 µm nylon membrane filer and diluted up to 25 mL with methanol. 40 µL of this solution was transferred into injection vial and then the volume made up to 1 mL with the mobile phase. 10 µL of sample solution was injected into the HPLC system.

Results and Discussion

The procedure for the simultaneous analysis of paracetamol, phenylephrine hydrochloride, oxolamine citrate and chlorpheniramine maleate using isocratic HPLC method has been reported. The chromatographic conditions were optimized to obtain good baseline separation and peak shapes. Various compositions of mobile phase consisting of 0.026 M phosphate buffer and acetonitrile were used in the study and the composition of 15:85 was selected as it gave best elution, reasonable retention time and least tailing. The retention times of standards are 1.18 min for paracetamol, 2.18 min phenylephrine HCl, 2.80 min for oxolamine citrate and 3.34 min for chlorpheniramine maleate. A typical HPLC chromatogram of standard mixture solution was given in Figure 1.

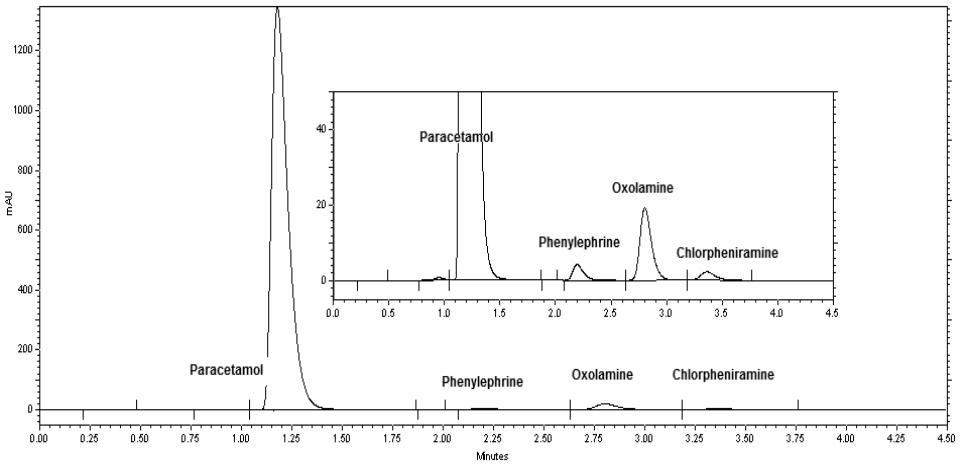

Figure 1. HPLC chromatogram of standard mixture solution

Calibration and linearity

In this study, an external method was used for the simultaneous determination of four ingredients. Seven concentrations were chosen, ranging between 20 and 120 µg/mL for paracetamol, 8 and 48 µg/mL for oxolamine citrate, 0.4 and 2.4 µg/mL for phenylephrine hydrochloride, 0.16-0.96 µg/mL for chlorpheniramine maleate. Each concentration of standard mixture solutions was injected in triplicate and the mean value of peak area was taken for the calibration curve. Calibration curves were constructed using three series of standard solutions in the range of that mentioned above. Peak area was recorded for all the peaks and a calibration graph was obtained by plotting peak area *versus* concentration of standard drugs [Figure 2 (A), (B), (C) and (D)]. The calibration graphs were found to be linear in the mentioned concentrations and correlation coefficients were given in Table 1.

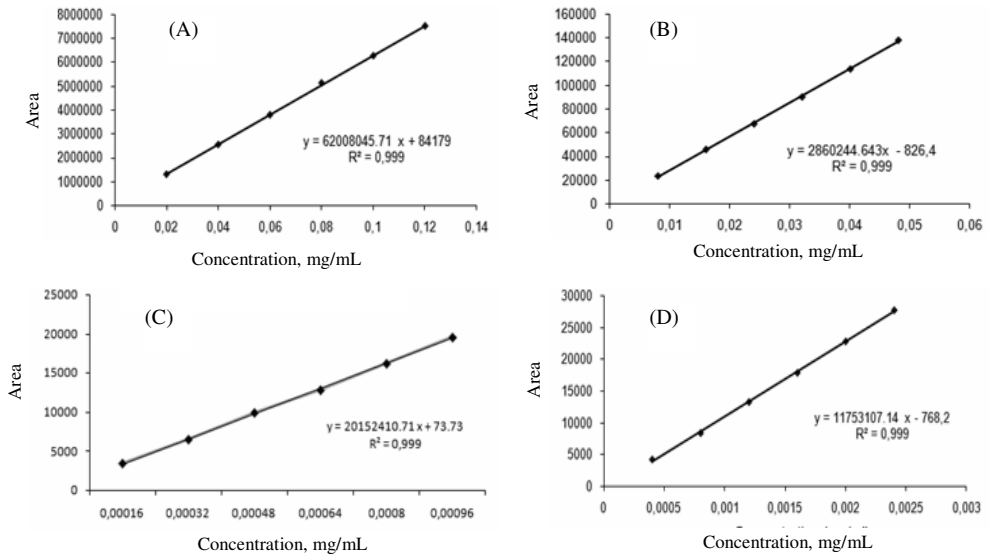

Figure 2. Calibration graphics of standard drugs (A: paracetamol, B: oxolamine citrate, C: chlorpheniramine maleate, D: phenylephrine hydrochloride)

Repeatability

For evaluation of the precision estimates, repeatability was performed at six concentration levels for each compound. Ten replicates was performed for each concentration. The results in Table 1 indicate that the RSD (%) is less than 2% and the method is reliable.

Table 1. Results of precision and linearity of the study

Ingredients	Precision, % RSD	Coefficient of correlation	Linearity, µg/mL
Paracetamol	0.12	0.999	0.02-0.12
Oxolamine citrate	0.18	0.999	0.008-0.048
Phenylephrine HCl	0.36	0.999	0.0004-0.0024
Chlorpheniramine maleate	0.59	0.999	0.00016-0.00096

Recovery

The accuracy of the proposed method was tested by recovery experiments. Recovery tests were performed by adding a known amount of each drug to placebo. The mean results of five analyses were ranged from 99.6 to 100.56 and can be considered to be good recoveries (Table 2).

Table 2. Results of the recovery tests

Ingredients	Amount added, mg	Recovery %, RSD
Paracetamol	250.0	99.99 (0.04)
Oxolamine citrate	100.0	100.20 (1.20)
Phenylephrine HCl	5.0	100.56 (1.56)
Chlorpheniramine maleate	2.0	99.60 (0.65)

The proposed HPLC method was applied to simultaneous determination of paracetamol, phenylephrine HCl, oxolamine citrate and chlorpheniramine maleate in Forza Tablet® and in Oledro Tablet®. The quantitative results of these assays are summarized in Table 3. Satisfactory results were obtained for each compound in good agreement with label claims.

Table 3. Analyses of two different tablets by the proposed method

Commercialized formulations	Ingredients	Labelled amount, mg	Found amount, mg	Found amount, %
Forza Tablet®	Paracetamol	250.0	250.06	100.02
	Oxolamine citrate	100.0	100.06	100.06
	Phenylephrine HCl	5.0	5.02	100.40
	Chlorpheniramine maleate	2.0	2.01	100.50
Oledro Tablet®	Paracetamol	250.0	250.06	100.02
	Oxolamine citrate	100.0	100.02	100.02
	Phenylephrine HCl	5.0	5.01	100.20
	Chlorpheniramine maleate	2.0	2.01	100.50

Conclusion

A simple and quick, new analytical method has been developed to be applied for the analysis of mentioned compounds. The method uses a simple, easily prepared mobile phase composition. The rapid run time of 3.5 minutes allows the analysis of large number of samples with less mobile phase that proves to be cost effective. The proposed method has been found suitable for the routine analysis of the pharmaceutical tablet forms in quality control and R&D laboratories.

Acknowledgment

This study was supported by Gazi University Research Fund (02/2009-19).

References

1. Heydari R, *Anal Lett.,* 2008*,* **41(6),** 965-976.
2. Garcia A, Ruperez F J, Marin A, de la Maza A and Barbas C, *J Chromatogr B,* 2003, **785**, 237-243.
3. Olmo B, Garcia A, Marin A and Barbas C, *J Chromatogr B,* 2005, **817**, 159-165.
4. Senyuva H and Ozden T, *J Chromatogr Sci.*, 2002, **40**, 97-100.
5. Das Gupta V and Heble A R, *J Pharm Sci.*, 1984, **73(11)**, 1553-1556.
6. Kanumula G V, Raman B and Bhoir I C, *Indian Drugs*, 2001, **38(4)**, 203-207.
7. Krieger D J, *J Assoc off Anal Chem.*, 1984, **67(2)**, 339-341.
8. Marin A, Garcia E, Garcia A and Barbas C, *J Pharm Biomed Anal.*, 2002, **29**, 701-719.