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Simultaneous Estimation of Nimesulide, Cetirizine Hydrochloride and Pseudoephedrine Hydrochloride in Combined Tablet Dosage Form Using RP-HPLC Method

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A simple, accurate and precise RP-HPLC method has been developed for the simultaneous estimation of nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride in commercially available tablet formulations. The chromatographic separation was achieved on Luna C_8 column using acetonitrile:phosphate buffer:triethyl amine (pH 6.5 ± 0.1) (50:50:0.1 % v/v/v) as mobile phase at a flow rate of 1.0 mL/min. Quantitation was carried out at λ_{max} of 266, 230 and 256 nm for nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride, respectively. The method was validated as per ICH guidelines. The method may be applied for the routine simultaneous estimation of the above mentioned drugs in tablet dosage form.

Key Words: RP-HPLC, Nimesulide, Cetirizine hydrochloride, Pseudoephedrine hydrochloride, Simultaneous estimation.

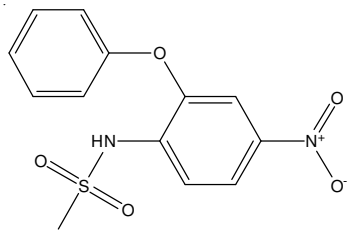
INTRODUCTION

Nimesulide (N[4-nitro-2-phenoxyphenyl]methane sulphonamide), is a nonsteroidal antiinflammatory drug (NSAID) with antiinflammatory, antipyretic and analgesic properties. It inhibits prostaglandin synthetase/cyclooxygenase, which limits prostaglandin production. Its cyclooxygenase inhibiting potency is intermediate, but is relatively selective for the cyclo-oxygenase-2 (COX-2)[1,2].

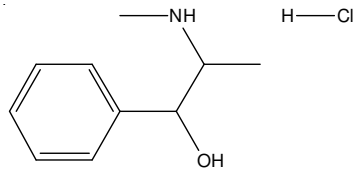
Cetirizine hydrochloride (2-[2-[4-[(4-chlorophenyl)-phenylmethyl]piperazin-1-yl]ethoxy]acetic acid dihydrochloride), is a potent and highly selective antagonist of the peripheral histamine H_1-receptor on effector cells in the gastrointestinal tract, blood vessels and respiratory tract. Cetirizine also inhibits release of histamine and of cytotoxic mediators from platelets as well as eosinophil chemotexis during the secondary phase of the allergic response[1-3].

Pseudoephedrine hydrochloride (2-(methyl amino)-1-phenylpropan-1-ol hydrochloride), is both α- and β-adrenergic receptor agonist. It causes vasoconstriction *via* direct stimulation of α-adrenergic receptors of the respiratory mucosa. It also directly stimulates β-adrenergic receptors causing bronchial relaxation. The structures of drugs are shown in Fig. 1[1-3].

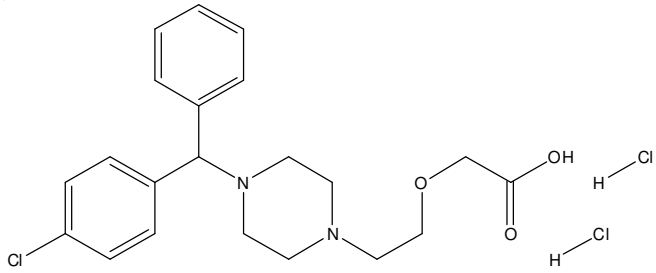
Assay of nimesulide in bulk and in dosage form is official in British Pharmacopoeia (2004). Several analytical methods have been reported for the determination of nimesulide in dosage form, in biological fluids and in urine using HPLC, LC/MS, capillary electrophoresis and UV[4-7].



Nimesulide



Pseudoephedrine hydrochloride



Cetirizine hydrochloride

Fig. 1. Chemical structures of nimesulide, pseudoephedrine hydrochloride and cetirizine hydrochloride

Assay of cetirizine hydrochloride in bulk and in dosage form is official in Indian Pharmacopoeia (2007) and British Pharmacopoeia (2004). Several analytical methods have been reported for the determination of cetirizine hydrochloride in dosage form, in biological fluids and in urine using UV, HPLC, HPTLC, LC/MS and CE[8-11].

Assay of pseudoephedrine hydrochloride in bulk and in dosage form is official in Indian Pharmacopoeia (2007), British Pharmacopoeia (2004). Several analytical procedures have been reported for the determination of pseudoephedrine hydrochloride, most frequently by using UV, HPLC, GC and LC/MS procedures[12-15].

This paper describes a novel method for the simultaneous estimation of nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride in tablets dosage form. The procedure, based on the use of reversed-phase high-performance liquid chromatography, is simple rapid and provides accurate and precise results. The proposed methods were optimized and validated according to current International Conference on Harmonization (ICH) guidelines[16].

EXPERIMENTAL

Nimesulide and cetirizine hydrochloride were provided by Schon Pharmaceuticals Limited (Indore, India) and pseudoephedrine hydrochloride was obtained from Cipla Ltd. (Pithampur, India) as gratis sample. All the chemicals and reagents used were of HPLC grade and purchased from Merck Ltd. (Mumbai, India). The percentage purity of nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride were found to be 100.1, 99.51 and 99.86 %, respectively.

Chromatographic system and conditions: The LC system consisted of LC $10AT_{VP}$ (Shimadzu, Japan) gradient pump with universal loop injector (Rheodyne 7725i) of 20 L injection capacity, photodiode array detector (PDA) SPD-10 AVP and Phenomenex Luna C_8 (25 cm × 5 m × 4.6 mm i.d.) column, controlled by a PC work station equipped with software CLASS-Vp (software M-10, version 1.6).

The mobile phase consisted of a mixture of acetonitrile, phosphate buffer and triethyl amine (pH 6.5 ± 0.1 (50:50:0.1 % v/v/v). Mobile phase was filtered through a 0.45 µm membrane filter and delivered at a flow rate of 1.0 mL/min.

Standard stock solutions: The equivalent of 10 mg each of nimesulide, cetirizine hydrochloride and 100 mg of pseudoephedrine hydrochloride were accurately weighed, different dilutions were prepared for each drug having concentration from 10, 20, 30, 40 and 50 µg/mL for nimesulide, 5, 10, 15, 20 and 25 µg/mL for cetirizine hydrochloride and 200, 300, 400, 500 and 600 for pseudoephedrine hydrochloride with mobile phase. 20 µL of these solutions were injected into the LC system with the help of Hamilton syringe. The chromatograms were recorded at 266, 230 and 256 nm for nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride, respectively. Peak areas were used to prepare calibration curve against their respective concentrations.

Analysis of tablets: As the results of mixed standard analysis were found satisfactory, the method was applied for the quantitative study of all drugs in commercially available tablet. 20 tablet of Namcold were weighed and powder equivalent to 5 mg of cetirizine hydrochloride was taken in 100 mL volumetric flask and dissolved in 10 mL of mobile phase acetonitrile, phosphate buffer and triethyl amine (50:50:0.1 % v/v/v) (pH 6.5 ± 0.1) with vigorous shaking for 5-10 min. The supernatant liquid was transferred to 100 mL of volumetric flask through a whatman # 41 filter paper. The residue was washed twice with solvent and the combined filtrate was suitably diluted. Five replicates of sample solutions were prepared and 20 µL of each replicates were injected. The concentrations of these drugs were extrapolated from their respective calibration curves by using the area.

Recovery study: To check the accuracy of the developed method recovery study was carried out in triplicate as per ICH guideline. 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 using three replicates over three concentration levels of within range expressed as % RSD values.

RESULTS AND DISCUSSION

For the RP-HPLC method, chromatographic conditions were optimized to achieve the best resolution and peak shape for nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride. Mobile phase contaning acetonitrile:phosphate buffer:triethyl amine (pH 6.5 ± 0.1, 50:50:0.1 % v/v/v) was selected as optimal for obtaining well-defined and resolved peaks. The quantitation was carried out at λ_{max} of 266, 230 and 256 nm for nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride, respectively (Fig. 2). Table-1 summarizes linearity range, limit of detection (LOD), limit of quantitation (LOQ), λ_{max} values for all three drugs and system suitability parameters for the RP-HPLC method.

The proposed methods were also evaluated in the assay of commercially available tablets containing nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride. Five replicates determination were performed on the accurately weighed amounts of tablets (Table-2). Linearity range was found to be in the range of 10-120, 4-50 and 100-1250 µg/mL with LOQ of 1.84, 0.90 and 48.94 for nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride, respectively, the recovery study showed an acceptable range of variation below RSD of 2. The solution was found to be stable in precision study for long period of time.

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

Parameters	NIM	CET	PSE
Linearity range, (µg/mL)	10-120	4-50	100-1250
$\lambda_{max,}$ (nm)	266	230	256
Limit of detection, (µg/mL)	0.60	0.28	16.15
Limit of quantitation, (µg/mL)	1.84	0.90	48.94
Theoretical plate number	7494	4476	2356
Retention time, (min)	6.86	4.285	2.68
HETP[a]	0.0033	0.0055	0.0106
Tailing factor	1.33	1.45	1.81
Capacity factor, (k')	1.55	0.59	–
Resolution	8.82	6.39	–

[a]HETP = Height equivalent to theoretical plate, cm; NIM = nimesulide, CET = cetirizine hydrochloride, PSE = pseudoephedrine hydrochloride

TABLE-2
RESULTS OF COMMERCIAL TABLET ANALYSIS AND STATISTICAL VALIDATION OF RECOVERY STUDY

Particulars	Conc. of drug added (%)	NIM Conc. found (%)†	CET Conc. found (%)†	PSE Conc. found (%)†
Recovery study	80	100.40 ± 0.72	99.51 ± 0.70	100.96 ± 0.29
	10	100.35 ± 0.38	100.62 ± 0.86	100.85 ± 1.00
	120	98.86 ± 0.33	99.18 ± 0.25	99.2 ± 0.35
Commercial tablet analysis		99.54 ± 0.63*	99.47 ± 0.81*	98.65 ± 0.33*

†Mean ± RSD (n = 3). *10 µg/mL for NIM, 5 µg/mL for CET and 250 µg/mL for PSE, respectively (% RSD, n = 5); NIM = nimesulide, CET = cetirizine hydrochloride, PSE = pseudoephedrine hydrochloride

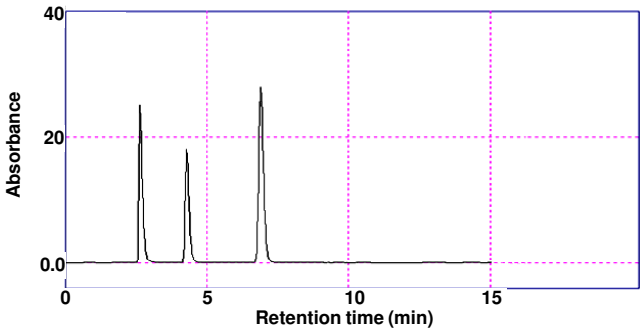


Fig. 2. Chromatograms of 500 µg/mL pseudoephedrine hydrochloride, 10 µg/mL cetirizine hydrochloride and 20 µg/mL nimesulide at 240 nm in acetonitrile:phosphate buffer:triethyl amine (pH 6.5 ± 0.1) (50:50:0.1 % v/v/v) as mobile phase

Conclusion

The validated RP-HPLC method developed here found to be simple, fast, accurate, precise and sensitive. The developed method was validated based on ICH guidelines. Thus, it can be used for routine analysis of nimesulide, cetirizine hydrochloride and pseudoephedrine hydrochloride in combined tablet dosage form.

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REFERENCES

1. British Pharmacopoeia, The Department of Health, Great Britain, pp. 415, 1378, 1662 (2004).
2. K.D. Tripathi, Essential of Medical Pharmacology, Jaypee Brothers Medical Publishers, New Delhi, edn. 5, pp. 114,142,179 (2003).
3. Indian Pharmacopoeia, The Controller of Publication, Government of India, Delhi, India, edn. 5, pp. 275,1005 (2007).
4. S. Altino and O.O. Dursun, *J. Pharm. Biomed. Anal.*, **22**, 175 (2000).
5. D. Castoldi, V. Monjani and O. Toffaneti, *J. Chromatogr.*, **425**, 413 (1988).
6. P. Kovarikova, M. Mokry and J. Klimes, *J. Pharm. Biomed. Anal.*, **31**, 827 (2003).
7. P. Ptacek, J. Macek and J. Klima, *J. Chromatogr. B*, **758**, 183 (2001).
8. S. Azhagvuel and R. Sekar, *J. Pharm. Biomed. Anal.*, **43**, 813 (2007).
9. A.F.M. Walily, M.A. Kornay and M.F. Bedair, *J. Pharm. Biomed. Anal.*, **17**, 435 (1998).
10. J. Moncrieff, *J. Chromatogr.*, **583**, 128 (1992).
11. B.S. Nagaralli, J. Seetharamappa, B.G. Gowda and M.B. Melwanki, *J. Chromatogr. B*, **798**, 49 (2003).
12. M. Ming, F. Fang, S. Yulan, C. Shuangjin and L. Han, *J. Chromatogr. B*, **846**, 105 (2007).
13. M.M. Mabrouk, H.M. El-Fatatry, S. Hammad, A. Aziz and M. Wahbi, *J. Pharm. Biomed. Anal.*, **33**, 597 (2003).
14. T.G. Altuntas, S.S. Zanooz and D. Nebioglu, *J. Pharm. Biomed. Anal.*, **17**, 103 (1998).
15. S. Karakus, I. Kucukguzel and S.G. Kucukguzel, *J. Pharm. Biomed. Anal.*, **46**, 295 (2008).
16. ICH Q2 (R1) Guideline, Validation of Analytical Procedures: Text and Methodology (CPMP III/ 5626/94), ICH, Geneva, Switzerland (2005).