Asian Journal of Chemistry Vol. 14, No. 2 (2002), 1004–1008

Simultaneous Estimation of Nimesulide and Paracetamol in Tablets by Reverse Phase High Performance Liquid Chromatography

K.E.V. NAGOJI, S. VIJAYA SRINIVAS*, S. SRINIVASA RAO† and S.S. PATRO
Roland Institute of Pharmaceutical Sciences, Berhampur-760 010, India

A simple, precise, fast, reproducible and selective reverse phase HPLC method has been developed for the simultaneous estimation of nimesulide and paracetamol from tablets. The analyte was resolved by using a mobile phase (acetonitrile and water in the ratio 60 : 40) at a flow rate of 0.7 mL/min. on an isocratic HPLC system consisting of LC-10 AT liquid pump, SPD-10A UV-Visible detector, an ODS C-18 RP column (4.6 mm I.D. × 25 cm) at a wavelength of 230 nm. The linear dynamic range for both nimesulide and paracetamol was 0.25 to 40.0 μg/mL by this method. Ibuprofen was used as an internal standard.

Key Words: Estimation, Nimesulide, Paracetamol, HPLC.

INTRODUCTION

Nimesulide[1] is a non-steroidal anti-inflammatory, analgesic and antipyretic agent with minimal side effects. Chemically it is N-(4-nitro-2-phenoxyphenyl) methane sulfonamide. It is commonly prescribed for the treatment of inflammatory conditions associated with rheumatoid arthritis, respiratory tract infections, soft tissue and oral cavity inflammations, urogenital diseases and postoperative pain[2]. It is also used in the treatment of cataract, asthma[2] etc. A few HPLC methods[3–6], a very few HPTLC methods[7, 8], and a gas chromatographic method[9] have been reported for the estimation of nimesulide alone.

Paracetamol[10–13] is also a non-steroidal anti-inflammatory, analgesic and antipyretic drug. Chemically it is N-(4-hydroxyphenyl) acetamide. A few HPLC methods[14–20] and a very few HPTLC methods[21–23] have been reported for the estimation of paracetamol alone. Fixed dose combination containing nimesulide and paracetamol is available in the tablet form in the market. However only one reverse phase HPLC method[24] has been reported so far for the simultaneous determination of these drugs from the tablets.

In this communication we report a new reverse phase HPLC method for simultaneous determination of nimesulide and paracetamol from tablets which is simple, rapid, selective, precise and reproducible.

†Asmara University, Asmara, Eritria, North-East Africa.

EXPERIMENTAL

An isocratic HPLC system (Shimadzu) consisting of LC-10 AT liquid pump, SPD-10A UV-Visible detector, an ODS C-18 RP column (4.6 mm I.D. × 25 cm), 25 mL Hamilton injecting syringe and window based single channel software was used. Afcoset electronic balance was used for weighing the materials.

Pure samples of nimesulide, paracetamol and ibuprofen were obtained from Dr. Reddy's Laboratories, Hyderabad; acetonitrile used was of HPLC grade and obtained from E. Merck (India) Ltd., Mumbai. Water used was triple distilled prepared by all-glass distillation apparatus.

Standard graph: Standard stock solutions of nimesulide and paracetamol were prepared by dissolving 25 mg of the drug in 25 mL of the mobile phase (acetonitrile and water in the ratio 60 : 40) to get 1 mg/mL solution and these solutions were suitably diluted to prepare stock solutions of concentration 10 μg/mL and 100 μg/mL. Stock solution of ibuprofen was prepared by dissolving 25 mg of the drug in 25 mL of the mobile phase to get 1 mg/mL solution and suitably diluted to get a solution of concentration 200 μg/mL.

Working standard solutions containing nimesulide and paracetamol in various concentrations and ibuprofen (internal standard) in the concentration of 10 μg/mL were prepared in the mobile phase as per Table-1. 25 μL of each solution was injected in the HPLC system to obtain the chromatogram. The ratios of AUC of nimesulide to internal standard and the ratios of AUC of paracetamol to internal standard were calculated. The results are shown in Table-1.

TABLE-1
STANDARD GRAPH FOR THE ESTIMATION OF NIMESULIDE AND PARACETAMOL FROM TABLETS

Concentration (μg/mL) of			Ratio of AUC of	
Nimesulide	Paracetamol	Ibuprofen	Nimesulide to I.S.	Paracetamol to I.S.
0.25	0.25	10	0.05982	0.04723
0.50	0.50	10	0.12728	0.09170
1.00	1.00	10	0.25550	0.18940
5.00	5.00	10	0.95480	0.92380
10.00	10.00	10	1.88000	1.73660
20.00	20.00	10	3.75310	3.42700
40.00	40.00	10	7.22900	6.72790
Slope (m):			0.1808	0.168100
Intercept (b):			0.04777	0.029321
Corr. Coeff. (r):			0.99980	0.999900

All the values are the averages of three determinations.

Estimation of nimesulide and paracetamol in the combined dosage form: The quantities of the formulations containing nimesulide and paracetamol equivalent to 25 mg of nimesulide were weighed accurately and taken into 25

mL volumetric flask. Nimesulide and paracetamol were extracted in acetonitrile and the volume was adjusted to 25 mL, mixed and filtered. From the filtrate 0.125 mL was pipetted in 25 mL volumetric flask and spiked with the required aliquot of internal standard solution and then the volume was adjusted to 25 mL with the mobile phase such that the concentration of internal standard in each solution was 10 μg/mL solution. 25 μL of this solution was injected into HPLC system to obtain the chromatogram and the concentration of nimesulide and paracetamol corresponding to the ratio of AUC of nimesulide to AUC of internal standard and AUC of paracetamol to the AUC of internal standard respecetively in the formulations were calculated from the standard graph (Fig. 1). The results are given in Table-2.

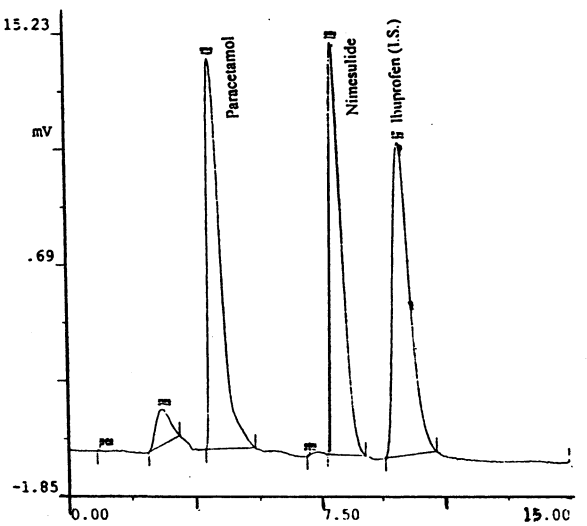

Fig. 1. A typical chromatogram of nimesulide, paracetamol and ibuprofen (I.S.)

TABLE-2
ANALYSIS OF TABLETS CONTAINING NIMESULIDE AND PARACETAMOL

Pharmaceutical formulation	Amount of Nimesulide (mg)		Amount of Paracetamol (mg)		% Recovery	
	Labelled	Found	Labelled	Found	Nimesulide	Paracetamol
Tablet-1 (NICIP PLUS)	100	99.750	325	322.00	99.750	100.750
Tablet-2 (DOLAMIDE)	100	100.250	500	505.02	99.865	100.250
Tablet-3 (SUMO)	100	98.862	500	501.25	98.980	100.852

All the values are the averages of three determinations.

Recovery studies: Recovery experiments by adding known amounts of nimesulide and paracetamol to the previously analysed pharmaceutical preparations were carried out and the results are given in Table-2.

Optimized chromatographic conditions

The optimized chromatographic conditions were as follows:

Chromatograph	Shimadzu HPLC system
Mobile phase	acetonitrile : water (60 : 40)
Column	ODS C-18 (4.6 mm I.D. × 25 cm)
Flow rate	0.7 mL/min.
Detection	U.V. set at 230 nm
Injection volume	25 µL
Temperature	Ambient
Retention time:	
of nimesulide	7.96–8.00 min.
of paracetamol	4.26–4.30 min.
of internal standard	9.97–10.04 min.
Run time	15 min.

RESULTS AND DISCUSSION

The extracts of the formulations containing nimesulide and paracetamol showed no significant peaks at the retention times other than the retention times of nimesulide and paracetamol which indicates that the excipients in the tablets are not interfering in the estimation by this method and therefore this method is specific.

The values of recovery studies given in Table-2 indicate that the method is accurate. As the mobile phase is only a mixture of acetonitrile and water, the run time is only 15 min. and the flow rate of the mobile phase is 0.7 mL/min. The method is rapid and economical.

ACKNOWLEDGEMENTS

The authors are grateful to Dr. Reddy's Laboratories, Hyderabad for providing gift samples of nimesulide, paracetamol and ibuprofen. The authors are also grateful to M/s Roland Inst. of Pharm. Sciences, Berhampur for providing the necessary facilities to carry out the research work.

REFERENCES

1. The Merck Index, 12th Edn., p. 1125 (1996).
2. Davis Glick and R.N. Brogden, *Drugs*, **48**, 431 (1994).
3. S.F. Chang, *J. Pharm. Sci.*, **66**, 1700 (1977).
4. Zhu Zeng and Hamping Zhang, *Shongguo Yaoxue Zazhi*, **31**, 610 (1996).
5. A. Nonzioli, G. Luque and C. Ferdnandez, *J. High Resolut. Chromatogr.*, **12**, 413 (1989).

6. D. Castoldi, V. Monzani and O. Tofanetti, *J. Chromatogr. Biomed. Appl.*, **69**, (*J. Chromatogr.*, 425), 413 (1988).
7. K.K. Pandya, M.C. Satia, I.A. Modi, R.I. Modi, B.K. Chakravarti and T.P. Gandhi, *J. Pharm. Pharmacol.*, **49**, 773 (1997).
8. R.T. Sane, G. Sameer Navalgund, H. Deepa Khanolkar, S. Padmaja Prabhu and S. Prafulla Sahasrabudhe, *Indian Drugs*, **35**, 757 (1998).
9. G. Sameer Navalgund, H. Deepa Khanolkar, S. Padmaja Prabhu and S. Prafulla Sahasrabudhe, *Indian Drugs*, **36**, 173 (1999).
10. European Pharmacopoeia, 1288, 1001 (1997).
11. USP XXIII, 16,785,981.
12. British Pharmacopoeia, 994,713 (1998).
13. Indian Pharmacopoeia, 554,387 (1996).
14. R.H. Chang, *Yaowu Fenxi Zhazi*, **18**, 198 (1998).
15. S.V. Erram and H.P. Tipnis, *Indian Drugs*, **30**, 116 (1993).
16. O.T. Aloba, P.S. Adusumilli and A.G. Nigalaye, *J. Pharm. Biomed. Anal.*, **9**, 335 (1991).
17. A.I. Gasco Lopaez, Izquievdo, R. Hornillos and A. Jimmiinez, *J. Chromatogr. A*, 18, **775**, 179 (1997).
18. S. Ravishankar, M. Vasudevan, M.J. Nanjan and B. Bijukarian Suresh, *Indian Drugs*, **34**, 663 (1997).
19. M. Masuda, T. Satoh, M. Handa, Y. Itoh and K. Sagana, *Buneki Kagaku*, **46**, 777 (1997).
20. X.L. Tian, and M.C. Zhang, *Yaowu Fenxi Zhazi*, **17**, 346 (1997).
21. P.D. Sethi, HPTLC Quantitative Analysis of Pharmaceutical Formulations, 158, 160, 206, 214.
22. P.P. Shirke, M.K. Patel, V.A. Tamhane, V.B. Tirodkar and P.D. Sethi, *Indian Drugs*, **30**, 653 (1993).
23. T.K. Save, D.V. Parmar and P.V. Devrajan, *J. Chromatogr. B. Biomed. Appl.* 7, **690**, 315 (1997).
24. (Ms.) Bhanu Raman and Dhanajay Patil, *Indian Drugs*, **37**, 437 (2000).

(*Received*: 7 January 2001; *Accepted*: 15 February 2002) AJC-2624