Eurasian Journal of Analytical Chemistry

Eurasian J Anal Chem 7(1): 1-6, 2012

Validated Method Development for Estimation of Naproxen sodium as Bulk Drug and in Tablet Dosage Form by HPTLC

Padmanabh. B. Deshpande, Santosh. V. Gandhi[a*], Rajiv A. Mantri, Khushbu P. Luniya, Shalaka U. Dubey and Shriniwas K. Bharani

Department of Pharmaceutical Analysis, AISSMS College of Pharmacy, Kennedy Road, Near R. T. O., Pune – 411 001

Received: *22/07/2009****; Accepted:*** *17/07/2011*

Abstract

Naproxen sodium is a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties. The present work describes a simple, precise and accurate HPTLC method for its estimation as bulk and in tablet dosage form. The chromatographic development was carried out on precoated silica gel 60 F_{254} aluminium plates using mixture of toluene : ethyl acetate: acetic acid (7.5: 1.5: 1 v/v/v) as mobile phase and densitometric evaluation of band was carried out at 230 nm using Camag TLC Scanner-3 with win CAT 1.4.2 version software. The R_f value of drug was found to be 0.63 ± 0.013. The accuracy and reliability of the proposed method was ascertained by evaluating various validation parameters like linearity (100-500 ng band^{-1}), precision (intra-day RSD 0.56-0.87 %, inter-day RSD 0.49-1.39 %), accuracy (99.313 ± 0.467) and specificity according to ICH guidelines. The method was also evaluated by the assay of commercially available tablets. The % assay (Mean ± S.D., n = 6) was found to be 99.34 % ± 0.146. The proposed method can analyse ten or more formulation units simultaneously on a single plate and provides a faster and cost-effective quality control tool for routine analysis of naproxen sodium as bulk drug and in tablet formulation.

Keywords:

Naproxen sodium; HPTLC

1. Introduction

Naproxen sodium, chemically ((+)-(*S*)-2-(6-methoxynaphthalen-2-yl)propanoic acid is commonly used for the reduction of moderate to severe pain, fever and inflammation [1]. Literature review reveals that several methods like HPLC [2-11], GLC [12-13] and spectrophotometry [14] have been reported for estimation of naproxen sodium in single and combined form with other drugs, but no HPTLC method is reported so far. The present study illustrates development and validation of a simple, accurate, economical and reproducible procedure for determination of naproxen sodium by HPTLC as bulk and in tablet dosage form.

2. Materials and methods

Pharmaceutical grade naproxen sodium working standard was a generous gift from Maxim Pharmaceuticals (Pune, India) Fixed dose tablets (Naproxen-500) containing 500 mg of naproxen sodium (LRPG Life Sciences Ltd. Ankleshwar) were procured from local market.

* **Corresponding Author**
E-mail: santoshvgandhi@rediffmail.com
ISSN: 1306-3057,

Silica gel 60 F_{254} TLC plates (20×20 cm, layer thickness 0.2 mm, E. Merck, Germany) were used as stationary phase. All chemicals and reagents used were of analytical grade and were purchased from Merck Chemicals Corporation Ltd. Mumbai, India. A Camag HPTLC system containing Camag Linomat V semiautomatic sample applicator, Hamilton syringe (100 µL), Camag TLC Scanner-3 with win CAT software version 1.4.3 and Camag twin- trough chamber (20×20 cm) were used for the present study.

2.1. Chromatographic conditions

TLC plates were pre-washed with methanol. Activation was done in oven at 105 ºC for 20 min. The plates were allowed to cool at room temperature. The chromatographic estimations were performed using following conditions: stationary phase: precoated silica gel 60 F_{254} aluminium plates (20 cm×20 cm×250 µm); mobile phase: toluene: ethyl acetate: acetic acid (7.5: 1.5: 1 v/v/v); chamber saturation time: 20 min; wavelength of scanning: 230 nm; slit dimensions: 6.00 × 0.30 mm; spotting parameters used were, band width: 8 mm and space between two bands: 15.4 mm.

2.2. Preparation of standard solution

Naproxen sodium (10 mg) was weighed accurately and transferred to 10 mL volumetric flask. The volume was made upto 10 mL with methanol to obtain concentration of 1 mg mL^{-1}. 0.5 mL of the above solution was further diluted 10 mL with methanol to obtain the concentration 50 ng μL^{-1} of naproxen sodium.

2.3. Validation of method

The method was validated as per the ICH guidelines in terms of linearity, accuracy and specificity, intra-day and inter-day precision, repeatability of measurement of peak area as well as repeatability of sample application [15].

2.4. Preparation of calibration curve

For the preparation of a calibration curve, aliquots 2, 4, 6, 8, 10 µL of standard stock solution of naproxen sodium (50 ng μL^{-1}) were applied on the TLC plate under nitrogen stream. TLC plates were developed under above established conditions. Area under peak was calculated and plotted against concentration.

2.5. Specificity

The specificity of the method was ascertained by analyzing standard drug and sample. The spot for drug was confirmed by comparing the R_f and spectra of the sample spots with that of standard drugs.

2.6. Recovery Studies

To check the accuracy of the method, recovery studies were carried out by addition of standard drug solution to pre-analyzed sample solution at three different levels 50, 100 and 150 %. Chromatogram was developed and the peak areas were noted. At each level of the amount, three determinations were carried out.

2.7. Intra-day and inter-day precision

The intra-day precision was determined by analyzing standard solutions of naproxen sodium in range 100-500 ng $band^{-1}$ for three times on the same day while inter-day precision was determined by analyzing corresponding standards on three different days over a period of one week

2.8. Repeatability of measurement of peak area as well as repeatability of sample application

Repeatability of measurement of peak area was determined by applying 4 µL of standard drug solution on TLC plate. After developing the plate, band of drug was scanned six times without changing position of the plate and RSD value was calculated. Repeatability of sample application was assessed by applying 4 µL of standard drug solutions six times on a TLC plate by semiautomatic applicator, followed by development of plate and recording the peak areas for six spots. The RSD for the peak area values was calculated.

2.9. Robustness studies

Robustness studies were carried out by examining the effect of small, deliberate variation of the analytical conditions on the peak areas of the drug. Factors varied were volume of mobile phase (± 0.5 %), time from application to development (0, 10, 20, and 30 min) and from development to scanning (0, 30, 60, and 90 min). One factor at a time was changed to study the effect. The robustness of the method was checked at amount of 200 ng band^{-1}.

2.10. Assay of the marketed formulation

For analysis of tablet dosage form, twenty tablets were weighed and their average weight was calculated. The tablets were finely powdered and powder equivalent to 10 mg of naproxen sodium was accurately weighed and suspended in 5 mL of methanol. The solution was filtered through Whatman filter paper no. 41, the residue was washed with methanol and volume was adjusted to 10 mL with the same solvent. 0.5 mL of this solution was further diluted with methanol so as to have sample concentration 50 ng µL^{-1}. Four µL volume of this solution was applied to the plate which was then developed as described above. The amount of naproxen sodium was determined from the standard calibration curve. Procedure was repeated six times for the analysis of homogenous sample.

3. Results and discussion

Literature survey revealed that several HPLC, GLC and spectrophotometry methods have been reported for estimation of naproxen sodium which are sophisticated but costly and time consuming. As no HPTLC method has been reported so far for estimation of naproxen sodium, the present study was aimed at development of a versatile, speedy and cost effective HPTLC technique for determination of naproxen sodium as bulk and in tablet dosage form.

Since naproxen sodium is freely soluble in methanol, tablet powder was extracted with methanol. Centrifugation for 15 min at 600 rpm helped to completely extract the drug from tablet matrix. The mixture of toluene: ethyl acetate: acetic acid (7.5: 1.5: 1 v/v/v) as mobile phase gave better peak shape. The R_f value of drug was found to be 0.63 ± 0.013 (Fig. 1).

The method was found to be linear in the range of 100-500 ng band^{-1}. The spectrum of naproxen sodium extracted from tablet compared with spectrum of standard naproxen sodium showed good correlation, confirm the specificity of the proposed method. The results of recovery study indicate that the proposed method is accurate for estimation of drugs in tablet dosage form (Table 1).

The intra-day and inter-day relative standard deviations were found in the range 0.56-0.87 % and 0.49-1.39 % respectively. The smaller values of intra-day and inter-day variation in the analysis indicate that the method is precise. RSD for repeatability of measurement of peak area and repeatability of sample application were found to be 0.56 % and 1.23 %, respectively. The RSD values for measurement of peak area and sample application were both

below the instrumental specifications (1 % and 3 %, respectively), ensuring proper functioning of HPTLC system. Robustness of the method checked after deliberate alterations of the analytical parameters showed that areas of peaks of interest remained unaffected by small changes of the operational parameters (% RSD < 2). The results are given in Table 2.

The proposed method was also evaluated by the assay of commercially available tablets. The % assay (Mean ± S.D., n = 6) was found to be 99.34 % ± 0.146.

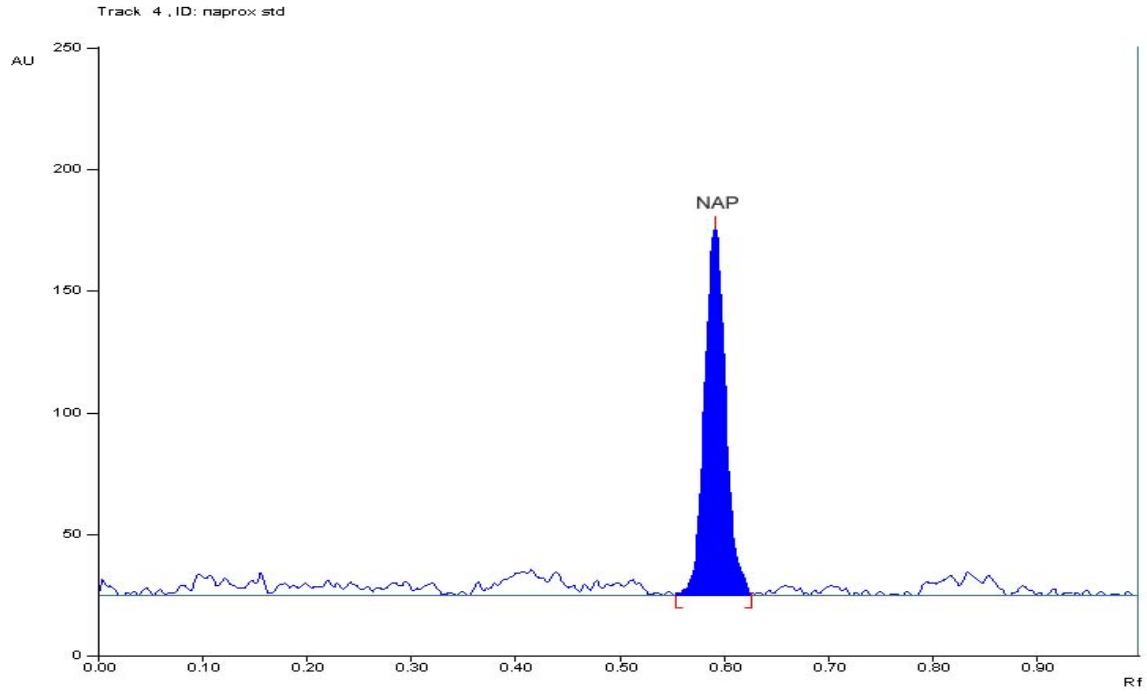

Fig. 1 Densitogram of Naproxen sodium (200 ng band^{-1}, *R*f = 0.63 ± 0.013)

Table 1. Recovery studies of Naproxen sodium

Drug	Amount taken (ng µL^{-1})	Amount added (ng µL^{-1})	Total amount found (ng µL^{-1})	Recovery[a], %	RSD, %
Naproxen sodium	200	100	297.470	99.15	0.438
	200	200	395.822	98.95	0.652
	200	300	499.204	99.84	0.594

[a]Average of three determinations

Table 2. Robustness Data in Terms of Peak Area

Sample No.	Parameter Varied	RSD, %
1	Volume of mobile phase	0.86
2	Time from application to development (Mins.)	1.35
3	Time from development to scanning (Mins.)	0.89

Conclusion

This validated HPTLC method proved to be simple, less expensive, fast, accurate, precise and robust and can thus be used for routine analysis of naproxen sodium in tablet dosage forms.

Acknowledgements

Authors are thankful to Maxim Pharmaceuticals (Pune, India) for providing gift sample of Naproxen Sodium. The authors are also thankful to Dr. K. G. Bothara, Principal, AISSMS College of Pharmacy for providing necessary facilities.

References

1. Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, and Gilman AG (1996) Goodman and Gilman's The Pharmacological Basis of Therapeutics, 9th Edition, McGraw- Hill INC., New York, p 640.
2. Shimek JL, Rao NG and Khalil SK (1982) An isocratic high- pressure liquid chromatographic determination of naproxen and desmethylnaproxen. J Pharm Sci 71: 4.
3. Dusci LJ and Hackett LP (1979) Determination of some anti-inflammatory drugs in serum by high performance liquid chromatography. J Chromatogr 172: 516.
4. Broquair M, Rovei V and Braithwaite R (1981) Quantitative determination of naproxen in plasma by simple high performance liquid chromatographic method. J Chromatogr 224: 43.
5. Slattery JT and Levy G (1979) Determination of naproxen and its desmethyl metabolite in human plasma by high performance liquid chromatography. Clin Biochem 12:100.
6. Ekpe A, Tong JH and Rodriguez L (2001) High-performance liquid chromatographic method development and validation for the simultaneous quantitation of naproxen sodium and pseudoephedrine hydrochloride impurities. J Chromatogr Sci 39: 81.
7. Dinc E, Ozdemir A, Aksoy H, Ustundag O and Baleanu D (2006) Chemometric determination of naproxen sodium and pseudoephedrine hydrochloride in tablets by HPLC. Chem Pharm Bull 54: 415.
8. Monser L, Darghouth F (2003) Simultaneous determination of naproxen and related compounds by HPLC using porous graphitic carbon column. J Pharm Biomed Anal 32: 1087.
9. Tashtoush B M and Al-Taani B M (2003) HPLC determination of naproxen in plasma. Pharmazie 58: 614.
10. Mikami E, Goto T, Ohno T, Matsumoto H and Nishida M (2000) Simultaneous analysis of naproxen, nabumetone and its major metabolite 6-methoxy-2-naphthylacetic acid in pharmaceuticals and human urine by high-performance liquid chromatography. J. Pharm. Biomed. Anal. 23: 917.
11. Zakeri-Milani P, Barzegar-Jalali M, Tajerzadeh H, Azarmi Y and Valizadeh H (2005) Simultaneous determination of naproxen, ketoprofen and phenol red in samples from rat intestinal permeability studies: HPLC method development and validation. J. Pharm. Biomed. Anal. 39: 624.
12. Runkel R, Chaplin M, Boost G and Segre E (1974) Absorption, distribution,

metabolism and excretion of naproxen in various laboratory animals and human subjects. J Pharm Sci 61: 703.

13. Desager JP, Vanderbist M and Harvengt C (1976) Naproxen plasma levels in volunteers after single-dose administration by oral and rectal routes. J. Clin. Pharmacol. 16: 189.
14. Anttila M (1977) Fluorometric determination of naproxen in serum. J. Pharm. Sci. 66: 433.
15. ICH (1994) Text on validation of analytical procedures, ICH harmonized tripartite Guidelines, adapted 27 Oct 1994.