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Research Article

RP-HPLC METHOD FOR THE ESTIMATION OF NABUMETONE IN BULK AND PHARMACEUTICAL FORMULATIONS

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ABSTRACT

A simple, specific, accurate reverse phase liquid chromatographic method was developed for the determination of Nabumetone in bulk and in tablet dosage forms. A Waters C-18, 5 µm column having 250×4.6 mm i.d., with mobile phase containing acetonitrile: triple distilled water (70:30 v/v) was used. The retention time of Nabumetone was 5.58 min. The linearity for Nabumetone was in the range of 50-150 µg/ml. The recovery was found to be in the range of 99.4-100.3%. The LOD and LOQ were found to be 0.1628 µg/ml and 0.4872 µg/ml, respectively. The proposed method was validated and successfully applied to the estimation of Nabumetone in tablet formulations.

Keywords: Nabumetone, reverse phase liquid chromatography, validation

INTRODUCTION

Nabumetone[1], a non-steroidal anti-inflammatory drug[2] which is chemically 4-(6-methoxy-2-naphthalenyl)-2-butanone[3] is rapidly metabolized in the liver to a major active metabolite, 6-methoxy-2-naphthyl acetic acid.

As found with previous NSAIDs, nabumetone's active metabolite inhibits the cyclooxygenase enzyme preferentially blocks cyclo-oxygenase-2 activity which is indirectly responsible for the production of inflammation and pain during arthritis by way of enhancing the production of endoperoxides and prostaglandins E2 and I2 (prostacyclin). Nabumetone belongs to a new class of NSAID with a low potential for causing gastrointestinal mucosal irritancy and inhibition of platelet function and has little effect on renal prostaglandin secretion and had less of an association with CHF (congestive heartfailure) than other traditional drugs of the class.

There are few papers published reporting analytical methods for nabumetone[4]. Different methods employed HPLC with UV-detection[5] and fluorescence detection[6] were reported. Also methods employed HPLC using photodiode array (PDA) detector and mass spectrometric detection for the determination of Nabumetone and its metabolites[7]. The interactions with β-cyclodextrin were also studied by fluorescence measurements[8]. A novel colorimetric method using 1, 10 phenanthroline was also published[9].

We here present a new method for the determination of Nabumetone in bulk and pharmaceutical dosage forms which utilizes a very cheap solvent system on a Waters ODS C18 analytical column. This type of method leads to better retention, very sharp and symmetrical peak shapes and exhibits a very good selectivity for Nabumetone.

MATERIALS AND METHODS

The liquid chromatographic system of Younglin make containing Variable wavelength programmable UV/Vis detector and Rheodyne injector with 20 µl fixed loop was used. Chromatographic analysis was performed using Autochro 3000 software. A waters C18 column with 250×4.6mm i.d. and 5 µm particle size was used. Acetonitrile, triple distilled water (E. Merck, Mumbai, India) were of LC grade, used for the preparation of mobile phase.

Preparation of mobile phase and stock solution

The Stock solution was prepared by weighing (25 mg) and transferring analytically pure Nabumetone to 25 ml volumetric flask. Volume was made up to the mark with diluent (Acetonitrile and Water 50:50), which gave 1000 µg/ml of the drug. The solution was further diluted with the same diluent to obtain final concentration of 100 µg/ml.

Chromatographic conditions

A reverse phase C18 column equilibrated with mobile phase Acetonitrile: Triple Distilled water (70:30 v/v) was used. Mobile phase flow rate was maintained at 1 ml/min and effluents were monitored at 230 nm. The sample was injected using a 10 µl fixed loop, and the total run time was 10 min.

Calibration curve for Nabumetone

Appropriate aliquots of stock solution were taken in different 10 ml volumetric flasks and diluted up to the mark with mobile phase to obtain final concentrations of 50,60,80,100,120,140,150 µg/ml of Nabumetone, respectively. The solutions were injected using a 10 µl fixed loop system and chromatograms were recorded (Fig 1). Calibration curve was constructed by plotting average peak area versus concentration and regression equation was computed for Nabumetone.

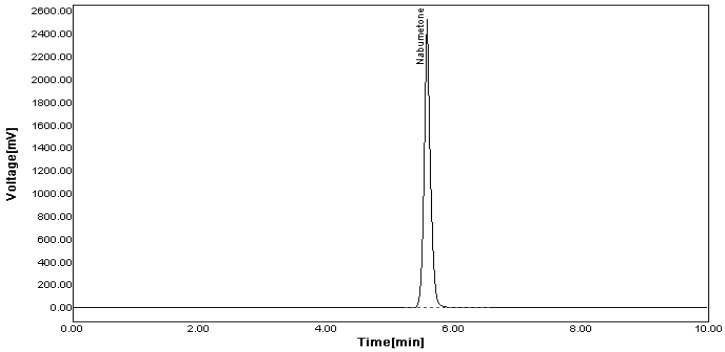

Fig. 1: Chromatogram of Nabumetone (Standard)

Determination of Nabumetone in pharmaceutical formulations

Twenty tablets were weighed and finely powdered. Powder equivalent to 25 mg Nabumetone was accurately weighed and transferred to a 25 ml volumetric flask and 20 ml of Acetonitrile was added to the same. The flask was sonicated for 20 min and volume was made up to the mark with Acetonitrile. The above solution was filtered using Whatman filter paper (No.1). Appropriate volume of the aliquot was transferred to a 25 ml volumetric flask and the volume was made up to the mark with mobile phase to obtain 100 µg/ml of Nabumetone.

The solution was sonicated for 10 min and injected under above chromatographic conditions, the chromatogram was recorded (Fig 2) and the peak area was measured.

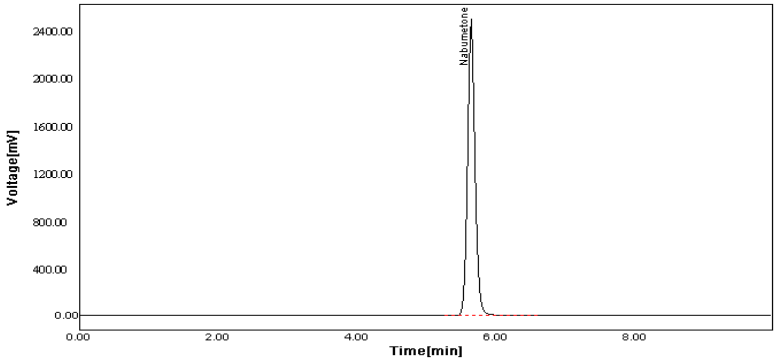

Fig. 2: Chromatogram of Nabumetone (Sample)

Validation

The calibration curve was obtained at 7 concentration levels of Nabumetone standard solutions. The solutions (10 µl) were injected into liquid chromatographic system (n=7) with chromatographic conditions previously given. The linearity was evaluated by least square regression method. The accuracy of the method was determined by calculating recoveries of Nabumetone by method of standard addition. Known amount of drug were added to a pre-quantified sample solution and the amounts were estimated.

The intra-day and inter-day precision study was carried out by estimating the corresponding responses 3 times on the same day and on 3 different days (first, second and third day) for 3 different concentrations of Nabumetone which represents low, medium and high concentrations in the analytical range. The specificity was estimated by spiking commonly used excipient (starch, talc and magnesium stearate) into a pre weighed quantity of drug. The chromatogram was taken by appropriate dilutions and the quantities of drugs were determined. The detection limit is defined as the lowest concentration of an analyte that can reliably be differentiated from background levels. Limit of quantification (LOQ) of an individual analytical procedure is the lowest amount of analyte that can be quantitatively determined with suitable precision and accuracy. Limit of Detection (LOD) was the concentration that yielded signal to noise ratio (S/N) 3:1 and LOQ was the concentration that yielded signal to noise ratio (S/N) 10:1.

RESULTS AND DISCUSSION

Optimization of mobile phase was carried out by taking different proportions of aqueous and organic phases to obtain rapid, simple assay method for Nabumetone with appropriate run time, asymmetric factor and theoretical plates. Mobile phase consisting of Acetonitrile: Triple Distilled Water (70:30v/v) was found to be satisfactory which gave symmetric and sharp peak for Nabumetone at a 1 ml/min flow rate. For quantitative analytical purpose wavelength was set at 230 nm, which provided better reproducibility with minimum interference than the other UV bands. Under the chosen experimental conditions, the liquid chromatogram of Nabumetone showed a single peak of the drug around retention time (Rt) 5.58 min with asymmetry 1.06 .

The calibration curve for Nabumetone was obtained by plotting the peak area versus concentration. It was found to be linear in the range of 50-150 µg/ml. Peak area and concentrations were subjected to least square regression analysis to calculate calibration equation and correlation coefficient. The data of the calibration curve are shown in [Table 1]. The correlation coefficient (r) was found to be 0.999, showing good linearity. Accuracy of the method was examined by performing recovery studies by standard addition method. The recovery of the added standard to the sample was calculated and it was found to be 99.4-100.3%, which indicated good accuracy of the method. Precision studies were carried out at 3 different concentration levels and the results of the intra-day and inter-day studies are reported in terms of RSD [Table 1]. The LOD value was found to be 0.1628 µg/ml which is the concentration that yields signal to noise (S/N) ratio 3:1. The LOQ was 0.4872 µg/ml with S/N ratio of 10:1. [Table 2]

The proposed liquid chromatographic method was applied to the determination of Nabumetone in Tablet formulation A and B. The results obtained were satisfactorily accurate and precise as indicated by the good recovery values [Table 3].

The method was validated and found to be simple, sensitive, accurate and precise. Statistical analysis proved that method was repeatable and selective for the analysis of Nabumetone without any interference from the excipient.

Table 1: Statistical data for linearity and calibration range

Drug	Nabumetone
Concentration range(µg/ml)	50-150
Slope(m)	170.19
Intercept(c)	150
Correlation coefficient	0.9999
% RSD	0.672
Standard error of estimate	39.59

Table 2: System suitability parameters

Validation parameter	Results
Theoretical plates(N)	9862.2
Tailing factor	1.06
Retention time(min)	5.58
Area (%)	98.68
LOD (µg/ml)	0.1628
LOQ (µg/ml)	0.4872

Table 3: Recovery studies

Sample	Labelled claim (mg/tablet)	Amount recovered (mg/tablet) Mean ± S.D	% Recovery*
A	250	247.65 ± 0.58	99.06
B	500	498.75 ± 0.35	99.75

*Average of three determinations at three levels

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REFERENCES

1. The Merck Index, Merck Research laboratories, White house station, NJ, 13th edition, Pg no.6369
2. Gonzalo-Garijo MA, Cordobes-Duran C, Lamilla-Yerga AM, Moreno-Gaston I., "Severe immediate reaction to Nabumetone". *Journal of investigational allergology & clinical immunology,* 2007, 17 (4): 274–276
3. www.Rxlist.com
4. Małgorzata starek and jan krzek, "A review of analytical techniques for determination of oxicams, nimesulide and Nabumetone", *Talanta*, volume 77, issue 3, 15 January 2009, pages 925-94
5. Prafulla kumar sahu, M. Mathrusri annapurna, "Analysis of Nabumetone in bulk and tablet formulation by a new and validated reverse phase high performance liquid chromatography", *e-journal of chemistry*, 2009, 6(s1), s59- s64
6. E. Mikami, T. Goto, T. Ohno, H. Matsumoto and M. Nishida, "Simultaneous analysis of naproxen, Nabumetone and its major metabolite 6-methoxy-2-naphthylacetic acid in pharma-ceuticals and human urine by high-performance liquid chromatography", *Journal of Pharmaceutical and Biomedical Analysis,* Volume 23, Issue 5, October 2000, Pages 917-925
7. Nobilis M, Holcapek M, Kolarova L, Kopeck J, Kunes M., "Identification and determination of phase II Nabumetone metabolites by high-performance liquid chromatography with photodiode array and mass spectrometric detection", *Journal of chromatography*, 2004, vol. 1031, 229-236
8. YS Rao, KPR Chowdary, J.V.L.N Seshagiri Rao, "A colorimetric Assay Method for Nabumetone", *Indian Journal of Pharmaceutical sciences*, 2003 Vol. 65, Issue 2, Page : 206-207.