Development of UV-spectroscopic method for nabumetone in tablet formulation

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ABSTRACT

Nabumetone is a non steroidal anti-inflammatory drug with good analgesic and anti-rheumatic properties. Various methods for analysis of the same are available but are time consuming and expensive. Here we have developed a new, precise and simple UV spectrophotometric method for estimation of nabumetone from bulk and tablet formulation. The drug obeyed the Beer's law and showed the regression line (Y = 0.024 X – 0.003) and correlation coefficient 0.9998. It showed absorption maxima at 261 nm; in methanol. The linearity was observed between 5 – 45 µg/mL. The results of analysis were validated by recovery studies. The % recovery was found to be 99.2 – 100.2%. The method was found to be simple, accurate, precise, economical and robust.

Keywords: Nabumetone, UV–Vis Spectrophotometry, Recovery, Validation

INTRODUCTION

Nabumetone, 4-(6-methoxy-2-naphthyl)-butan-2-one, is a nonsteroidal anti-inflammatory drug (NSAID) of naphtylalkanone class. The drug has proved to be effective in the treatment of rheumatoid arthritis, osteoarthritis and acute soft tissue injuries[1,2]. Nabumetone is a prodrug which undergoes extensive first pass metabolism to 6-methoxy-2-naphthylacetic acid (6-MNA), the major circulating metabolite. 6- MNA is largely responsible for the therapeutic efficacy of nabumetone. It decreases prostaglandin synthesis via inhibition of cyclooxygenase, an enzyme involved in the arachidonic acid conversion pathway[3].

It is official in United States Pharmacopoeia, British Pharmacopoeia. Several analytical techniques like colourimetric[4], liquid chromatography[5,6,7], spectrophotometric[8], high performance liquid chromatography[9,10], micelle-stabilized room temperature phosphorescence[11], flow injection analysis[12] and voltametric[13] have been reported for the determination of nabumetone. However some of these methods are costlier and time consuming. To overcome these difficulties spectrophotometric analysis serves to be the quickest, promising and reliable method for routine analytical needs.

The aim of the present study is to develop a new simple, rapid, reliable and precise UV

spectrophotometric method for analysis of nabumetone from tablet formulation; method is based on measurement of UV absorbance of nabumetone in methanol.

MATERIALS AND METHODS:

Instrument Used

A. Perkin Elmer UV-Vis Spectrophotometer Model Lambda 25 with,
  a. Software: UV Winlab 5.2.0

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  b. Spectral bandwidth of 1 nm
  c. Matched quartz cell 1cm
B. Bath Sonicator
C. Shimadzu Analytical balance Model AUX – 220

Reagents and Solution:

All the reagents used in this assay were of analytical grade. Nabumetone pure drug was obtained as a gift sample from Sekhsaria Chemicals Limited, Thane, Mumbai. Tablets of nabumetone were purchased from local market for analysis.

EXPERIMENTAL:

Determination of ?max:

Weighed amount of nabumetone was dissolved in methanol to obtain a 100µg/mL stock solution. Absorption maxima was studied by diluting the above solution to 20µg/mL and scanned from 200 – 400nm.

Standard Stock Solution:

A stock solution containing 1000 µg/mL of pure drug was prepared by dissolving 50mg of nabumetone in sufficient methanol to produce 50 mL solution in a volumetric flask.

Linearity and Calibration:

The aliquots standard stock solution was diluted serially with sufficient methanol to obtain the concentration range of 5 – 45 µg/mL. A calibration curve for nabumetone was obtained by measuring the absorbance at the λmax of 261 nm. Statistical parameters like the slope, intercept, coefficient of correlation, Beer's law limit, Molar Absorptivity, Sandell's sensitivity were determined.

Assay:

Twenty tablets of abumetone were weighed; average weight was determined and powered in glass mortar. Amount equivalent to 50 mg of abumetone was transferred to 50mL volumetric flask, dissolved in sufficient quantity of methanol, sonicated and made up the volume with methanol to obtain concentration of 1000 µg/mL. This solution was then filtered through Whatmann filter paper no. 41. From this filtrate, 0.25mL withdrawn and transferred to 10 mL volumetric flask, volume was adjusted to the mark and absorbance was recorded against
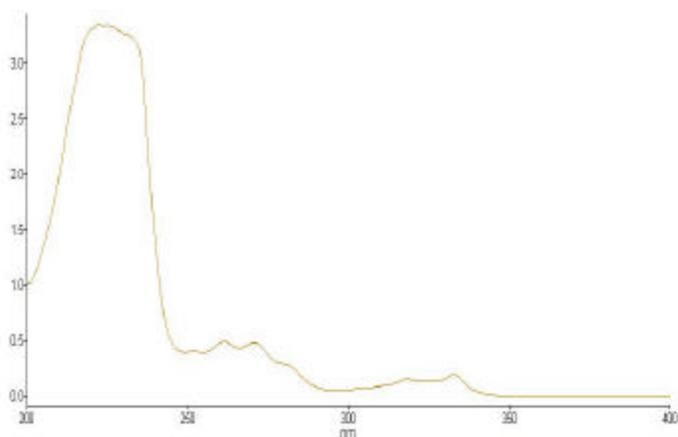
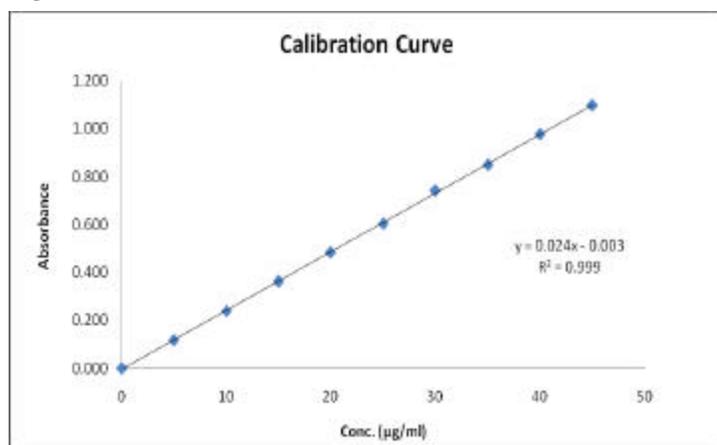**Figure1. Scan of Nabumetone in methanol**

Figure 2. Calibration Curve of Nabumetone at 261 nm

Table 1: Optical Characteristics and Regression Equation for Nabumetone

Parameter	Value
? max (nm)	261
Beer's range (µg/mL)	5 – 45
Regression equation	Y = 0.024x – 0.003
Intercept (a)	0.003
Slope (b)	0.024
Correlation coefficient (r^2)	0.9998
Molar Absorptivity (lit/mole/cm)	5615.348
Sandell's sensitivity (µg/sq.cm/0.001)	0.040656
L.O.D.(µg/mL)	0.210
L.O.Q. (µg/mL)	0.636

Table 2: Assay of Nabumetone Tablets 500mg

Formulation	Label Claim*	% Claim found	% R.S.D
F-I	500 mg	99.7 ± 0.38	0.38
F-II	500 mg	100.1 ± 0.42	0.42

Mean of five observations

Table 3: Results of Recovery study for Nabumetone Tablets 500mg

Labelled amount (mg)	Amount of drug added (%)	Amount of drug recovered* (mg)	Percentage recovery	% relative stand. devi.
500	80	400.8	100.2 ± 0.22	0.22
500	100	499.6	99.9 ± 0.19	0.19
500	120	601.0	100.2 ± 0.18	0.18

Mean of three observations

Table 4: Results of repeatability studies

Label Claim	Amount taken* [µg/mL]	Amount found[%]	%R.S.D
500 mg	25	99.9 ± 0.34	0.34

Mean of six observations

Table 5: Intra-day and Inter-day precision for 500mg

Sr.. No	Concentration (µg/mL)	Intra-day*%R.S.D		Inter-day*	%R.S.D
1	20	19.97 ± 0.02	0.31	19.87 ± 0.03	0.41
2	25	25.02 ± 0.07	0.62	24.01 ± 0.09	0.80
3	30	30.08 ± 0.23	1.45	29.81 ± 0.21	1.35

Mean of three observations

Table 6: Results of Ruggedness study

Label Claim	Analyst I Amt. found* (%)	%RSD	Analyst II Amt. found* (%)	%RSD
500mg	99.48 ± 0.62	0.65	99.46 ± 0.73	0.74

methanol as a blank at 261nm (Table 2)

Accuracy:

To assess the accuracy of the proposed method, recovery studies were carried out three different levels i.e. 80%, 100% and 120%. To the pre-analyzed sample solution a known amount standard drug solution was added at three different levels, absorbance was recorded. The % recovery was then calculated as % Recovery = [(A – B) / C] x 100, Where A is total amount of drug estimated; B is amount of drug found on preanalyzed basis; C is amount of pure drug added to formulation (Table 3)

Precision:

Precision of the method is studied as repeatability, intra-day and inter-day precision. Repeatability was determined by analyzing abumetone (25µg/mL) for six times (Table 4). Intra-day precision was determined by analyzing the 15, 20 and 25µg/mL of nabumetone for three t imes in the same day. Inter-day precision was determined by analyzing the same concentration of the solutions daily for three days (Table 5). In intermediate precision study, % R.S.D. values were not more than 1.0 % in all the cases.

Ruggedness:

Ruggedness of the proposed method is determined by analysis of aliquots from homogenous slot by two analyst using same operational and environmental conditions (Table 6)

Limit of detection and Limit of quantitation:

Limit of detection (LOD) and Limit of quantitation (LOQ) were determined by using the formula based on the standard deviation of the response and the slope. Limit of detection (LOD) and Limit of quantitation (LOQ) were calculated by using the equations LOD = 3 × s/S and LOQ = 10 × s/S, where s is standard deviation of intercept, S is the slope of the line. (Table 1)

RESULTS AND DISCUSSION:

A simple, rapid sensitive and accurate UV-Spectrophotometric method has been developed for estimation of Nabumetone in bulk and pharmaceutical formulation. In methanol, nabumetone showed absorbance maxima at 261nm. Linearity was observed in the concentration range 5-45 µg/mL with correlation coefficient value 0.9998. The value of correlation coefficient (r^2) greater than 0.999 indicating good linearity response in entire range. The proposed

method was applied to pharmaceutical formulation and Percent amount of drug estimated was found in good agreement with the label claim. The recovery experiment was carried out at three different levels i.e., 80 %, 100 % and 120 %. The percentage recovery was found to be in the range 99.9 – 100.2%; the low values of % R.S.D. are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intra-day and inter-day and repeatability. Ruggedness of the proposed method was studied with the help of two analysts. Repeatability of the samples also carried out which show low values of % R.S.D. The Limits of Detection and Quantitation for abumetone with a lower concentration were 0.210 and 0.636µg/mL respectively, values which are under the lowest expected concentrations in the sample.

CONCLUSION:

The present study was undertaken with an objective of developing simple, sensitive and reliable analytical method like UV-Visible spectrophotometry for estimation of nabumetone in tablet dosage form. The method has sufficiently good accuracy, precision and permitted as a cost effective as other methods. The analytical method is simple, sensitive, rapid and specific. Further it can be conveniently employed for the routine analysis and the quality control of nabumetone in tablet formulation.

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