WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 8, 1357-1365. Research Article ISSN 2277– 7105

DEVELOPMENT, VALIDATION AND STABILITY STUDY OF UV SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF NABUMETONE IN BULK AND PHARMACEUTICAL DOSAGE FORMS

Poulkar Madhuri*

Department of Quality Assurance, Channabasweshwar Pharmacy College, Latur (MS), India-413512.

Article Received on
24 May 2020,

Revised on 15 June 2020,
Accepted on 05 July 2020,

DOI: 10.20959/wjpr20208-17970

***Corresponding Author**
Poulkar Madhuri
Department of Quality Assurance, Channabasweshwar Pharmacy College, Latur (MS), India-413512.

ABSTRACT

A simple, specific and economic UV spectrophotometric method has been developed using as a solvent methanol: water (80:20) to determine the Nabumetone content in bulk and pharmaceutical dosage formulations. The quantitative determination of the drug has been carried out at a predetermined λ_{max} of 270nm, it was proved linear in the range 2-12 µg/mL and exhibited good correlation coefficient (R^2=0.997) and excellent mean recovery (98-100.09%). The method was validated statically and by recovery studies for linearity, precision, repeatability and reproducibility as per ICH guideline. The obtained results proved that the method can be employed for the routine analysis of Nabumetone in bulk as well as in the commercial formulations.

KEYWORDS: Nabumetone, UV Spectroscopy, Validation, Stress Studies.

INTRODUCTION

Nabumetone, 4-(6-methoxy-2-naphthyl)-butan-2-one,(fig 1) 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.

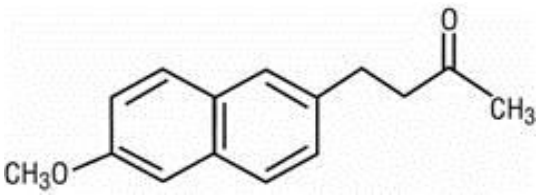


Fig 1: Chemical structure of Nabumetone.

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] [14] 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: water (80:20).

1. MATERIALS AND METHODS

1.1 Equipment

A Shimadzu UV–visible spectrophotometer (UV1800, Shimadzu Corporation, Kyoto, Japan) was used for all absorbance measurements with matched quartz cells.

1.2 Materials

All chemicals and reagents were of analytical grade. Nabumetone in the form of powder with certificate of analysis was provided by Arch Pharmalab Limited, Dombivli (East)Thane.

1.3 Determination of wavelength of maximum absorption

A standard stock solution of Nabumetone (100µg/mL) was prepared using diluents to further obtain 10µg/mL. An UV spectroscopic scanning (200-400 nm) was carried out with final diluted solution to determine λ_{max} for the detection of Nabumetone using diluents as a blank.

1.4 Linearity and Range

For linearity study, six solutions at different concentrations (2, 4, 6, 8, 10 and 12 mg/mL) were prepared using six different aliquots of stock solution, and the obtained data were used for the linearity calibration plot. Limit of detection (LOD) and limit of quantification (LOQ) for the assay were also calculated.

1.5 Intra-day precision (repeatability) and inter-day precision study (intermediate precision)

Nabumetone sample stock solution of 10mg/mL was prepared following the same dilution pattern of stock solution. Three different aliquots of stock solution were then diluted to 10 mL to obtain the concentrations of 4, 6 and 8 mg/mL. This procedure was repeated in the following days.

1.6 Stability study

Samples prepared for repeatability study were preserved for 24 h at room temperature and analyzed on the following day to test for short-term stability.

1.7 Accuracy/recovery study

This study was carried out using pre-formulated granules containing pure Nabumetone and common excipients. Calculation was done from the label claim and the average weight of the final product. Previously used dilution pattern was followed for the granules to obtain three concentrations-80%, 100% and 120% of reference solution.

1.8 Specificity in the presence of excipients

The test for the specificity was carried out using only excipients. Spectra for placebo granules, blank, and sample were compared. Secondly the specificity was determined by subjecting the sample solution to accelerated degradation by heat (60°C) for 48 h in order to verify that none of the degradation products interfered with the quantification of the drug.

1.9 Assay of content of Nabumetone in selected marketed brands

Market brands of Nabumetone tablet from different manufacturers were randomly selected and analyzed using the newly developed and validated method. Sample solutions of each brand (10 mg/mL) were also prepared and assayed for content of Nabumetone against the standard. The content of Nabumetone in the marketed brands was determined using standard calculations.

Stress degradation studies

i. Photolytic Degradation

Specific amount of drug Nabumetone was weighed accurately & putted into the UV chamber for three days. After three days 10mg drug was weighed and made stock solution (100µg/mL) with diluents. Then an appropriate concentration (10µg/mL) was prepared & absorbance was measured in UV spectrophotometer.

ii. Thermal Degradation

Drug was taken in a Petri dish which was previously cleaned & dried then was put it into the oven for 48 hrs then it was taken out & weighed 10mg drug was weighed and made stock solution (100µg/mL) with diluents. Then an appropriate concentration (10µg/mL) was prepared & absorbance was measured in UV spectrophotometer.

iii. Acid Degradation

0.01N HCl was taken in a 10 ml volumetric flask then accurately weighed 10mg drug Nabumetone was dissolved in it. Then the solution was refluxed for 4 hrs then from this solution an appropriate concentration (10µg/mL) was prepared using diluents & absorbance was measured in UV spectrophotometer.

iv. Alkali Degradation

0.01N NaOH was taken in a 10 ml volumetric flask then accurately weighed 10mg drug Nabumetone was dissolved in it. Then the solution was refluxed for 4 hrs then from this solution an appropriate concentration (10µg/mL) was prepared using diluents & absorbance was measured in UV spectrophotometer.

v. Oxidation with H_2O_2

3% H_2O_2 solution was taken in a 10 ml volumetric flask then accurately weighed 10mg drug Nabumetone was dissolved in it. Then the solution was kept in dark for 4 hrs then from this solution an appropriate concentration (10µg/mL) was prepared using diluents & absorbance was measured in UV spectrophotometer.

2. RESULTS AND DISCUSSION

2.1 Method development and optimization

Nabumetone is almost insoluble in aqueous medium and freely soluble in organic solvents like methanol. During the development phase, the use of methanol with water as the diluent

resulted in preferable outcome in UV analysis. The solvent composition was optimized to Methanol (80) and water (20). The pre-determined wavelength of maximum absorption (λ_{max}) was 270 nm. (Fig. 2).

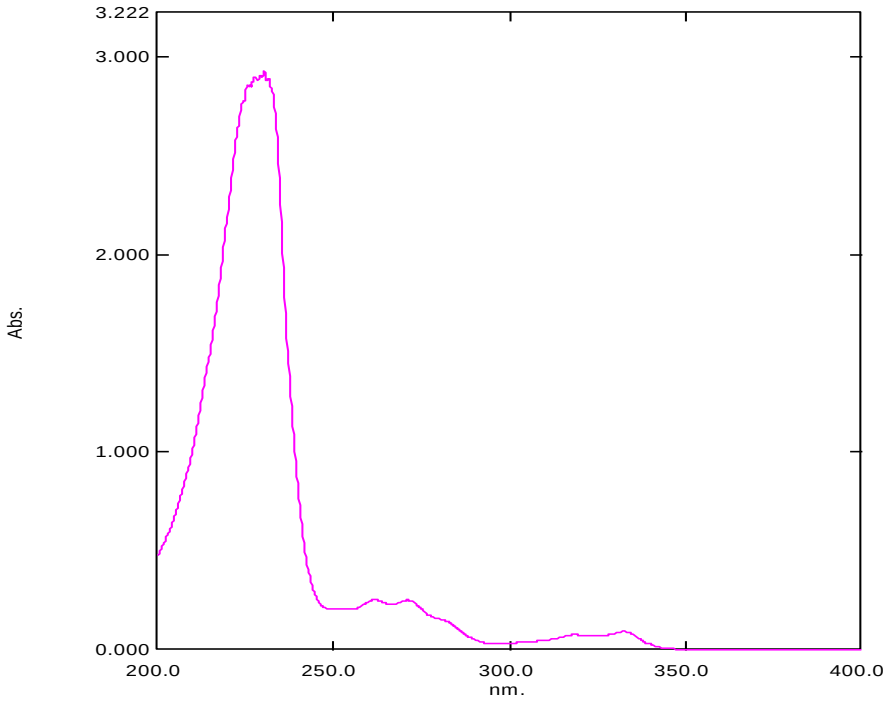


Figure 2: UV Spectrum of Nabumetone.

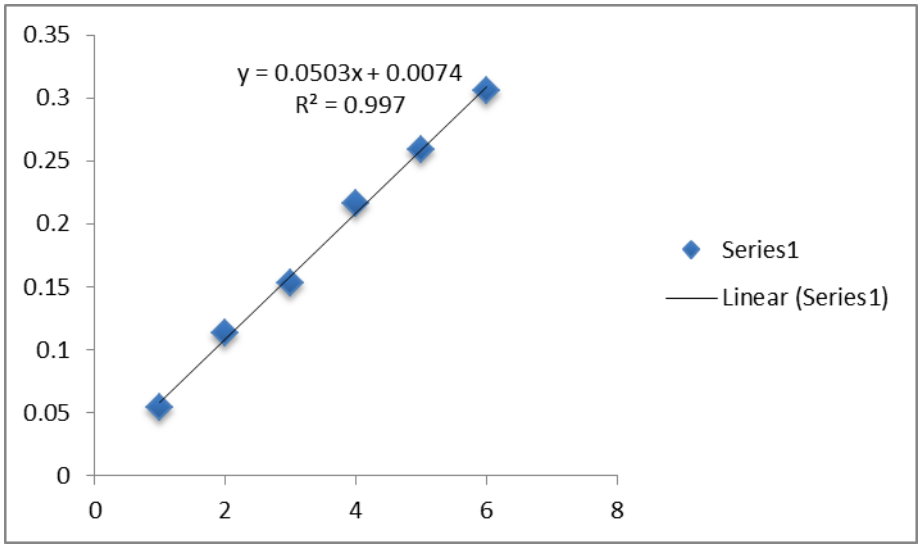
2.2 Method validation

2.2.1 Linearity and range

The calibration curve obtained was evaluated by its correlation coefficient. The absorbance of the samples in the range of 2.0–12.0µg/mL was linear with a correlation coefficient (R^2) greater than 0.997 (Table 1). The LOD and LOQ were calculated as 0.3788 mg/mL and 1.1479 mg/mL respectively.

Table 1: Linearity data.

Concentration µg/ml	Absorbance
2	0.054
4	0.113
6	0.153
8	0.216
10	0.259
12	0.306



Calibration Curve of Nabumetone

2.2.2 Intra-day and inter-day precision

The intra-day and inter-day precision study (Table 2) of the developed method confirmed adequate sample stability and method reliability where all the RSDs were below 2%.

Table 2: Intra-day and inter-day precision determined for three different concentrations of Nabumetone (n=3).

Concentration (µg/ml)	Intra-day precision		Inter-day precision	
	Absorbance mean	%RSD	Absorbance mean	%RSD
4	0.118	0.75798	0.115	1.050233
8	0.220	0.468034	0.221	0.609241
12	0.316	0.519168	0.309	1.272053

2.2.3 Stability

Stability study's results were within the acceptance range (Table 3) and indicated the samples stability over 24 h (short-term).

Table 3: Short term stability determined by the proposed method (n=3).

Concentration declared µg/mL	Concentration found µg/mL	RSD (%)	Average potency (%)
4	0.118	0.75798	98.39
8	0.220	0.468034	98.86
12	0.316	0.519168	98.56

2.2.4 Accuracy/Recovery

Results within the range of 98.00–100.97% ensure an accurate method (Table 4) as well as indicate non-interference with the excipients of formulation.

Table 4: Accuracy/Recovery for three different concentrations of Nabumetone by the proposed method.

Dosage form	Label Claim	Amount added	Recovery (%)
Pre-formulated granules	500mg	80	99.01
		100	99.25
		120	99.69

2.2.5 Specificity in the presence of excipients

The specificity of the analytical method was proved by comparing the spectra of placebo and degradation product of sample solution with that of accuracy sample (Fig. 3).

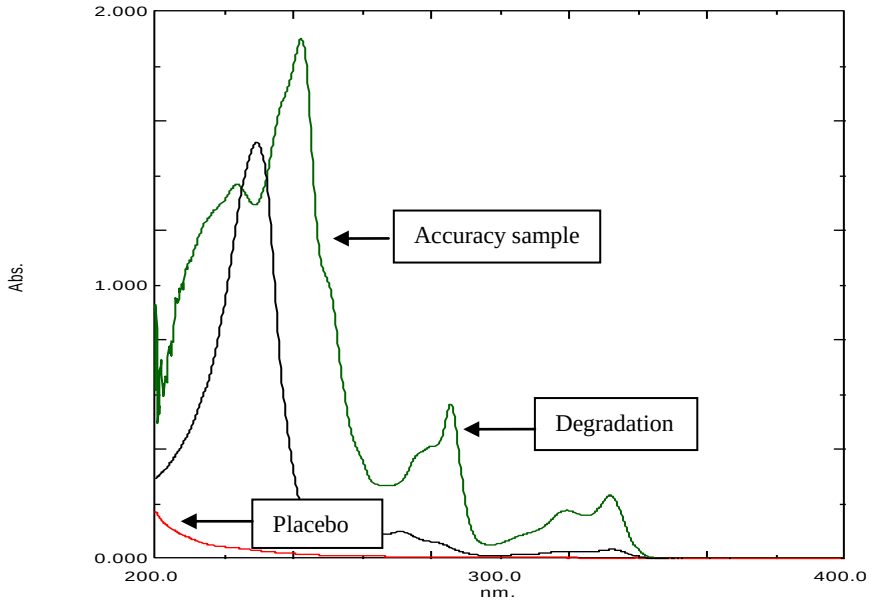


Figure 3: Specificity of the method determined by comparing the spectra of accuracy sample, placebo and degradation products

2.2.6 Stress degradation studies

The study conducted (Table 5) shows that there is degradation of drug under the stress conditions like photolytic, alkali & oxidation.

Table 5: Summary of stress degradation results.

Stress condition	Degradation %	Remark
Photolytic	42	Unstable
Thermal	11	Stable
0.01N HCl	19	Unstable
0.01N NaOH	89	Stable
H_2O_2	69	Unstable

2.2.7 Content of Nabumetone in marketed brands

Nabumetone content of three marketed products determined by the proposed method (Table 6) was in good agreement with the label claims and was in the range of 98.45–100.50% with the RSD values of 0.107–0.140% respectively.

Table 6: Content of Nabumetone in marketed products.

Labelled amount (mg)	Amount found	Potency	RSD (%)
500	497.9	100.5	0.23
500	498.5	99.8	0.19
500	496.8	99.9	0.17

3. CONCLUSION

The results and the statistical parameters demonstrate that the proposed UV spectrophotometric method is simple, rapid, specific, accurate and precise. Therefore, this method can be used for the determination of Nabumetone either in bulk or in the dosage formulations without interference with commonly used excipients and related substances.

ACKNOWLEDGMENT

Authors wish to thank Arch Pharma lab Limited, Dombivli (East) Thane for providing drug sample and also thank Principal Dr. Sanjay Thonte, Channabasweshwar Pharmacy College, Latur for providing facilities at college.

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