Original Article

First-order derivative spectrophotometric estimation of nabumetone and paracetamol in tablet dosage form

Abstract

Aim: To develop and validate a simple, precise and accurate spectrophotometric method for the simultaneous estimation of nabumetone and paracetamol in their combined tablet dosage form. This method is based on first-order derivative spectroscopy. **Materials and Methods:** For determination of sampling wavelengths, each of nabumetone and paracetamol were scanned in the wavelength range of 200–400 nm in the spectrum mode and sampling wavelengths were selected at 261 nm (zero crossing of nabumetone) where paracetamol showed considerable absorbance and at 248.2 nm (zero crossing of paracetamol) where nabumetone showed considerable absorbance. **Results:** Beer's law obeyed in the concentration range of 3-18 μg/ml for both the drugs. The correlation coefficients were found to be 0.9992 and 0.9998 for nabumetone and paracetamol, respectively. Mean recoveries were found satisfactory. **Conclusion:** The proposed method can be successfully applied for simultaneous estimation of nabumetone and paracetomol.

Key words: First-order derivative spectroscopy, nabumetone, paracetamol, spectrophotometric

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INTRODUCTION

Nabumetone (NBM) is frequently prescribed as a nonsteroidal anti-inflammatory drug for the symptomatic treatment of rheumatic and inflammatory conditions.[1,2] NBM is chemically known as 4-(6-methoxy-2-naphthyl)-butan-2-one. It is official in *United States Pharmacopoeia* and *British Pharmacopoeia*. Paracetamol (PRCM) [Figure 1] is official in *Indian Pharmacopoeia*, and it is chemically *N*-(4-hydroxyphenyl) acetamide and is an analgesic and antipyretic drug. The derivative spectrophotometric method is one of the advanced modern spectrophotometric techniques that offer a useful means for extracting both qualitative and quantitative information from the spectra composed of overlapped bands. It is based on using the first- or higher-order derivatives of absorbance with respect to wavelength from parent zero-order ones. Because derivatization can lead to the separation of unresolved signals and reduction of spectral background interferences, this technique permits the quantification of one analyte in the presence of others without initial separation or purification. The application of derivative spectrophotometry in pharmaceutical analysis has been critically reviewed.[3-5] Literature survey reveals that NBM can be estimated spectrometrically, [6] voltametrically,[7] and by high-performance liquid chromatography.[8] However, there is no analytical method reported for the estimation of NBM and PRCM in their combined tablet dosage form. The present work described the first-order derivative spectrophotometric method for the estimation of NBM and PRCM in tablet formulation.

MATERIALS AND METHODS

Instrumentation

Shimadzu UV-2450 double-beam spectrophotometer with 1-cm path length, supported by Shimadzu UV-Probe software, version 2.21, was used for all spectrophotometric estimations. Shimadzu balance (AUW-120D) was used for all weightings. Ultrasonicator was used for the sonication of all analytical solutions.

Materials

NBM and PRCM were supplied by IPCA Laboratories Pvt. Ltd., Ratlam, Gujarat, India. Formulation of NBM and PRCM in their combined tablet dosage form was purchased from the local market. Methanol (AR grade) was purchased from Fischer Scientific (India). Tablets NILITIS -P containing 500 mg of NBM and 500 mg of PRCM of IPCA Laboratories Pvt. Ltd. were procured from the local market.

Standard stock solution

A standard stock solution (1.0 mg/ml) each of NBM and PRCM was separately prepared by dissolving in methanol, and these stock solutions were further diluted to get a concentration of 200 µg/ml. These solutions were used as working standard stock solutions for further analysis.

Preparation of tablet sample solution

Twenty tablets were weighed accurately and powdered. A powder equivalent of 12 mg of NBM (containing 12 mg of PRCM) was weighed and transferred to a 100-ml volumetric flask. Then it was dissolved in 25 ml of methanol by shaking the flask for 15 min, and the volume was made up to the mark with methanol. The solution was filtered through Whatman filter paper no. 41. A 1.0 ml aliquot of the sample stock solution was transferred to a 10-ml standard volumetric flask, and the volume was made up to the mark with methanol. The sample solution of the final concentration of 12 µg/ml of NBM (containing 12 µg/ml of PRCM) was analyzed by the first-order derivative spectroscopic method, and absorbance was measured at 261 and 248.2 nm. The procedure was repeated six times for sample analysis.

Recovery

A recovery study was carried out by the addition of known amount of the standard drug in the preanalysed tablet formulation in 80, 100, and 120% of the label claim. At each level of amount, three determinations were performed.

RESULT AND DISCUSSION

Selection of analytical wavelengths

From appropriate dilutions of the working standard stock solution, 12 µg/ml of NBM and 12 µg/ml of PRCM were separately prepared and scanned in the UV range 200–400 nm. The overlain zero-order absorption spectra of NBM and PRCM were obtained [Figure 2]. These absorption spectra were converted to first-order derivative spectra by using the instrument mode. After observing the overlain first-order derivative spectra with scaling factor = 4 and $\Delta\lambda$ = 4 for NBM and PRCM [Figure 3], zero crossing points of drugs were selected for the analysis of other drugs. The first wavelength selected was 261 nm (zero crossing of NBM), where PRCM showed considerable absorbance. The second wavelength selected was 248.2 nm (zero crossing of PRCM), where NBM showed considerable absorbance.

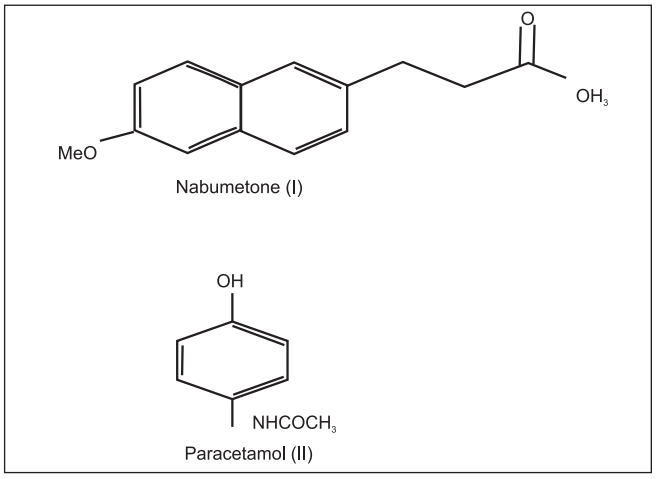

Figure 1: Structure of nabumetone and paracetamol

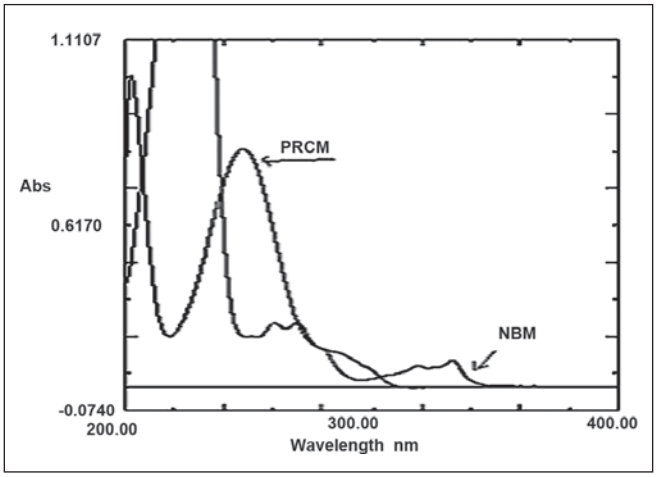

Figure 2: Overlain zero-order absorption spectra of 12 µg/ml nabumetone and 12 µg/ml paracetamol in methanol

Calibration curves

For each drug, linearity was observed by diluting appropriate aliquots of the working standard stock solution 0.15, 0.3, 0.45, 0.6, 0.75, and 0.9 ml into a series of 10-ml volumetric flasks with methanol to get a final concentration range of 3–18 µg/ml separately for both NBM and PRCM. The samples were scanned in the wavelength range 200400 nm, and the first-order derivative of the spectrum was taken. The dA/dλ of each of these solutions was measured at the selected wavelength and plotted against concentration to obtain the calibration graph. The statistical parameters of the calibration curve, such as correlation coefficient, regression equation, limit of detection, and limit of quantitation, for NBM and PRCM are given in Table 1.

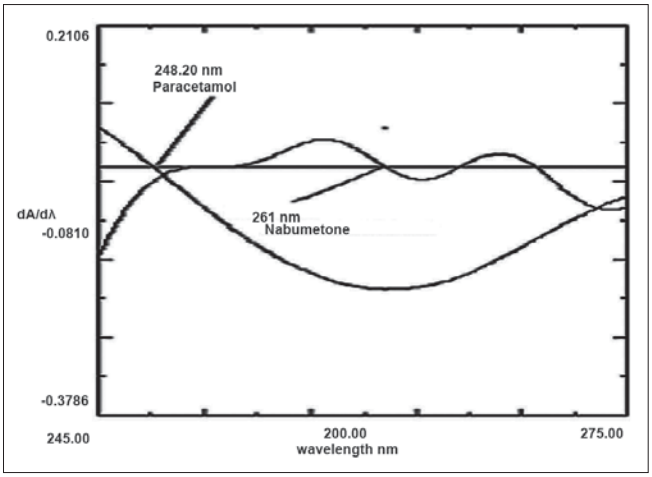

Figure 3: Overlain first-order derivative spectra of 12 µg/ml nabumetone and 12 µg/ml paracetamol in methanol

Table 1: Optical characteristics of the proposed method (first-order derivative method)

Parameters	Nabumetone	Paracetamol
Wavelength selected (nm)	248.20	261.00
Linearity range (µg/ml)	6–18	6–18
Regression equation ($y = mx + c$)		
Slope (m)	−0.00153	−0.01538
Intercept (c)	−0.00204	0.00064
Correlation coefficient	0.9992	0.9998
DL (µg/ml)	0.56	0.04
QL (µg/ml)	1.3	0.12

Analysis of tablet formulation

Twenty tablets were weighed accurately and powdered. A powder equivalent of 12 mg of NBM (containing 12 mg of PRCM) was weighed and transferred to a 100-ml volumetric flask. Then it was dissolved in 25 ml of methanol by shaking the flask for 15 min, and the volume was made up to the mark with methanol. The solution was filtered through Whatman filter paper no. 41. A 1.0 ml aliquot of the sample stock solution was transferred to a 10-ml standard volumetric flask, and the volume was made up to the mark with methanol. The sample solution of the final concentration of 12 µg/ml of NBM (containing 12 µg/ml of PRCM) was analyzed by the first-order derivative spectroscopic method, and absorbance was measured at 261 and 248.2 nm. The procedure was repeated six times for sample analysis. The concentrations of NBM and PRCM were calculated from the calibration graph. The results of analysis are given in Table 2.

Method Validation

Accuracy

The accuracy of the proposed method was determined by performing recovery study at 80, 100, and 120% level for NBM and PRCM. The recovery study was done by adding pure drug solution to the preanalyzed tablet formulation, and concentrations of NBM and PRCM were determined by using the calibration graph. The values of percent relative standard deviation and recovery studies were showing satisfactory accuracy. The results of the recovery study are shown in Table 3.

Precision

The precision of an analytical method was expressed as

Table 2: Results of commercial formulation analysis ($n = 3$)

Parameters	Drug	
	Nabumetone	Paracetamol
Label claim (mg per tablet)	500	500
Drug content % (±SD)	99.7 ± 1.2	98.84 ± 1.004
% RSD	1.203	1.01
Standard error	0.699	0.5796

Table 3: Result of recovery of nabumetone and paracetamol by first-order derivative method

Method/precision	% level of recovery	Taken µg/ml		% Mean*		% RSD		SEM	
		NA	PARA	NA	PARA	NA	PARA	NA	PARA
First-order derivative	80	8	8	101.4	101.2	1.10	0.249	0.649	0.146
	100	10	10	101.5	103.2	1.19	0.130	0.699	0.0776
	120	12	12	102.4	101.9	0.73	0.126	0.433	0.0745
Intraday	–	12	12	105	101.5	0.693	1.15	0.400	0.676
Inter-day	–	12	12	99.91	101.1	1.02	0.683	0.593	0.398

* = 3

the percent relative standard deviation and standard error of mean of the series of measurements. It was ascertained by the replicate estimation of standard drugs. It involves intraday and interday precision. For intraday precision, three replicates of the solutions containing 12 µg/ml of NBM and 12 µg/ml of PRCM were carried out three times on the same day, and for interday precision, three replicates of the solutions were carried out for the three consecutive days at the same concentration level. Results are summarized in Table 3.

Limit of detection and limit of quantitation

The detection limit (DL) and the quantitation limit (QL) were calculated on the basis of the standard deviation of the *y*-intercept and slope: DL = 3.3 σ/S and QL = 10 σ/S, where σ is the standard deviation of the response and *S* is the slope of the calibration curve of analyte. The DL and QL values 0.56 and 1.3 for NBM and 0.04 and 0.12 for PRCM showed good precision for the proposed method.

One-way analysis of variance test

One-way analysis of variance test was performed for the percent mean of intraday and interday precision of NBM and PRCM. The calculated *P* value was found to be 0.383 and 0.816 for NBM and PRCM, respectively, which is greater than the theoretical *P* value ($P > .05$). It shows that there is no statistically significant difference between the intraday and interday precision of NBM and PRCM.

CONCLUSION

The developed first-order derivative spectroscopic method proved to be simpler in procedure and produced more accurate results. Hence, the method is effective for the routine analysis of NBM and PRCM in bulk and tablet dosage form.

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