Original Article

UV-visible spectrophotometric simultaneous estimation of paracetamol and nabumetone by AUC method in combined tablet dosage form

Abstract

Introduction: The present study deals with development and validation of a simple, rapid, sensitive and economic area under curve method for simultaneous estimation of paracetamol and nabumetone in bulk and tablet dosage form. **Materials and Method:** Area under curve method includes determination of area of paracetamol and nabumetone at absorption maxima, which for paracetamol was 248.8 ± 10 nm and for nabumetone was 269.2 ± 10 nm. Beer's law was obeyed in the concentration range of 5–25 μg/mL for both paracetamol and nabumetone. Correlation coefficient was found to be 0.9983 and 0.9993 for paracetamol and nabumetone, respectively for area under curve method. **Results:** The analysis were validated statistically and by performing recovery studies. The mean percent recoveries were found satisfactory for the proposed method. The percentage recovery was found to be 101.67–102.43% for paracetamol and 96.69–98.49% for nabumetone. **Conclusion:** The proposed AUC method used for the simultaneous estimation of PARA and NAB in bulk and tablet dosage formrespectively.

Key words: Area under curve, nabumetone, paracetamol, UV spectrophotometric

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INTRODUCTION

Paracetamol (PARA) is chemically N-(4 hydroxyphenyl) acetamide.[1,2] It is used mainly as an analgesic and antipyretic. It is official in the Indian Pharmacopeia[3] [Figure 1]. Nabumetone (NAB) is chemically 4-(6-methoxynaphthalen-2-yl) butan-2-one. It is a nonsteroidal anti-inflammatory drug. It is used in the treatment of rheumatoid arthritis and osteoarthritis. It is official in the United States Pharmacopoeia.[4] Several methods are reported for the individual estimation of PARA and NAB.[5-7] For PARA, other methods are reported like spectrophotometrically,[8] High Performance Liquid Chromatography with UV detector (HPLC-UV)[9] individually and in combination with other drugs. Literature survey also reveals methods like spectrophotometrically,[10] Liquid Chromatography Mass Spectrometry (LC–MS/MS),[11] and HPLC[12] for estimation of nabumetone individually and in combination with other drugs. No ultraviolet (UV) spectrophotometric method is reported for the simultaneous estimation of PARA and NAB area under curve method (AUC). This paper describes the development and validation of a method to simultaneously quantify PARA and NAB by AUC in bulk and tablet dosage form.

MATERIALS AND METHODS

Instrumentation
Shimadzu UV-2450(Toshvin Analytical Instruments, Japan) double beam spectrophotometer with 1-cm path length, supported by Shimadzu UV-Probe software, version 2.21, Japan, was used for all spectrophotometric estimations.
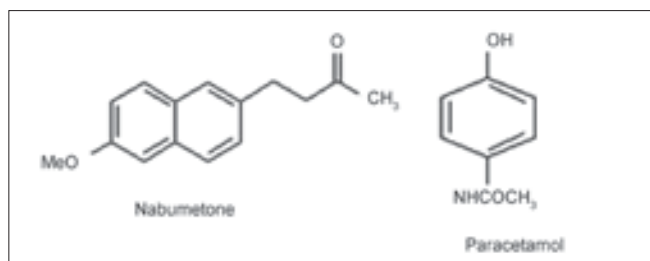
Figure 1: Structures of paracetamol and nabumetone

Figure 2: Ultraviolet spectra of paracetamol and nabumetone for area under curve method

Analytical balance (Shimadzu AUW-120D, Japan) was used for all weightings.

Reagents and chemicals
Active pharmaceutical ingredient of PARA was obtained from Kirti Pharmachem, Sinnar, Nashik, India, and NAB was obtained from IPCA Labs Ltd., Daman, Gujarat, India. Methanol HPLC grade was obtained from Fisher Scientific, India Marketed formulation (tablet NILTIS-P manufactured by, Ipca laboratories Ltd., India), containing 500 mg of paracetamol and 500 mg of nabumetone were used for the study.

Solution preparation
Standard stock solution
Accurately weighed 20 mg PARA and NAB were separately dissolved in sufficient quantity of methanol and further diluted with methanol to give concentration of 200 µg/mL respectively. These solutions were used as standard stock solution for the further analysis.

Working standard stock solution
From this, aliquot solution was pipetted out and further diluted with methanol to obtain working standard stock solution of 100 µg/mL.

Selection of analytical wavelength
Working standard stock solutions of both the drugs were diluted to obtain final concentration each containing 10 mg/mL of PARA and 10 mg/mL of NAB, respectively. Solutions were scanned in the wavelength range of 200 – 400 nm. The wavelengths selected should be such that at each wavelength the absorptivity difference between the two components should be as large as possible. Hence, the λ_{max} of both drugs was selected for the proposed method. PARA shows maximum absorption at wavelength (λ_{max}) 248.8 nm whereas NAB shows maximum absorption at wavelength (λ_{max}) 269.2 nm. The range 248.8 ± 10 nm for PARA and 269.2 ± 10 nm for NAB was selected for the AUC method [Figure 2].
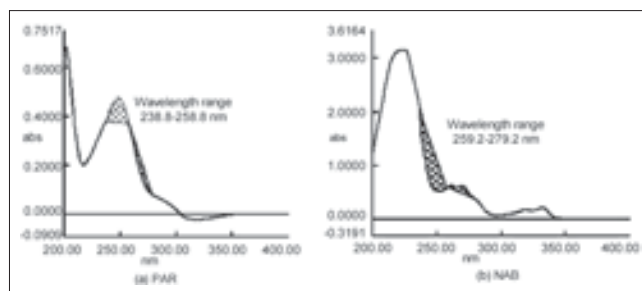
Analysis of the tablet formulation
Ten tablets were weighed accurately and powdered. Powder equivalent to 20 mg of PARA was weighed and transferred to 100 mL volumetric flask, then dissolved in 50 mL of methanol by shaking the flask for 15 min with the help of sonicator, and volume was made up to mark with methanol. The solution was filtered through whatman filter paper no. 41. An aliquot 0.5 mL of sample stock solution was transferred to a 10-mL standard volumetric flask and volume was made up to mark with methanol to get concentration 10 µg/mL of PARA and 10 µg/mL of NAB. The results of tablet analysis are shown in Table 1.

Recovery study
A recovery study was carried out by addition of known amount of standard drug in the pre-analyzed tablet formulation in 80, 100, and 120% of label claim. At each level of amount, three determinations were performed. Further, the area was put in the equation 1,a and 1,b to calculate the concentration. The results for recovery studies are given in Table 2. For determining the concentration of drugs by AUC method, the following equation was used. Amount of each drug was calculated using following formulae,

$$C_{PARA} = \frac{\begin{aligned}&AUC_{(259.2\text{-}279.2)} \times X^A_{(238.8\text{-}258.8)}\\&-AUC_{(238.8\text{-}258.8)} \times X^A_{(259.2\text{-}279.2)}\end{aligned}}{\begin{aligned}&X^D_{(259.2\text{-}279.2)} \times X^A_{(238.8\text{-}258.8)}\\&-X^D_{(238.8\text{-}258.8)} \times X^A_{(259.2\text{-}279.2)}\end{aligned}} \quad \text{...eq. 1,a}$$

$$C_{NAB} = \frac{\begin{aligned}&AUC_{(238.8\text{-}258.8)} \times X^D_{(259.2\text{-}279.2)}\\&-AUC_{(259.2\text{-}279.2)} \times X^D_{(238.8\text{-}258.8)}\end{aligned}}{\begin{aligned}&X^D_{(259.2\text{-}279.2)} \times X^A_{(238.8\text{-}258.8)}\\&-X^D_{(238.8\text{-}258.8)} X^A_{(259.2\text{-}279.2)}\end{aligned}} \quad \text{...eq. 1,b}$$

Where,

Table 1: Results of analysis of PARA and NAB by AUC method in tablet formulation

Sr. No.	Labeled amount in tablet (mg/tab)		Labeled amount found in tablet (mg/tab)		% of label claim	
	PARA	PARA	PARA	NAB	PARA	NAB
1.	500	517.5	517.5	9.97	103.56	99.75
2.	500	518.0	518.0	9.98	103.67	99.83
3.	500	520.0	520.0	10.03	104.05	100.34
Mean					103.76	99.97
±SD					0.2570	0.320
%RSD					0.2477	0.3201
±SEM					0.1465	0.1898

C_{PARA} and C_{NAB} are concentration of PARA and NAB respectively.

$AUC_{(238.8-258.8)}$ and $AUC_{(259.2-279.2)}$ are area under curve of solution at wavelength range between $238.8-258.8$ nm and $259.2-279.2$ nm. $X^D_{(238.2-258.8)}$, $X^D_{(259.2-279.2)}$; $X^A_{(238.8-258.8)}$, $X^A_{(259.2-279.2)}$ are absorptivities of PARA and NAB at respective wavelengths.

RESULTS AND DISCUSSION

Method validation
The newly developed method was validated according to the International Conference on Harmonisation guidelines with respect to linearity, Limit of Detection (LOD) and Limit of Quantitation (LOQ), and recovery studies.[13]

Recovery
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 101.67 – 102.43 for PARA and 96.69-98.49 for NAB. The low values of % relative standard deviation (RSD) are indicative of the accuracy and reproducibility of the method. [Table 2].

Linearity
PARA and NAB showed linearity in the range of 5–25 µg/mL. Linear regression equations and correlation coefficient (r^2) are, Y_{PARA}=0.2705x-0.0721 (r^2=00.9983) and Y_{NAB}=0.1542x + 0.0878 (r^2=0.9972) [Table 3].

Limit of detection and limit of quantitation
The LOD 0.2610 and 0.2609 and LOQ 0.7912 and 0.7908 was found for PARA and NAB, respectively [Table 3].

Table 2: Results of recovery studies of PARA and NAB (*n*=3)

Level of % recovery *n*=3	Mean % recovery		%RSD		±SEM	
	PARA	NAB	PARA	NAB	PARA	NAB
80	102.04	98.49	0.1092	0.07131	0.06344	0.04757
100	102.43	96.69	0.4834	0.3154	0.2858	0.177
120	101.67	97.64	0.1964	0.1307	0.1133	0.07494

Table 3: Optical parameters of PARA and NAB at 248.8 nm (±10 nm) and 269.2 nm (±10 nm) by AUC method

Parameters	PARA	NAB
Wavelength range	238.8-258.8 nm	259.2-279.2 nm
Beer's law range (µg/mL)	5-25	5-25
Regression equation* (y = mx + c)		
Slope (m)	0.2705	0.0516
Intercept (c)	−0.0721	0.0276
Correlation coefficient (r^2)	0.9983	0.9993
Limit of detection (LOD) µg/mL	0.2610	0.2609
Limit of quantitation (LOQ) µg/mL	0.7912	0.7908

Where y = absorbance and x = concentration, y = mx + c

CONCLUSION

The proposed AUC method for the simultaneous estimation of PARA and NAB in bulk and tablet dosage form is selective and sensitive. The value of the %RSD was satisfactory, indicating the reproducibility and accuracy of the proposed method.

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