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Research Article

Q-Analysis and Simultaneous Equation Method for Estimation of Domperidone and Naproxen by UV Spectrophotometry in Bulk and Tablet Dosage Form

Leela Bhaskar K, Sri Lakshmi D*, Sumalatha G, Suji G and Anil Teja Kumar K

Vikas Institute of Pharmaceutical Sciences, Rajahmundry, India

***Corresponding author:** D Sri Lakshmi, Associate Professor, Vikas Institute of Pharmaceutical Sciences, Rajahmundry, India

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Abstract

An accurate, specific and precise UV spectrophotometric method was developed for the simultaneous determination of domperidone (DOM) and naproxen (NAP) in tablet dosage form. The optimum conditions for the analysis of the drug were established. The maximum wavelength (λmax) was found to be 286 nm for DOM and 270nm for NAP respectively. The linearity of the proposed method was found in the range of 10-50 µg/ml and 5-25 µg/ml for DOM and NAP respectively. Calibration curves showed a linear relationship between the absorbance and concentration. The line equation for DOM Y = 0.020X + 0.006 with r2 of 0.999 and for NAP Y = 0.008X - 0.004 with r^2 of 0.999 was obtained. Validation was performed as per ICH guidelines for linearity, accuracy, precision, LOD and LOQ. The LOD and LOQ were found to be within the range. The proposed method was simple, sensitive, precise, accurate, quick and useful for routine analysis of DOM and NAP in bulk and tablet dosage forms.

Keywords: Simultaneous equation method; Validation; Domperidone; Naproxen; UV spectrophotometry

Introduction

Domperidone acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of domperidone are related to its peripheral dopamine receptor blocking properties. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure. Antiemetic: The antiemetic properties of domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone, located just outside the blood brain barrier, which - among others - regulates nausea and vomiting (Figure 1).

As with other non-selective NSAIDs, naproxen exerts it's clinical effects by blocking COX-1 and COX-2 enzymes leading to decreased prostaglandin synthesis [3]. Although both enzymes contribute to prostaglandin production, they have unique functional differences [3]. The COX-1 enzymes is constitutively active and can be found in normal tissues such as the stomach lining, while the COX-2 enzyme is inducible and produces prostaglandins that mediate pain, fever and inflammation [4]. The COX-2 enzyme mediates the desired antipyretic, analgesic and anti-inflammatory properties offered by Naproxen, while undesired adverse effects such as gastrointestinal upset and renal toxicities are linked to the COX-1 enzyme (Figure 2).

Simultaneous equation method

By using the below equations the concentrations in the samples were obtained

$$CX = A1ay2 - A2ay1 / ax1ay2 - ax2ay1 \quad \text{Eq. 1}$$

$$CY = A1ax2 - A2ax1 / ay1ax2 - ay2ax1 \quad \text{Eq. 2}$$

where A1 and A2 are absorbances of mixture at 286nm and 270nm respectively, ax1 and ax2 are absorptivities of DOM at λ1 and λ2 respectively, ay1 and ay2 are absorptivities of NAP at λ1 and λ2 respectively, Cx and Cy are concentrations of DOM and NAP respectively.

Q-Analysis/Isobestic point method

Concentrations in the samples were obtained by using following equations:

$$Cx = (Qm-Qy / Qx-Qy). A/ax \quad \text{Eq. 3}$$

$$Cy = (Qm-Qx / Qy-Qx). A/ay \quad \text{Eq. 4}$$

Where,

Cx, Cy - Concentrations of DOM and NAP respectively (g/100ml).

Qx - Ratio of absorptivity of DOM at 286nm and 270nm.

Qy - Ratio of absorptivity of NAP at 286nm and 270nm.

Qm - Ratio of absorbance of Mixture at 286nm and 270nm.

A - Absorbance of Mixture at Isobestic point.

Ax - Absorptivity of DOM at Isobestic point.

Ay - Absorptivity of NAP at Isobestic point.

By using the above two methods estimation of both drugs by UV spectrophometry has been done.

Literature is enriched with several reports indicating UV spectrophotometry as vital tool for analytical method development [1,2]. Several analytical procedures have been proposed for the

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quantitative estimation of domperidone and naproxen separately and in combination with other drugs. HPLC [3] and UV [4] methods for estimation of domperidone alone in pharmaceutical preparation have been reported. Methods for simultaneous estimation of domperidone in combination with pantoprazole [4], rabeprazole [5], omeprazole [6] and paracetamol [7] are also available. Similarly, methods for simultaneous estimation of naproxen in combination with other drugs are reported in literature [8,9]. In continuation of our work on analytical method development [10,11], present work was directed toward development of a simple, rapid, accurate, specific and economic UV spectrophotometric method for the estimation of NAP and DOM in bulk and tablet dosages form. The method was further validated as per ICH guidelines [12-16] for the parameters like precision, accuracy, sensitivity, and linearity. The result of analysis was validated statistically and by recovery studies.

Reagents

Methanol (AR grade) was obtained from Qualigens Fine Chemical, Mumbai.

Instruments

UV Visible Double beam spectrophotometer (LABINDIA UV 3000+), Weighing Machine (ATY 224), Pipettes, Burettes and Beaker (BOROSILL).

Materials and Methods

Domperidone and Naproxen were obtained as a gift sample from pharmtrain and the tablets were purchased from the local market (Domperidone 10mg and Naproxen 550mg).

Preparation of standard stock solutions: Accurately weighed about 1mg of DOM and transferred to 10ml volumetric flask, sonicated with diluent methanol for 10min and diluted to 10ml with the diluent to get the concentration of 100µg/ml.

An accurately weighed quantity of about 5mg of NAP was taken in 10ml volumetric flask dissolved in sufficient quantity of methanol, sonicated for 15min and diluted up to the mark with same solvent to get the concentration of 50µg/ml. From this solution, 5ml solution was pipetted out in 10ml volumetric flask and volume was made up to the volume with methanol to get concentration of 5µg/ml and these solutions were used for making dilutions of calibration curve.

Determination of λmax

The standard solution of DOM and NAP were separately scanned at different concentrations in the range of 200-400 nm and the λmax was determined.

Preparation of calibration curve

For each drug, appropriate aliquots were pipetted out from standard stock solution into the series of 10ml volumetric flask and the volume was made up to the mark with methanol to get concentration of 10-50 µg/ml of DOM and 5-25 µg/ml of NAP. Solutions of different concentrations for each drug were analysed at their respective wavelengths and absorbances were recorded.

Simultaneous equation method

Two wavelengths were selected for the method (286nm and 270nm) as the absorbance maxima of DOM and NAP respectively in methanol. Standard stock solutions (100µg/ml and 50µg/ml for both drugs) were prepared separately in methanol. The stock solutions of both drugs were further diluted separately with methanol to get series of standard solutions of 5-25 µg/ml for NAP and 10-50 µg/ml for DOM. The absorbances were measured at the selected wavelengths and absorptivities (A 1%, 1cm) for both the drugs at both wavelengths were determined. Concentrations in the samples were obtained by using following equations 1 & 2.

Q-Analysis method

Two wavelengths were selected for the method (270nm and 275nm) as one is the maximum wavelength for NAP and the other is the isobestic point respectively in methanol. Standard stock solutions (100µg/ml and 50µg/ml for both drugs) were prepared separately in methanol. The stock solutions of both drugs were further diluted separately with methanol to get series of standard solutions of 5-25 µg/ml for NAP and 10-50 µg/ml for DOM. The absorbances were measured at the selected wavelengths and absorptivities (A 1%, 1cm) for both the drugs at both wavelengths were determined. Concentrations in the samples were obtained by using the equations 3 & 4.

Preparation of tablets for assay

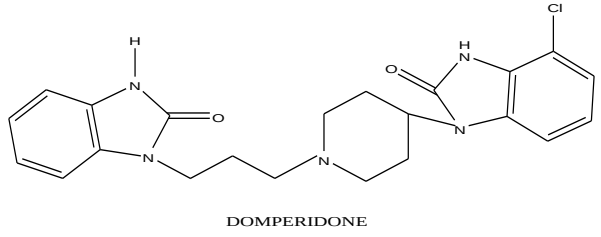
The developed procedure was extended to formulation of DOM and NAP, the combination was available in the market in the strength of 10mg and 550mg of DOM and NAP respectively. Average weight of twenty tablets were taken and crushed to make powder, weighed powder containing 10mg DOM was transferred to 10ml of volumetric flask and volume was made up to the mark with Methanol (DOM 100µg/ml and NAP 50µg/ml). From the stock solution further dilutions were done to get the concentration of 10µg/ml and 5µg/ml DOM and NAP respectively. The same procedure as mentioned for the pure drug was followed for the formulation. The concentrations of both DOM and NAP were determined by measuring absorbance at 286nm and 270nm.

Recovery study

To check the accuracy of the developed method, recovery studies were carried out as per ICH guidelines. To the analysed solutions, standard solutions of all the two drugs were added equivalent to 50, 100 and 150% of its drug content. Recovery studies were carried by doing replicate studies.

Method validation

The analytical method was validated with respect to parameters such as linearity, limit of detection (LOD), limit of quantitation (LOQ), precision, accuracy, robustness, and recovery according to the ICH guidelines. Linearity was established by least squares linear regression analysis of the calibration curve. Accuracy was studied



DOMPERIDONE

Figure 1: DOM.

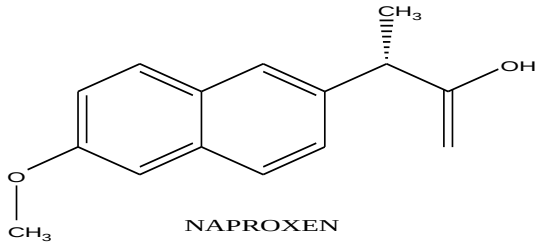


Figure 2: NAP.

Table 1: Analysis of tablet dosage form.

Formulations	Drugs	Lable Claim(mg)	% Label claim (mean±SD)
Tablets	Domperidone	10	104.08±0.002
	Naproxen	550	99.89±0.003

by adding two different amounts (corresponding to 50%, 100% and 150% of the test preparation concentrations) of NAP and DOM to the placebo preparation and comparing the actual and measured concentrations. For each level, three solutions were prepared and each was estimated in duplicate. The precision of the method, as intra-day repeatability was evaluated by performing six independent assays of the test sample preparation and calculating the %RSD. The intermediate (interday) precision of the method was checked by performing same procedure on different days by another person under the same experimental conditions. The LOD and LOQ of NAP and DOM were calculated by mathematical equations:

$$LOD = 3.3 \times SD/S \quad \text{Eq. 5}$$

$$LOQ = 10 \times SD/S \quad \text{Eq. 6}$$

Robustness of proposed method was performed by changing UV analyst and keeping the remaining conditions (solvent, dilution, UV spectrophotometer) same (Figure 3).

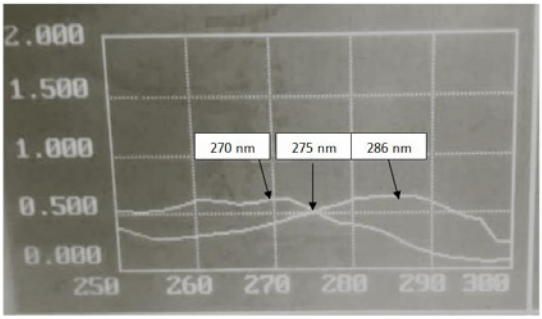


Figure 3: Isobestic Point.

Statistical analysis

Means, standard deviation (SD), relative standard deviation (RSD) and linear regression analysis were calculated using Microsoft Excel 2007.

Results and Discussion

The UV scanning showed spectrum exhibiting λmax of 286nm and 270nm for DOM and NAP respectively (Figure 2).

The linearity of the proposed method was investigated in the range of 10-50 µg/ml and 5-25 µg/ml for DOM, NAP respectively. Calibration curves showed a linear relationship between the absorbance and concentration. The line equation for DOM y = 0.020x+0.005 with r^2 of 0.9999 and for NAP y = 0.022x - 0.003 with r^2 of 0.9999 was obtained. Calibration curves showed a linear relationship between the absorbance and concentration of DOM and

Table 2: Accuracy data of DOM and NAP for Simultaneous Equation method.

DOM						
%Level (n=3)	Target sample solution	Amt. of std. spiked	Total conc. (µg/mL)	Mean abs ± SD	Found conc (µg/mL)	% Recovery
50	10	5	15	0.321±0.002	15.48	103.23
100	10	10	20	0.408±0.001	20.512	102.56
150	10	15	25	0.535±0.001	26.087	104.35
NAP						
50	5	2.5	7.5	0.172±0.002	7.51	100.12
100	5	5	10	0.231±0.003	9.98	99.89
150	5	7.5	12.5	0.287±0.002	12.48	99.86

Table 3: Accuracy data of DOM and NAP for Q-Analysis Method.

DOM						
%Level (n=3)	Target sample solution	Amt. of std. spiked	Total conc. (µg/mL)	Mean abs ± SD	Found conc (µg/mL)	% Recovery
50	10	5	15	0.331±0.001	14.84	98.98
100	10	10	20	0.418±0.003	19.8	99.02
150	10	15	25	0.544±0.001	25.31	101.23
NAP						
50	5	2.5	7.5	0.170±0.001	7.67	102.33
100	5	5	10	0.236±0.002	10.13	101.36
150	5	7.5	12.5	0.288±0.001	12.79	102.32

Table 4: Assay data of DOM and NAP for Simultaneous Equation method & Q-Analysis Method.

Drug	Prepared Concentration	Assay Mean %	
		Simultaneous equation Method	Q-Analysis Method
DOM	10	98.47	102.73
NAP	550	103.52	104.28

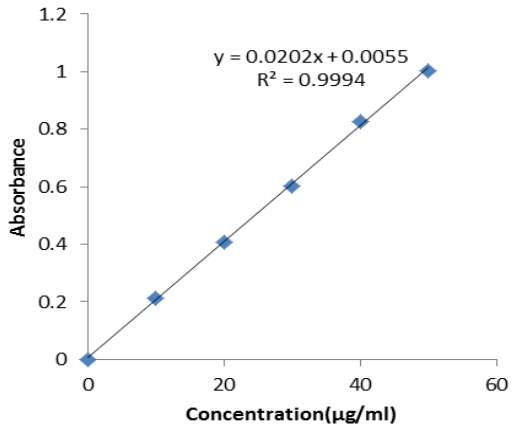


Figure 4: Linearity of DOM 286nm.

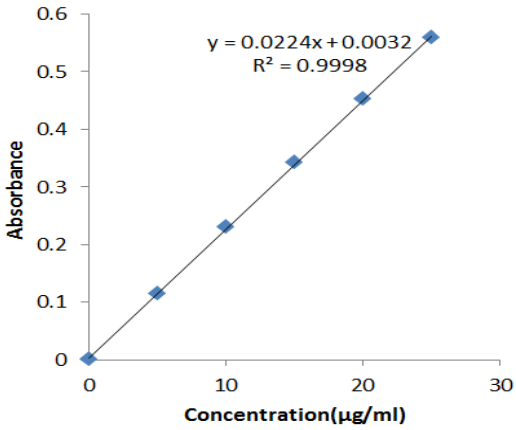


Figure 5: Linearity of NAP 270nm.

NAP (Figure 4 and 5).

Linearity Graph

The present research works discuss the development of a UV spectrophotometric method for the estimation of DOM and NAP in tablet dosages form. The optimum conditions for the analysis of the drug were established. During analysis of commercial formulation (Table 2), absorbances were recorded at the respective wavelengths. The LOD of DOM and NAP was 0·541µg/ml and 0·662µg/ml and LOQ for DOM and NAP was 0·133µg/ml and 3.26µg/ml respectively (Table 1).

Conclusion

The proposed method is simple, sensitive, accurate and reproducible and can be used for routine analysis for simultaneous determination for naproxen and domperidone in bulk as well as in pharmaceutical preparation by UV spectrophotometry. The results of statistical analysis carried out reveal the accuracy and precision of the method. The relative standard deviation (RSD) for all parameters was found to be less than one, which establishes the validity of the method. The method can be implemented for routine analysis for simultaneous estimation of Domperidone and Naproxen.

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