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RESEARCH ARTICLE

SIMULTANEOUS ESTIMATION OF NAPROXEN AND DOMPERIDONE USING UV SPECTROPHOTOMETRY IN TABLET DOSAGE FORM

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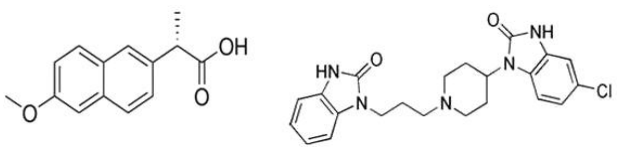
An accurate, specific and precise UV spectrophotometric method was developed for the simultaneous determination of naproxen (NAP) and domperidone (DOM) in tablet dosage form. The optimum conditions for the analysis of the drug were established. The maximum wavelength (λ_{max}) was found to be 271 nm for NAP and 287 nm for DOM. The linearity of the proposed method was found in the range of 10-35 μg/ml and 5-30 μg/ml for NAP and DOM respectively. Calibration curves showed a linear relationship between the absorbance and concentration. The line equation for NAP Y = 0.0222X - 0.0226 with r^2 of 0.9999 and for DOM Y = 0.0292X - 0.0149 with r^2 of 0.9998 was obtained. Validation was performed as per ICH guidelines for linearity, accuracy, precision, LOD and LOQ. The LOD was found to be 0.0454 and 0.656 μg/ml for NAP and DOM and the LOQ was found to be 0.151 and 2.18 μg/ml for NAP and DOM respectively. The proposed method was simple, sensitive, precise, accurate, quick and useful for routine analysis of NAP and DOM in tablet formulations.

Key words: Simultaneous equation method, Validation, Naproxen, Domperidone, UV spectrophotometry.

INTRODUCTION

Naproxen (NAP) is a proprionic acid derivative related to the arylacetic acid group of nonsteroidal anti-inflammatory drugs which is chemically (2S)-2-(6-methoxynaphthalen-2-yl)propanoic acid (**Figure 1a**). Naproxen is used to treat pain or inflammation caused by conditions such as arthritis, ankylosing spondylitis, tendinitis, bursitis, gout, or menstrual cramps. It works by reducing hormones that cause inflammation and pain in the body. Like other NSAIDs, naproxen produces disturbances in the gastrointestinal tract (Drugs.com). Domperidone (DOM) is chemically 5-chloro-1-[1,3- (2,3-dihydro-2-oxo-1*H*-benzimidazol-1yl) propyl)-4-piperdinyl-1,3-dihydro-2*H*-benzimidazol-2-one] (**Figure 1b**), a dopamine antagonist which is usually given along with proton pump inhibitors. Domperidone does not cross the blood brain barrier and therefore has fewer adverse CNS effects than other dopamine antagonist.



(a) (b)

Fig. 1. Structures of (a) NAP and (b) DOM

Domperidone increases the movements or contractions of the stomach and bowel. It is also used to treat nausea and vomiting caused by other drugs used to treat parkinson's disease (Drugs.com).

A novel formulation in combination of naproxen (NAP) 250 mg and domperidone (DOM) 10 mg is commercially available in Indian market for treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, fever and prevent some of the gastro-intestinal problems that NSAIDs can cause.

Literature is enriched with several reports indicating UV spectrophotometry as vital tool for analytical method development (Patil *et al* 2011; Shah *et al* 2011; Shukla *et al* 2011; Singh *et al* 2011). Several analytical procedures have been proposed for the quantitative estimation of domperidone and naproxen separately and in combination with other drugs. HPLC (Varalakshmi *et al* 2011) and UV (Kaushik and Banerjee, 2009) methods for estimation of domperidone alone in pharmaceutical preparation have been reported. Methods for simultaneous estimation of domperidone in combination with lansoprazole (Patel *et al* 2009), pantoprazole (Thanikachalam *et al* 2008), rabeprazole (Sabnis *et al* 2008), omeprazole (Patel *et al* 2007) and paracetamol (Karthik *et al* 2007) are also available. Similarly, methods for simultaneous estimation of naproxen in combination with other drugs are reported in literature (Haque *et al* 2008; Gondalia and Dharamsi, 2013).

In continuation of our work on analytical method development (Singh *et al* 2012a; Singh *et al* 2012b), 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 (ICH Q2(R1), 2005) for the parameters like precision, accuracy, sensitivity, and linearity. The result of analysis was validated statistically and by recovery studies.

MATERIAL AND METHODS

Samples

Naproxen (NAP) was obtained as gift sample from Glenmark Pharmaceuticals Limited, India and Domperidone (DOM) was received as gift sample from Sidmech Laboratories India Pvt. Ltd., Dehradun. The pharmaceutical formulation Naprodom tablets (Naproxen - 250 mg and Domperidone - 10 mg) used in this study was procured from local market of Bareilly.

Reagents

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

Instruments

UV-Visible double beam spectrophotometer (UV-3200 LAB INDIA) with 1cm matched quartz cells, digital balance (K- Roy Electronic), hot air oven (CLE-101, coslab) was used in the study.

Preparation of standard stock solutions

Accurately weighed quantity of about 50 mg of NAP was taken in 50 ml volumetric flask, dissolved in sufficient quantity of methanol, sonicated for 10 min and diluted to 50 ml with the same solvent so as to get the concentration of 1000 μg/ml. An accurately weighed quantity of about 50 mg of DOM was taken in 50 ml volumetric flask dissolved in sufficient quantity of methanol, sonicated for 15 min and diluted up to the mark with same solvent so as to get the concentration of 1000 μg/ml. From this solution, 5 ml solution was pipetted out in 50 ml volumetric flask and volume was made up with methanol to get concentration of 100 μg/ml which was used for making dilutions of calibration curve.

Determination of λ_{max}

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

Preparation of calibration curve

For each drug, appropriate aliquots were pipetted out from standard stock solution into the series of 10 ml volumetric flask and the volume was made up to the mark with methanol to get concentration of 10-35 μg/ml of NAP and 5-30 μg/ml of DOM. Solutions of different concentrations for each drug were analyzed at their respective wavelengths and absorbances were recorded.

Simultaneous equation method

Two wavelengths were selected for the method (271 nm and 287 nm) as the absorbance maxima of NAP and DOM respectively in methanol. Standard stock solutions (100 μg/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 10-35 μg/ml for NAP and 5-30 μg/ml for DOM. The absorbances were measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs at both wavelengths were determined. Concentrations in the samples were obtained by using following equations:

$$CX = A1ay2 - A2ay1 / ax1ay2 - ax2ay1 \quad \text{Eq. 1}$$
$$CY = A1ax2 - A2ax1 / ay1ax2 - ay2ax1 \quad \text{Eq. 2}$$

where A1 and A2 are absorbances of mixture at 271 nm and 287 nm respectively, ax1 and ax2 are absorptivities of NAP at λ1 and λ2 respectively, ay1 and ay2 are absorptivities of DOM at λ1 and λ2 respectively, Cx and Cy are concentrations of NAP and DOM respectively.

Preparation of tablets for assay

Twenty NAP and DOM tablets (250 mg NAP and 10 mg DOM) were weighed and powdered. A portion equivalent to 250 mg of NAP was weighed into 100 ml clean and dry volumetric flask, about 70 ml of methanol was added. The solution was sonicated for 20 minutes and volume was made up to the mark with methanol. The contents of the solution were mixed well and filtered through Whatman filter paper No. 41. First few ml of filtrate was discarded, 5 ml of filtrate was pipetted out and diluted to 50 ml with methanol. The absorbances were recorded at the respective wavelengths.

Recovery study

To check the accuracy of the developed method, recovery study was carried out as per ICH norms where to a reanalyzed sample solution, standard solutions of all the two drugs were added equivalent to 80, 100 and 120% of its drug content. Recovery study was carried by doing replicate study.

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 (ICH Q2R1 2003). Linearity was established by least squares linear regression analysis of the calibration curve. Accuracy was studied by adding two different amounts (corresponding to 80%, 100% and 120% 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:

$$LOD = 3.3 \times \text{standard deviation} \div \text{slope} \quad \text{Eq. 3}$$
$$LOQ = 10 \times \text{standard deviation} \div \text{slope} \quad \text{Eq. 4}$$

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

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 λ_{max} of 271 nm and 287 nm for NAP and DOM respectively (**Figure 2**).

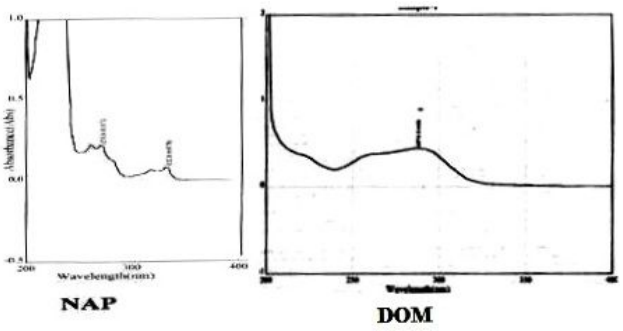


Fig. 2. λ_{max} of NAP and DOM

The linearity of the proposed method was investigated in the range of 10-35 g/ml and 5-30 g/ml for NAP, DOM respectively. Calibration curves showed a linear relationship between the absorbance and concentration. The line equation for NAP y = 0.0222x - 0.0226 with r^2 of 0.9999 and for DOM y = 0.0292x - 0.0149 with r^2 of 0.9998 was obtained. Calibration curves showed a linear relationship between the absorbance and concentration of NAP and DOM (**Figure 3a, 3b**).

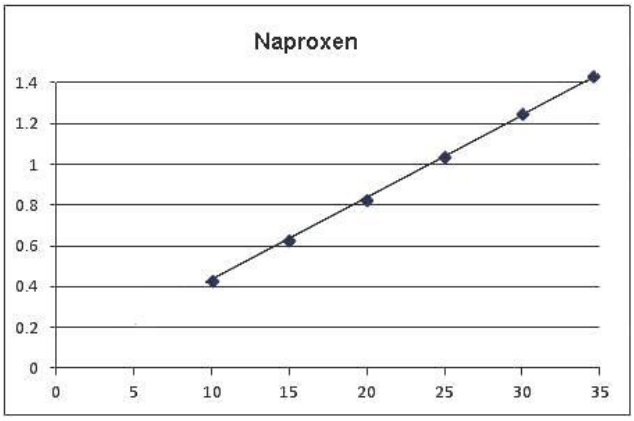


Fig. 3a. Calibration curve of NAP

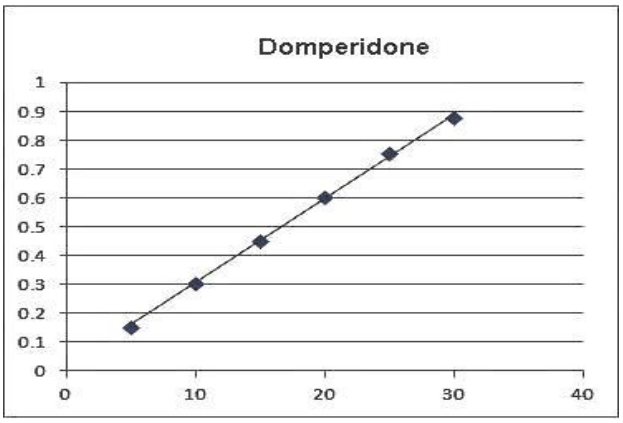


Fig. 3b. Calibration curve of DOM

The present research work discuss the development of a UV spectrophotometric method for the estimation of LAN and NAP in tablet dosages form. The optimum conditions for the analysis of the drug were established. During analysis of commercial formulation (**Table 1**), absorbances were recorded at the respective wavelengths.

The LOD of NAP and DOM was 0·454 μg/ml and 0·656 μg/ml and LOQ for NAP and DOM was 0·151 μg/ml and 2.18 μg/ml respectively (**Table 2**).

Table 1. Analysis of tablet dosage form

Formulation	Drugs	Label claim	% Label claim (mean±SD)
Tablet	Naproxen Domperidone	250 mg 10 mg	100·16±0·012757 98±0.000573

Table 2. Validation parameters for NAP and DOM

Validation parameter	Mean±SD	
	Naproxen	Domperidone
Linearity range	10-35 μg/ml	5-30 μg/ml
Correlation coefficient	0.9999	0.9998
Slope	0.0222	0.0292
Intercept	0.0226	0.0149
Interday		
1st day	101%±0·0018626	106±0.000566
2nd day	97%±0·0014136	94±0.000404
3rd day	97%±0·000375	100.7±0.000499
Intraday		
(1st h)	98%±0·001002	94±0.000927
(2nd h)	96%±0·002631	94±0.000432
(3rd h)	98%±0·000608	94±0.00034
Recovery		
80%	107%±0·00391	98±0.0059
100%	105%±0·00254	96±0.00033
120%	106%±0·00928	99±0.00091
LOD (mg/ml)	0·454 μg/ml	0.657 mg/ml
LOQ (mg/ml)	0·151 μg/ml	2.18 mg/ml
Robustness	106%±0·00389	91±0.000125

CONCLUSION

The proposed method is simple, sensitive and reproducible and hence it can be used in routine analysis for simultaneous determination for naproxen and domperidone in bulk as well as in pharmaceutical preparation by UV spectrophotometry. Statistical analysis of the results has been carried out revealing high accuracy and good precision. The relative standard deviation (RSD) for all parameters was found to be less than one, which established the validity of the method. So, the proposed method can be used for routine quantitative simultaneous estimation of both the drug.

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http://www.drugs.com/naproxen.html

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