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Research Article

DEVELOPMENT AND VALIDATION OF UV-SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS ESTIMATION OF PARACETAMOL AND DOMPERIDONE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

Two new simple, accurate and precise spectrophotometric methods have been developed for simultaneous determination of Paracetamol and Domperidone in a binary mixture. In Method I absorbance were measured at 243.4 nm and 284.12 nm corresponding to the absorbance maxima of Paracetamol and Domperidone. In Method II, two wavelengths 284.12 nm, the λmax of Domperidone and 270 nm, an iso-absorptive point were selected. Linearity range was observed in the concentration range of 15-30 µg/ml for Domperidone and 11-16µg/ml for Paracetamol. Concentration of each drug was obtained by using the absorptivity values calculated for both drugs at wavelengths, 243.4 nm, 284.12 nm and 270 nm. Developed method were applied to marketed formulation. The methods were validated statistically and recovery study was performed to confirm the accuracy of both methods. The methods were found to be rapid, simple, accurate and precise.

Keywords: Domperidone, Paracetamol, Ultraviolet spectroscopy, Simultaneous equation method, Q Analysis Method.

INTRODUCTION

Chemically, Paracetamol (PARA) is 4-hydroxy acetanilide. It has centrally and peripherally acting non-opioid analgesic and antipyretic activity.[1-2] Domperidone (DMP) is chemically 5-chloro-1-[1-[3-(2-oxo-2, 3-dihydro-1 H -benzimidazol-1yl) propyl]-piperidin-4-yl]-1, 3-dihydro-2 H benzimidazol-2-one used as an antiemetic drug. A combination of these drugs, DMP (20 mg), and PARA (500 mg) is available as tablets for clinical practice. Their combination is used for the treatment of migraine. A Survey of literature reveals that various methods like HPLC [3-5], UV [6-14] are available for individual determination of domperidone and paracetamol or in combination with other drugs. However there is only one spectrometric method available for the simultaneous determination of paracetamol and domperidone[15]. Aim of present work was to develop simple, precise, accurate and economical spectrophotometric methods for simultaneous determination of binary drug formulation. The proposed methods were optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines[16].

MATERIALS AND METHODS

Apparatus

The instrument used in the present study was double beam Shimadzu UV-1800 UV visible spectrophotometer with 10 mm matched quartz cells.

Materials

Standard gift samples of Paracetamol and Domperidone were procured from Macro labs, Banglore. Tablets containing both Paracetamol and Domperidone were purchased from local market.

Stock solutions

The standard stock solutions (100 µg/ml) of each of Paracetamol and Domperidone were prepared separately by dissolving accurately about 10mg of drug in 20ml of 0.5M Methanolic HCl and volume was made up to 100 ml with Distilled water.

Preparation of calibration curves

Solutions of 10µg/ml of PARA and DOM were prepared separately. Both the solutions were scanned in the spectrum mode from 200.0 nm to 400.0 nm. The maximum absorbance of PARA and DOM were observed at 243.4 nm and 284.12 nm, respectively.

PARA and DOM showed linearity in the concentration range of 11-16 µg/ml and 15-30 µg/ml at their respective maxima. Accurately measured standard stock solution of Paracetamol (1.1, 1.2, 1.3, 1.4, 1.5, 1.6 ml) & standard stock solution of Domperidone (15, 18, 21, 24, 27, 30 ml) were transferred to a separate series of 10 ml of volumetric flasks & diluted to the mark with disilled water. The absorbance of each solution was measured at wavelength 243.4 nm & 284.12 nm. The coefficient of correlation was found to be 0.9995 for PARA and 0.9991 for DOM.

Method 1: Simultaneous equation method

Paracetamol and Domperidone were dissolved separately in 20ml of 0.5 M Methanolic HCl and the volume was made up to 100 ml with Distilled water. These solutions were then diluted suitable in distilled water to get the concentration of 10 µg/ml and the solutions were scanned in the wavelength range of 200–400 nm (Fig 1).

From the overlain spectrum of PARA and DOM, two wavelengths namely 243.4 nm and 284.12 nm, λmax of Paracetamol and Domperidone respectively were selected. The calibration curves were constructed in the concentration range of 15-30µg/ml for DOM and 11-16µg/ml PARA. The absorptivity coefficients were determined for both the drugs at the selected wavelengths and following equations were made.

$A1 = 0.0661\ Cx + 0.0091\ Cy$ .....(1)

$A2 = 0.0101\ Cx + 0.0279\ Cy$ .... (2),

Where, A1 and A2 are absorbance of sample at 243.4 nm and 284.12 nm, respectively.

0.0661 and 0.0101 are absorptivities of Paracetamol at 243.4 nm and 284.12 nm respectively.

0.0091 and 0.0279 are absorptivities of Domperidone at 243.4 nm and 284.12 nm respectively.

Cx and Cy are concentrations of and Paracetamol and Domperidone respectively.

Method 2: Absorption Ratio / Q Analysis Method

From the overlain spectrum of Paracetamol and Domperidone (Fig 1), two wavelengths were selected, one at 284.12 nm, the λmax of Domperidone and other at 270 nm, an iso-absorptive point for both the drugs. The solutions were prepared in the similar manner as mentioned in the previous method. The absorbance values were measured at selected wavelengths. The concentration of each component were calculated by mathematical treatment of the following mentioned equations.

For Domperidone,

$$Cx = \frac{Qm-Qy}{Qx-Qy} \cdot \frac{A}{ax_1} \quad \ldots$$

For Paracetmol,

$$Cy = \frac{Qm-Qx}{Qy-Qx} \cdot \frac{A}{ax_2} \quad \ldots$$

Where,

Cx and Cy are concentrations of Domperidone and Paracetamol, respectively.

A is the absorbance of sample solution at isoabsorptive wavelength 270 nm

ax_1 and ax_2 are the absorptivity of Domperidone and Paracetamol at isoabsorptive wavelength 270 nm

Cx and Cy are concentrations of Domperidone and Paracetamol respectively.

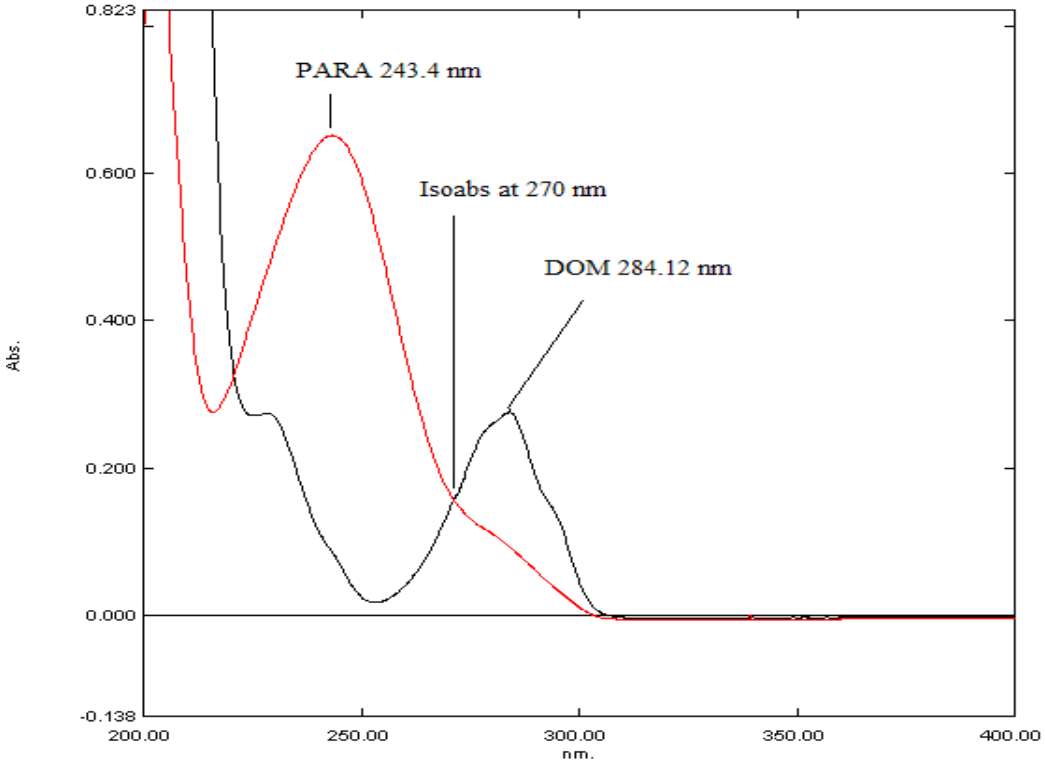

Fig. 1: It shows Overlain spectrum of PARA and DOM

Analysis of tablet formulation

For the estimation of drugs in the marketed preparations, 20 tablets containing 10 mg of Domperidone and 500 mg paracetamol (Domcet) were weighed and finely powdered. A quantity of powder equivalent to 10 mg Domperidone and 500 mg Paracetamol was accurately weighed and transferred to a 100 ml volumetric flask, dissolved in 20ml of 0.5M Methanolic HCl. This solution were shaken upto 10 mins until clear solution appeared and the volume was made up to 100 ml with Distilled water and the solution was filtered through Whatman filter paper no.1. Aliquots of this tablet solution were diluted to get the concentrations ~ 1µg/ml of Domperidone and ~50 µg/ml of Paracetamol. The sample solutions were scanned over the range of 200-400nm. Absorbance of the sample solutions at 243.4 nm, 284.12 nm and 270 nm were measured and from the absorbance values, the concentration of drugs in the sample solution were determined by using both methods. The accuracy of the proposed method was ascertained by carrying out recovery studies by standard addition method. The proposed methods were validated statistically and the results are represented in Table 1.

Table 1: Shows Assay of tablets

Method	Label Claim (mg/tab)		Amount Claim (mg/tab)		% Label Claim found		% Recovery	
	PARA	DOM	PARA	DOM	PARA	DOM	PARA	DOM
I	500	10	496.0	10.0	99.20	100	99.76	99.09
II	500	10	496.0	10.08	99.20	100.08	100.06	99.02

Table 2: Shows optical characteristics of the proposed method

Parameter	Method I		Method II	
	DOM	PARA	DOM	PARA
Beer's law limit (µg/ml)	15-30	11-16	15-30	11-16
Coefficient of Correlation	0.9991	0.9995	0.9993	0.9998
Intercept	0.0075	0.0343	0.0026	0.0170
Slope	0.0279	0.0661	0.0147	0.0177
Molar absorptivity(lit/mole/cm)	11882.9169	9992.337	6260.60	2675.707

RESULTS AND DISCUSSION

The overlain spectra of drugs showed the λmax of 243.4 nm and 284.12 nm for PAR and DOM respectively. Both the drugs obeyed linearity range 5-20µg/ml and 6-30µg/ml respectively and correlation coefficient (r^2) were found to be <1 in both cases. The absorptivity values were calculated and along with absorbances, these values were submitted in equation (1) and (2) to obtain concentration of drugs. The percentage purity of drugs in combined dosage form was found to be 99.20 ± 0.01 % for PARA and 100.04 ± 0.54 % for LAR. The accuracy of both methods were determined by performing recovery study by standard addition method. The % recoveries were found to be 99.76 % and 99.09 % for PARA and DOM for method 1, and 99.45% and 99.02% for method 2. The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. The methods were found to be precise as % RSD for intra-day and inter-day precision were < 2.

Validation

The methods were validated with respect to specificity, accuracy, precision and linearity.

Linearity

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of DOM and PARA. For simultaneous equation method and Q analysis, the Beer- Lambert's concentration range was found to be 15-30µg/ml for DOM and 11-16µg/ml PARA.

Accuracy

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). Percent recovery for DOM and PARA, by both the methods, was found in the range of 99.93% to 101.68%.

Precision

Precision was studied to find out intra and inter-day variations in the test method of DOM and PARA. Calibration curves prepared in medium were run in triplicate in same day and for three different days. %RSD (relative standard deviation) were calculated which is less than 2 %.

Table 3: Shows Precision Study of DOM and PARA

Day	Method I		Method II	
	% Label claim estimated (Mean ± % R.S.D.)		% Label claim estimated (Mean ± % R.S.D.)	
	DOM	PARA	DOM	PARA
Intraday	100.8 ± 0.660	99.20 ± 0.09124	100.74 ± 0.571	98.77 ± 0.259
Interday	103 ± 0.438	99.46 ± 0.85	100.0 ± 0.660	99.20 ± 0.6224

Limit of detection

It is the lowest amount of analyte in a sample that can be detected but not necessarily quantitated under the stated experimental conditions. Limit of detection can be calculated using following equation as per ICH guidelines.

LOD = 3.3 × N/S

Where,

N = Standard deviation of the responce and

S = Slope of the corresponding calibration curve.

Limit of quantification

It is the lowest concentration of analyte in a sample that can be determined with the acceptable precision and accuracy under stated experimental conditions. Limit of quantification can be calculated using following equation as per ICH guidelines.

LOQ = 10 × N/S

Where,

N = Standard deviation of the response and

S = Slope of the corresponding calibration curve

Table 4: Shows LOD and LOQ Values.

Parameter	Method I		Method II	
	DOM	PARA	DOM	PARA
L.O.D. (µg / ml)	0.412	0.149	0.05185	1.03474
L.O.Q. (µg / ml)	1.25089	0.453	1.57	3.13

CONCLUSION

The proposed methods are simple, precise, and accurate and can be used for routine quantitative analysis of Paracetamol and Domperidone in pure and tablet dosage form.

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