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Research Article

SIMULTANEOUS ESTIMATION AND VALIDATION OF PARACETAMOL AND DOMPERIDONE IN BULK AND TABLET DOSAGE FORM BY USING DIFFERENT SPECTOPHOTOETRIC METHOD

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ABSTRACT
Three 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 258 nm and 292 nm corresponding to the absorbance maxima of Paracetamol and Domperidone. Concentration of each drug was obtained by using the absorptive values calculated for both drugs at wavelengths 258 nm, and 292 nm. Method II by Dual wavelength method, Paracetamol and Domperidone were quantified using principle that absorbance difference between two points on mixture spectra was directly proportional to concentration of component of interest and independent of interfering component. Method III describes Area under Curve and involves measurement of area under curve in the range of 288-296 nm (For PARA) and 247-269 nm (For DOM) for the analysis in methanol. Linearity range was observed in the concentration range of 5-30 µg/ml for Paracetamol and Domperidone. Developed methods were applied to marketed formulation. The methods were validated statistically and recovery study was performed to confirm the accuracy of both methods.
Keywords: Paracetamol, Domperidone, Ultraviolet spectroscopy, Simultaneous equation Method, Dual Wavelength Method, Area under Curve Method.

INTRODUCTION

Paracetamol, N-(4hydroxy phenyl) acetamide has analgesic and antipyretic. It is commonly used for the relief of headaches, relief of fever, and minor aches and pains, which is act by inhibition of cyclooxygenase (COX). Domperidone 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, Domperidone is a dopamine antagonist with antiemetic properties. Acts by selectively antagonizing the peripheral dopaminergic D2 receptors in the gastrointestinal wall, thereby enhancing gastrointestinal peristalsis and motility and increasing lower esophageal sphincter tone and which is used as an antiemetic drug[1]. Both the drugs show absorbance range between 200-400 nm. The combination was used for the treatment of migraine. Some analytical methods used for simultaneous estimation of Paracetamol and Domperidone include U.V spectrophotometry[2,3], HPLC[4] and RP-HPLC[5] in pharmaceutical preparation.

MATERIALS AND METHODS

Materials

UV-visible double beam spectrophotometer, Jasco model 680 with spectral bandwidth of 1 nm, wavelength accuracy of ± 0.3 nm and a pair of 10 mm matched quartz cells was used. The commercially available tablet, Domcet (Label claim: Paracetamol I.P.-500 mg, Domperidone I.P.-10 mg) was procured from commercial market.

Selection of common solvent

After assessing the solubility of drugs in different solvents 0.1N NaOH was used as common solvent for developing spectral characteristics.

Preparation of standard stock solution

The standard stock solutions (100 µg/ml) of each of Paracetamol and Domperidone were prepared separately by dissolving accurately about 10 mg of drug in 20 ml of 0.1N NaOH and volume was made up to 100 ml with 0.1N NaOH. Working standard solutions of 10 µg/ml were scanned in the entire UV range of 200 - 400 nm to obtain the absorbance.

Preparation of calibration curves

Solutions of 10 µg/ml of PARA and DOM each were prepared separately. Both the solutions were scanned in the spectrum mode from 200-400 nm. The maximum absorbance of PARA and DOM were at 258 nm and 292 nm, respectively. PARA and DOM obeys Beers-Lamberts law in the concentration range of 5-30 µg/ml at their respective maxima[6,7]. Accurately measured standard stock solution of PARA and DOM (0.5, 1.0, 1.5, 2.0, 2.5, 3.0 ml) were transferred to a separate series of 10 ml of volumetric flasks and diluted to the mark with 0.1N NaOH. The absorbance of each solution was measured at wavelength 258 nm and 292 nm. The coefficient of correlation was found to be 0.995 and 0.997 for PARA and DOM respectively.

Method I: Simultaneous Equation Method

Sample stock solution was appropriately diluted with 0.1N NaOH to obtain final concentration of 10 µg/ml for PARA and DOM. These solutions were scanned in the wavelength range of 200 – 400 nm. From the overlain spectrum, two wavelengths namely 258 nm and 292 nm, λ-max of PARA and DOM respectively were selected. The calibration curves were constructed in the concentration range of 5-30 µg/ml for PARA and DOM. The concentration of drugs was determined by using the Equations 1 and 2. Mention in paragraph where would be[8-10]; Figure 1.

$$A1 = 0.0859\ Cx + 0.0337Cy \quad \text{.....(1)}$$
$$A2 = 0.00093\ Cx + 0.0267Cy \quad \text{.... (2)}$$

Where, A1 and A2 are absorbance of sample at 258 nm and 292 nm, respectively. 0.0859 and 0.0337 are absorptivities of PARA at 258 nm and 292 nm respectively. 0.0093 and 0.0267 are absorptivities of DOM at 258 nm and 292 nm respectively. Cx and Cy are concentrations of and PARA and DOM respectively.

Method II: Dual Wavelength Method

In this method, PARA was determined by plotting the difference in absorbance at 247 nm and 269 nm (difference was zero for DOM) against the concentration of PARA (Figure 2). Similarly for the determination of DOM, the difference in absorbance at 288 nm and 296 nm (difference was zero for PARA) was plotted against the concentration of DOM (Figure 3). Standard solutions were prepared having concentration 5-30 µg/ml for both drugs. The difference in absorbance at 247 nm and 269 nm were plotted against the concentration of PARA and that at 288 nm and 296 nm were plotted against the concentration of DOM to construct two separate calibration curves for DOM and PARA[3,11].

Method III: Area under Curve Method

For the simultaneous determination using the Area under curve method, suitable dilutions of the standard stock solutions (100 µg/ml) of PARA and DOM were prepared separately in 0.1 N NaOH. The solutions of drugs were scanned in the range of 200 nm - 400 nm. For Area Under Curve method, calibration curve was plotted and the sampling wavelength ranges selected for estimation of PARA and DOM are 242 nm - 275 nm (λ1-λ2) and 284 nm - 302 nm (λ3-λ4) respectively (Figure 4) and area were integrated between these selected wavelength ranges for both drugs, which showed linear response with increasing concentration hence the same wavelength range were used for estimation of tablet formulations. By using integrated areas two simultaneous equations were constructed and solved to determine concentrations of analytes[12-14]. Concentration of two drugs in mixed standard and the sample solution were calculated using equation (3) and (4).

$$CPARA = A2ay1 - A1ay2 / ax2ay1 - ax1ay2 \quad (3)$$
$$CDOM = A1ax2 - A2ax1 / ax2ay1 - ax1ay2 \quad (4)$$

Where, aX1 (859.80) and aX2 (337.83) are absorptivities of PARA at (λ1-λ2) and (λ3-λ4) respectively. aY1 (93.26) and ay2 (267.13) are absorptivities of DOM at (λ1-λ2) and (λ3-λ4) respectively. A1 and A2 are Absorbance of mixed standard at (λ1-λ2) and (λ3-λ4) respectively. CPARA and CDOM are the concentrations in g /100 ml.

Analysis of Tablet Formulation

Twenty tablets were weighed and crushed to a fine powder. An accurately weighed powder sample equivalent to 10 mg of Paracetamol was transferred to a 100 ml volumetric flask, dissolved in 100 ml 0.1N NaOH, shake for 10 minutes and the volume was made up to the mark with 0.1N NaOH. The solution was then filtered through Whatman filter paper no. 41. The solution was further diluted to get different concentrations in the range of 5-30 µg/ml of both the drugs. The spectra of Paracetamol and Domperidone when overlaid indicated that the spectra of Paracetamol and Domperidone satisfied this condition. The result of analysis of the formulation is shown in Table 1 and 2.

Validation of Method

Validation of the proposed methods was carried out for its accuracy, precision, specificity and linearity according to ICH guidelines[6,14].

Accuracy

Recovery studies were carried out at three different levels by adding the pure drug to previously analyzed tablet powder sample. Accurately weighed quantities of tablet powder equivalent to 80 %, 100 % and 120 % of label claim of PARA were taken in a series of 100 ml volumetric flasks and dilutions were made as under sample solution. The graphs of % label claim vs. absorbance were plotted for Method I, II and III. From the amount of drug total drug found, percentage recovery was calculated by proposed four methods and results are shown in Table 3.

Precision

Inter-day precision

It was done by analyzing the solutions by same analyst on alternate days till 5th day. Results indicate that the solution is stable up to 1 day, thereafter degradation may have taken place leading lower percent label claim.

Intra-day precision

It was done by analyzing the solutions by same analyst within a day. Results indicate that the solution is stable up to 4 hours and thereafter, degradation may have taken place in the solution.

Linearity

Linearity was checked by diluting standard stock solution at six different concentrations. Paracetamol was with the concentration range of 5–30 µg/ ml at 258 nm. Domperidone was linear in the concentration range of 5–30 µg/ ml at 292 nm. Calibration curves (n = 6) were plotted between concentration and absorbance of drugs. Optical parameters were calculated.

Limit of detection

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula and shown in Table 1.

$$LOD = 3.3 (\sigma / S)$$

Where, S = slope of calibration curve, σ = standard deviation of the response.

Limit of quantification

The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives a response that can be accurately quantified. LOQ was calculated using the following formula and shown in Table 1.

$$LOQ = 10 (\sigma / S)$$

Where, S = slope of calibration curve, σ = standard deviation of the response.

RESULT AND DISCUSSION

PARA and DOM has estimated at 258 nm and 292 nm in 0.1N NaOH solution, both drugs obey Beer-Lamberts law in concentration range of 5-30 µg/ml. The method was validated as per ICH and USP guidelines. The result of recovery study was found to be within the prescribed limit of 98 – 101 %. The assay results obtained by proposed methods as shown in Table 1 and 2. The % R.S.D. Linearity was observed by linear regression equation method for PARA and DOM in different concentration range. The Correlation coefficient of these drugs was found to be close to 1.00, indicating good linearity, hence it can be used for routine analysis of two drugs in combined dosage forms. There was no interference from tablet excipients was observed in these methods. These methods were accurate, simple, rapid, precise, reliable, sensitive, reproducible and economic.

Table 1: Spectral and linearity characteristics data

Parameters	Method I		Method II		Method III	
	PARA	DOM	PARA	DOM	PARA	DOM
Beer's Law limit (µg/ml)	5-30	5-30	5-30	5-30	5-30	5-30
Coefficient of correlation	0.9956	0.996	0.994	0.998	0.9949	0.9995
Intercept	0.0491	0.0078	0.005	0.008	0.3425	0.0029
Slope	0.0789	0.0283	0.007	0.013	0.5437	0.0866
LOD	0.3054	0.3153	0.3102	0.3363	0.3178	0.5084
LOQ	0.9255	1.9564	1.9400	1.7010	1.9631	1.1540

Table 2: Result of Analysis of tablet formulation

Methods	Standard Deviation		% Relative Standard Deviation		Standard Error Mean	
	PARA	DOM	PARA	DOM	PARA	DOM
Method I	0.7219	0.2676	0.5019	0.5514	0.2947	0.1092
Method II	0.0653	0.1325	0.4852	0.4852	2.1353	0.3305
Method III	5.2304	0.8095	0.5737	0.5328	0.0267	0.0541

Table 3: Result of recovery study

Method	Label Claim (mg/tab)		Amount Claim (mg/tab)		% Label Claim found		% Recovery	
	PARA	DOM	PARA	DOM	PARA	DOM	PARA	DOM
I	500	10	485.0	09.80	97.00	98.00	99.45	99.86
II	500	10	489.5	09.84	97.90	98.40	98.60	100.20
III	500	10	493.5	09.81	98.74	98.10	98.65	100.05

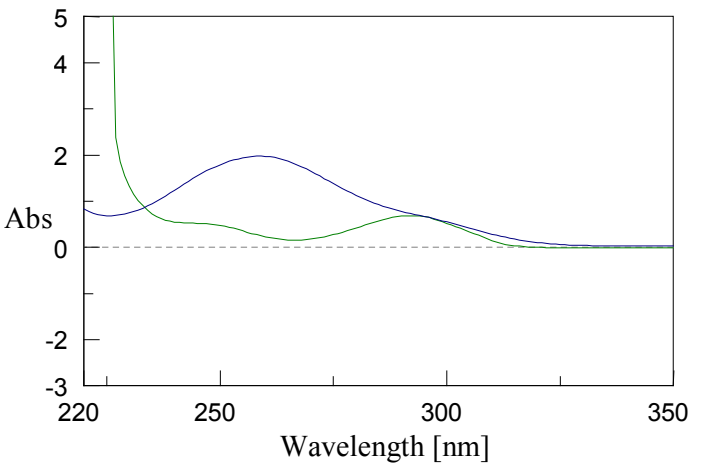

Figure 1: Overlay Spectrum for Paracetamol and Domperidone

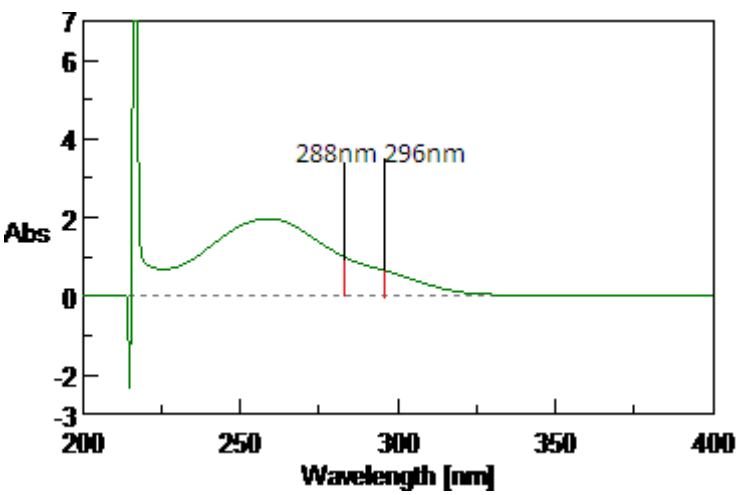

Figure 2: Spectra for Paracetamol in Dual Wavelength Method

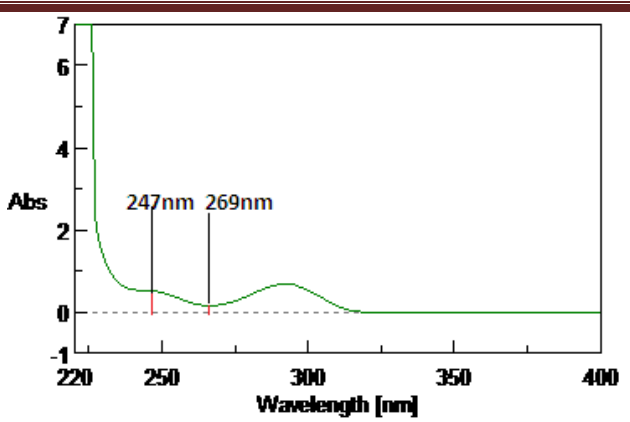

Figure 3: Spectra for Domperidone in Dual Wavelength Method

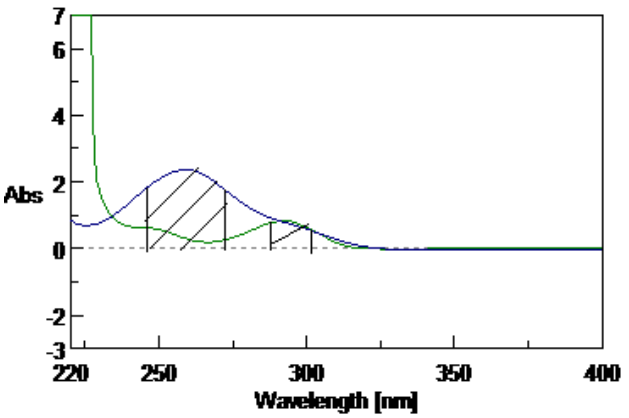

Figure 4: Overlay spectra for Paracetamol and Domperidone for AUC

CONCLUSION

Simple UV spectrophotometric methods were developed for the simultaneous determination of Paracetamol and Domperidone in bulk and tablet formulation, both the results of our study indicate that drugs analyzed ate wavelength 258 nm and 292 nm respectively. The main recovery was 98.9 % for PARA and 100.04 % for DOM respectively. Statistical analysis proves that, these methods are repeatable and selective for the analysis of PARA and DOM.

Abbreviations:
PARA- Paracetamol,
DOM- Domperidone

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