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Original Article

Different Methods for Spectrophotometric Estimation and Validation of Paracetamol and Domperidone in Pure and Tablet Dosage Form.

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Abstract

Two simple, accurate and precise spectrophotometric methods were developed for simultaneous determination of Paracetamol and Domperidone in combined pharmaceutical dosage form. The first method is Dual wavelength method principle for which is "the absorbance difference between two points on the mixture spectra is directly proportional to the concentration of the component of interest" and second method is Area under curve. In first method wavelengths selected for determination of paracetamol were 278.0 nm and 287.0 nm, whereas, the wavelengths selected for determination of Domperidone were 236.0 nm and 252.0 nm. In second method wavelength ranges of 237.0-251.0 nm and 275.0-289.0 nm were selected to determine PARA and DOM respectively by AUC. 0.5 M Methanolic HCl was taken as a solvent. Regression analysis of Beer's plots showed good correlation in concentration range of 5-25 µg/ml for PARA and 5-25 µg/ml for DOM. The precision by repeatability of method was found within limits. The proposed method was successfully applied to determination of these drugs in commercial tablets.

Keywords: Dual wavelength, Area under curve, Paracetamol, Domperidone.

1. Introduction

Chemically, Paracetamol (PARA) is 4-hydroxy acetanilide. It has centrally and peripherally acting non-opioid analgesic and antipyretic activity. Domperidone (DOM) 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, DOM (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, UV are available for individual determination of domperidone and paracetamol or in combination with other drugs. However there are no spectrometric Dual wavelength and AUC methods available for the simultaneous determination of paracetamol and domperidone by using methonolic HCl. 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.

2. Materials and Methods

2.1. Instrumentation

The instrument used for the present study was double beam UV/Visible spectrophotometer with 10 mm matched quartz cell. (Model Jasco 1700)

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2.2. Reagent and chemicals

Standard gift samples of Paracetamol and Domperidone were procured. Tablets containing both Paracetamol and Domperidone were purchased from local market. Tablet used for analysis was EMEGREN containing PCT 500 mg and DOM 20 mg per tablet. 0.5 M methanolic HCl and distilled water were used as solvent.

2.3. Preparation of standard stock solution and calibration curve

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.

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 244 nm and 284 nm, respectively. PARA and DOM both showed linearity in the concentration range of 5-25 µg/ml at their respective maxima. Accurately measured standard stock solution of Paracetamol and domperidone (0.5, 1.0, 1.5, 2.0, 2.5 ml) were transferred to a separate series of 10 ml of volumetric flasks & diluted to the mark with distilled water. The absorbance of each solution was measured at wavelength 244 nm & 284 nm. The coefficient of correlation was found to be 0.991 for PARA and 0.994 for DOM.

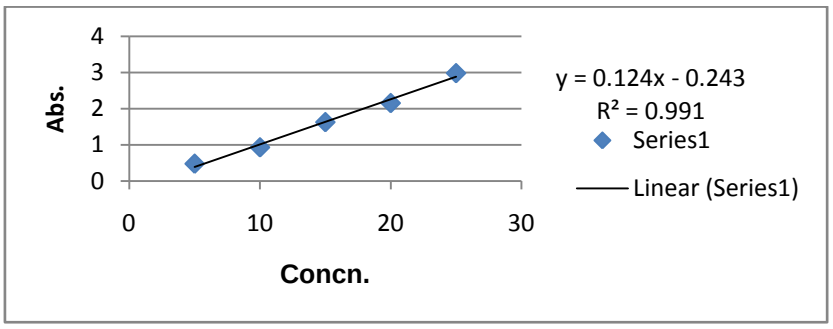

Fig 1: Linearity of PARA (5 – 25 µg/mL).

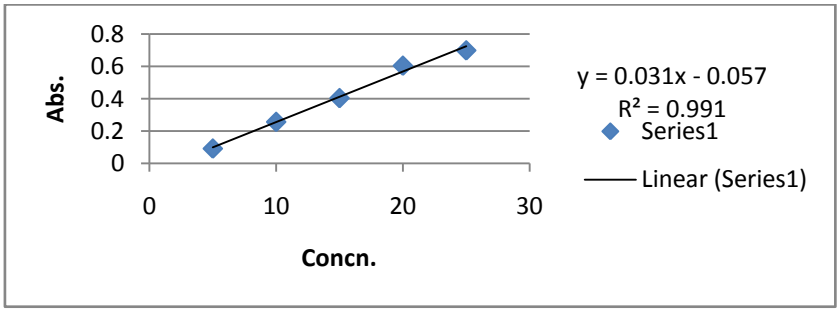

Fig 2: Linearity of DOM (5 – 25 µg/mL).

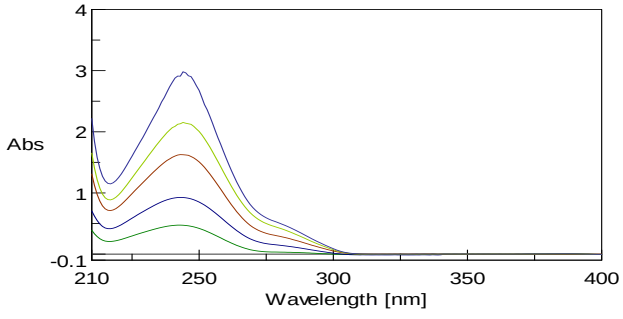

Fig 3: Overlay spectra of PCT (5 – 25 µg/mL).

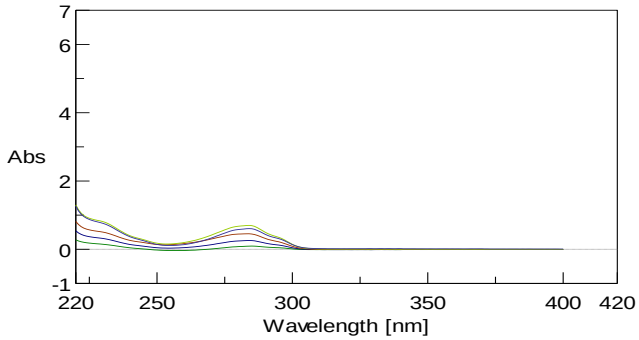

Fig 4: Overlay spectra of DOM (5 – 25 µg/mL).

2.4. Analysis of tablet formulation

For the estimation of drugs in the marketed preparations, 20 tablets containing 20 mg of Domperidone and 500 mg paracetamol (Emegren) were weighed and finely powdered. A quantity of powder equivalent to 10 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.41. Aliquots of this tablet solution were diluted to get the concentrations 5-25 µg/ml.

2.5. Theoretical Aspects

Method 1: Dual wavelength method

In this method difference in absorbance at two selected wavelength were calculated. The difference in absorbance at 278.0 and 287.0 nm was found to be zero for DOM. Hence these two wavelengths were selected for the determination of PARA. Similarly, 236.0 and 252.0 nm were selected for the determination of DOM, where the difference in absorbance was found to be zero for PARA. Zero order spectra were recorded for solutions of different concentration of DOM and PARA between 200:400nm. The difference in absorbance at and 278.0 nm and 287.0 nm were plotted against the concentration of PARA and that 236.0nm and 287.0 nm were plotted against the concentration of DOM to construct two separate calibration curves for PARA and DOM. The equations of line obtained to determine concentrations of PARA and DOM.

2.6. Method 2: Area under curve

For the simultaneous determination using the area under the curve method, suitable dilutions of the standard stock solutions (100 µg/mL) of PARA and DOM were prepared separately in 0.5 M methanolic HCl and distilled water. The solutions of drugs were scanned in the range of 200-400 nm. For Area under curve method, the sampling wavelength ranges selected for estimation of PARA and DOM were 237.0-251.0 nm (λ1-λ2) and 275-289 nm (λ3-λ4). Mixed standards were prepared and their Area under the Curve were measured at the selected wavelength ranges. Concentration of two drugs in mixed standard and the sample solution were calculated using equation (1) and (2).

CPARA = A2 × aX2 - A1 × ay2 / aX2 × aY1 - aX1 × aY2……(1)

CDOM = A2 - aX2 × CPARA/ aY2 …… (2)

2.7. Validation of proposed method

The proposed method was validated as per the ICH guidelines for various parameters like accuracy, repeatability, Limit of Detection, Limit of Quantitation etc.

2.7.1. Accuracy

It was done by recovery study using standard addition method at 80%, 100% and 120% level; known amount of standard PARA and DOM was added to pre-analyzed sample (10 µg/mL of PARA and DOM) and subjected them to proposed method. Results of recovery studies are shown in Table 1.

Table 1: Accuracy.

Sr. no.	Initial conc. (µg/mL)		Conc. of excess drug added to analyte (µg/mL)		Conc. found (µg/mL)		% Recovery		% RSD	
	PARA	**DOM**	**PARA**	**DOM**	**PARA**	**DOM**	**PARA**	**DOM**	**PARA**	**DOM**
1	10	0.4	8	0.32	17.94	0.718	99.33	99.37	0.918	0.311
2	10	0.4	10	0.4	19.93	0.78	99.3	95.58	0.755	1.8
3	10	0.4	12	0.48	21.91	0.883	99.24	100.6	0.885	1.21

2.7.2. Repeatability

Six test sample solutions containing 50 µg/mL of PARA and 2 µg/mL of DOM were scanned over range of 200-400 nm and absorbance are measured at 244 nm and 284 nm respectively, concentrations were determined with the help of proposed method and % RSD was calculated and results are given in Table 2.

2.7.3. Limit of Detection and Quantification (LOD & LOQ)

The LOD and LOQ were estimated from the standard calibration curve. It is calculated using the formula i.e. LOD = 3.3 × $\frac{\sigma}{S}$ and LOQ = 10 × $\frac{\sigma}{S}$ where, σ is the standard deviation of the response and S is slope of the calibration curve.

Table 2: Repeatability.

Sr. no.	Concentration found (µg/mL)	
	PARA	**DOM**
1	50.19	2.01
2	50.10	1.99
3	50.09	2.03
4	50.19	2.06
5	49.95	2.03
6	50.16	1.98
Mean	50.11	2.01
% RSD	0.1814	1.46

Table 3: Optical characteristics, Precision study and result of formulation analysis.

Parameter		**Paracetamol**		**Domperidone**	
		Method 1	**Method 2**	**Method 1**	**Method 2**
Wavelength (nm)		278 & 287	237 & 251	236 & 252	275 & 289
Beer's law limit (µg/mL)		5 – 25	5 - 25	5 -25	5 -25
Regression Equation*	**Slope (m)**	0.008	0.148	0.015	0.054
	Intercept (c)	-0.030	-0.475	0.021	0.003
Correlation coefficient (r)		0.997	0.996	0.996	0.998
Formulation Analysis (% Assay)		100.8	100.3	101.65	99
LOD (µg/mL)		0.267	0.261	0.275	0.262
LOQ (µg/mL)		0.812	0.792	0.836	0.798

RSD= Relative standard Deviation, Y= mX + C, where Y is the absorbance and X is the concentration in micrograms per milliliter.*

Result and Discussion

The overlain spectra of drugs showed the λ max of 244.0 nm and 284.0 nm for PARA and DOM respectively. Both the drugs obeyed linearity range 5-25µg/ml and 5-25µg/ml respectively and correlation coefficient (r2) were found to be <1 in both cases. The absorptivity values were calculated and along with absorbances, The percentage purity of drugs in combined dosage form was found to be 100.8 & 100.3% for PARA and 101.65 & 99% for DOM. The accuracy of both methods were determined by performing recovery study by standard addition method. The % recoveries were found to be 99.29 % for PARA and 98.51 for DOM. The precision was determined by performing repeatability study. The methods were found to be precise as % RSD were < 2.

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.

References

[1] The Indian Pharmacopoeia, Govt. of India, Ministry of Health and Family Welfare Controller of Publication, III, 2007, 1514.
[2] R. Sawant, L. Bhangale, R. Joshi, P. Lanke. J. Chem. Metrol., 4, 1 (2010) 21-27.
[3] Kapil Kalra, S. Naik, Jarmal Garima, N. Mishra. Asian J. Research Chem., 2, 2 (2009) 112-114.
[4] P. Venkatesh, K.D. Hepcy, Ravindra Reddy K. RJPBCS, 1, 3 (2010) 155-164.
[5] S. J. Babar, V. B. Mane, S. B. Bhise. International Journal of Pharmacy and Pharmaceutical Sciences, 4, 4 (2012) 206-209.

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