International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.6, No.1, pp 323-329, Jan-March 2014

Simultaneous Estimation and Development of UV Spectroscopic Method for Determination of Cinnarizine and Domperidone in Bulk and Pharmaceutical Formulation

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Abstract: The present work represents a UV spectrophotometric method for the simultaneous estimation of cinnarizine and domperidone in bulk and combined tablet dosage form. Methanol was used as solvent for preparation of stock solution and further dilutions were prepared in 1% v/v phosphoric acid. Cinnarizine and domperidone exhibit absorption maxima at 253 nm and 284 nm respectively. The developed simultaneous equation method obeyed Beer-Lambert's law in the concentration range of 5-30 µg/ml for both the drugs. The analytical method was validated for various parameters as per ICH (International Conference on Harmonization) guidelines. The proposed method was found to be simple, rapid, accurate and precise and can be applied for the routine quality control studies for assay of cinnarizine and domperidone in bulk and tablet dosage forms.
Keywords: UV spectrophotometry, cinnarizine, domperidone and validation.

Introduction

Cinnarizine (CIN) is chemically 1-(diphenyl methyl)-4-(3-phenyl-2-propenyl) piperizine (Figure 1). It is an antihistaminic drug blocking the histamine H1 receptors. It is weak antimuscarinic and shows local anesthetic activity. Cinnarizine is sedative calcium antagonist. Cinnarizine inhibits contractions of smooth muscle cells by blocking calcium channels [1, 2].

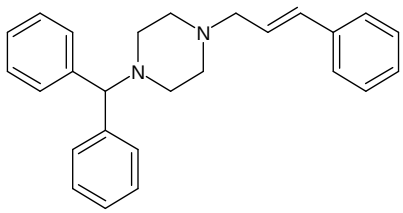

Figure 1: Structure of Cinnarizine

Domperidone (DOM) is chemically 5-Chloro-1-[1-[3-(2-oxo-1, 3-dihydrobenzimidazol-1-yl]-4-piperidyl]-1, 3-dihydrobenz imidazol-2-one maleate (Figure 2). Domperidone acts as a gastrointestinal emptying (delayed adjunct and peristaltic stimulant). The gastroprokinetic property of domperidone is related to its peripheral dopamine receptor blocking properties [3, 4].

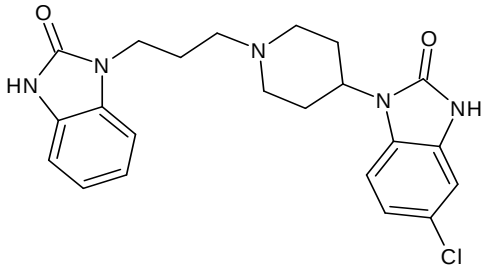

Figure 2: Structure of Domperidone

This paper is in continuation with our work [12-16] where we studied spectrophotometric method for single or multicomponent drugs. Literature survey revealed that UV and HPLC methods have been developed on single CIN and DOM or their combination with other drugs [7, 8, 9, 10, and 11]. But no UV spectrophotometric method is developed for simultaneous estimation of CIN and DOM in pharmaceutical dosage forms. The proposed method is found to be simple, rapid, accurate, and precise. It can be applied for the routine quality control studies for assay of CIN and DOM in bulk and tablet dosage forms.

Materials and Methods

Materials

Standard gift samples of CIN and DOM were kindly provided by Preet Remedies Ltd., Baddi, Himachal Pradesh. Combined dose tablet formulation Vertidome (20 mg of CIN and 15 mg of DOM, Manufactured by Geno pharmaceuticals), was purchased from local market of Nanded, (MS). All chemicals and reagents used were of AR grade and purchased from Rankem Pvt. Ltd.

Instrumentation

The Shimadzu UV/Vis 1800 double beam spectrophotometer with photomultiplier tube detector was used. The absorption spectra were recorded over the wavelength range 200-400 nm against the solvent blank. Anamed digital balance was used for weighing samples.

Method

Selection of solvent

Methanol gave spectra without noise, and as it is economical, it was selected as a solvent for the preparation of stock solution. Further dilutions were made with 1% v/v phosphoric acid in order to find the optimum conditions for spectrophotometric estimation of CIN and DOM.

Selection of analytical wavelength

Sample solutions were scanned over the wavelength range of 200 nm to 400 nm. λ_{max} for CIN and DOM were found at 253 nm and 284 nm respectively. Representative absorption spectra of DOM and CIN are shown in Figure 3 and 4 respectively. The overlain absorption spectrum is shown in figure 5.

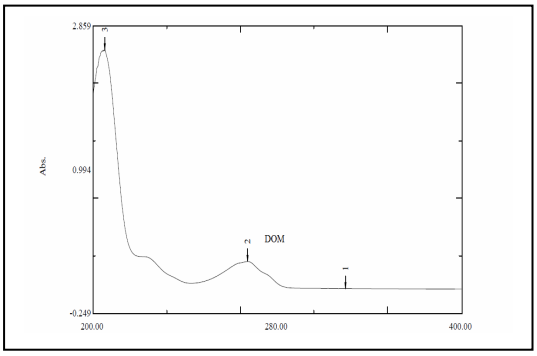

Figure 3: UV visible spectrum of DOM

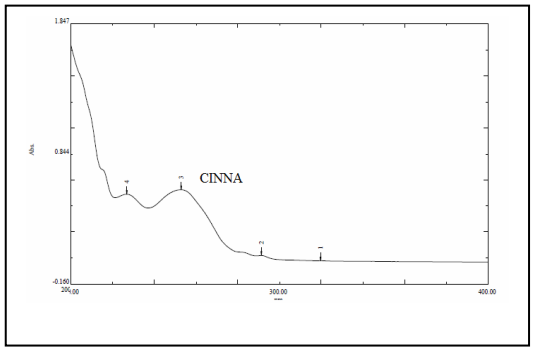

Figure 4: UV visible spectrum of CIN

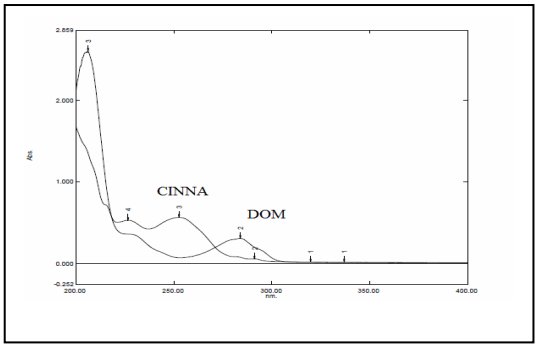

Figure 5: Overlain spectra of CIN and DOM

Preparation of stock solution

CIN stock solution (100µg/ml)

The stock solution of CIN was prepared in methanol. Accurately weighed 10 mg quantity was dissolved in 100 ml of methanol in 100 ml volumetric flask. It was sonicated for 10 min. Further dilutions were made in 1% v/v solution of phosphoric acid.

DOM stock solution (100µg/ml):

The stock solution of DOM was prepared in methanol. Accurately weighed 10 mg quantity was dissolved in 100 ml of methanol in 100 ml volumetric flask. It was sonicated for 10 min. Further dilutions were made in 1% v/v solution of phosphoric acid.

Procedure

Simultaneous equation method

Determination of E (1%, 1cm) of Drugs at Selected Wavelengths

For determination of E (1%, 1cm), aliquot portions of CIN and DOM were diluted separately by 1% v/v phosphoric acid to obtain concentration 10 and 7.5 µg/ml respectively. The absorbance of each resulting solution was measured at 253 nm and 284 nm. The E (1%, 1cm) values (ax1, ax2, ay1& ay2) were determined from five different concentrations of 10 and 7.5 µg/ml of CIN and DOM using following equation 1.

The absorptivity values of CIN and DOM are reported in Table No 1 and 2 respectively.

$$E = \frac{abs}{conc\ (g/100ml)} \quad \ldots \text{eq.1}$$

Table No. 1: Absorptivity values of CIN

Sr. no.	Conc. (gm/ml)	Absorbances		Absorptivity	
		253 nm	**284 nm**	**253 nm**	**284 nm**
1	0.01	0.812	0.056	81.2	5.60
2	0.01	0.810	0.055	81.0	5.50
3	0.01	0.812	0.055	81.2	5.50
4	0.01	0.811	0.054	81.1	5.40
5	0.01	0.811	0.053	81.1	5.30
			Mean	81.12	5.40
			SD	0.0836	0.1140

Table No. 2: Absorptivity values of DOM

Sr. no.	Conc. (gm/ml)	Absorbances		Absorptivity	
		253 nm	**284 nm**	**253 nm**	**284 nm**
1	0.01	0.073	0.377	7.30	37.7
2	0.01	0.072	0.376	7.20	37.6
3	0.01	0.072	0.378	7.20	37.8
4	0.01	0.074	0.377	7.40	37.7
5	0.01	0.075	0.374	7.50	37.4
			Mean	7.32	37.64
			SD	0.1303	0.1516

Analysis of tablet formulation

Twenty tablets were weighed; average weight was determined and triturated to produce fine powder. A quantity equivalent to 20 mg of CIN and 15 mg of DOM was weighed and transferred to 100 ml volumetric flask; the volume was made up with methanol. This solution was appropriately diluted with 1% v/v phosphoric acid to get concentration of 10 µg/ml of Cinnarizine and 7.5 µg/ml of domperidone. The absorbances of sample solutions were measured at 253 nm and 284 nm against blank. The contents of CIN and DOM in tablet dosage form were calculated using two framed simultaneous equations and the results of analysis of tablet formulation are reported in Table No 3.

Table No. 3: Analysis of tablet formulation

Drug	Labeled amount (mg)	Estimated amount (n)	% Estm. amt. ± SD	% RSD
CIN	20	19.98	99.90 ± 0.8679	0.8688
DOM	15	14.86	99.06 ± 0.7653	0.7723

(n) denotes average of 6 determinations.

Method Validation

The method was validated for linearity, accuracy (recovery), precision, and sensitivity. The method validation was performed as per ICH guidelines [5, 6].

Linearity

By appropriate dilution of the standard stock solution, different dilutions were prepared ranging from 5µg/ml to 30µg/ml of both CIN and DOM. Absorbances of all the dilutions were taken at λ_{max} of CIN and DOM i.e. 253 nm and 284 nm respectively. The absorbances were plotted against the respective concentrations to obtain the calibration curves (Figure 6 and 7). The r^2 value obtained was 0.999 for CIN and DOM respectively.

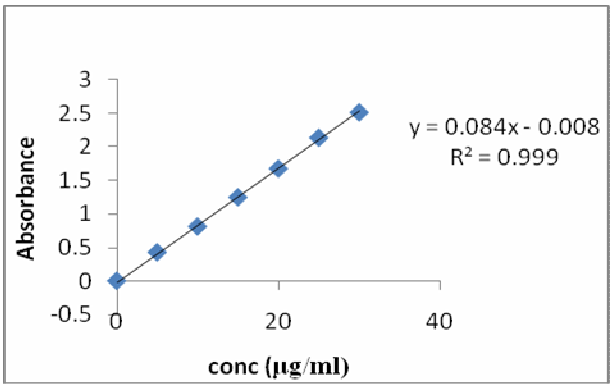

Figure 6: Calibration curve for CIN

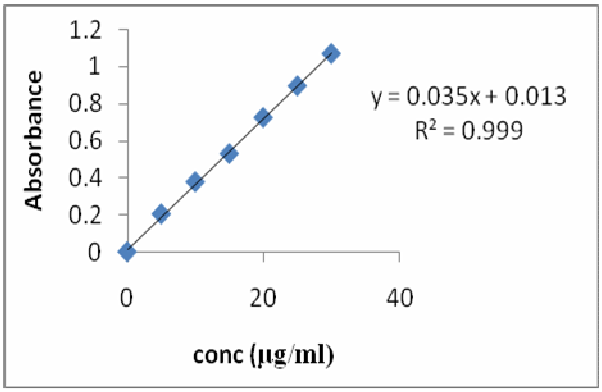

Figure 7: calibration curve of DOM

Precision

Precision of the method was verified by using tablet stock solution. The repeatability indicates the performance of the UV instrument. Intraday precision was determined by repeating assay six times in the same day and on different day for interday precision studies. The results of this analysis are shown in Table No 4.

Table No. 4: Precision Study

	Repeatability		Intraday		Interday	
	CIN	**DOM**	**CIN**	**DOM**	**CIN**	**DOM**
%Mean (n)	100.06	100.05	98.97	99.63	99.95	99.67
SD	0.2938	0.3057	0.0404	0.0519	0.1493	0.2983
% RSD	0.2936	0.3055	0.0408	0.0520	0.1494	0.2992

(n) denotes average of 6 determinations.

Accuracy

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. The recovery studies were performed by standard additional method. The results of recovery studies were found to be satisfactory and as reported in Table No. 5.

Table No. 5: Accuracy Study

Level (%)	% Mean (n) ± SD		% RSD	
	CIN	DOM	CIN	DOM
80	99.45 ± 0.1167	99.59 ± 0.0776	0.1173	0.0779
100	99.80 ± 0.0321	99.97 ± 0.0513	0.0322	0.0514
120	99.72 ± 0.4007	99.71 ± 0.3702	0.4017	0.3712

(n) denotes average of 6 determinations

LOD &LOQ

The limit of detection and limit of quantification i.e. LOD & LOQ were calculated by use of the equations LOD = 3.3 × σ/s and LOQ = 10 × σ/s, where σ is the standard deviation of the response areas of the drugs, taken as a measure of noise, and s is the slope of the corresponding calibration plot.

The LOD and LOQ were 0.0389 µg/ml and 0.1287 µg/ml for cinnarizine and 0.0933 µg/ml and 0.3088 µg/ml for domperidone respectively.

Result and Discussion:

The present study was carried out to develop a simple, rapid, sensitive, accurate, precise spectrophotometric method to determine cinnarizine and domperidone by simultaneous estimation of in tablet formulation. The standard deviation values were satisfactorily low and recovery was closed to 100% indicating the reproducibility, accuracy and precision of proposed method. The linearity study performed for both the components and absorptions were found to be linear in the concentration range 5 µg/ml to 30 µg/ml. Summary of analytical method validation is reported in Table No 6.

Table No. 6: Analytical Method Validation Summary

Parameter		CIN	DOM
Linearity		5-30 µg/ml	5-30 µg/ml
Correlation coefficient (r^2)		0.999	0.999
Precision (%RSD)	Intraday	0.0408	0.0520
	Interday	0.1494	0.2992
Accuracy (%)	80%	99.45	99.59
	100%	99.80	99.97
	120%	99.72	99.71
Repeatability		0.2936	0.3055
LOD (µg/ml)		0.0389	0.0933
LOQ (µg/ml)		0.1287	0.3088

Conclusion

The result indicates that the method was simple, accurate and precise. Hence it can be used for the analysis, which would involve detection of absorbance of sample and standard solution at two wavelength and single calculation.

Acknowledgement

Authors are thankful to 'Preet Remedies, Baddi, Himachal Pradesh' for providing us the gift sample of the pure drug and also to the Director of School of Pharmacy, S.R.T.M. University, Nanded, for providing research facilities.

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