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DEVELOPMENT AND VALIDATION OF NEW ANALYTICAL METHOD FOR THE SIMULTANEOUSS ESTIMATION OF PANTOPRAZOLE AND DOMPERIDONE BY UV-SPECTROPHOTOMETRY

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ABSTRACT

A simple, rapid and precise method is developed for the quantitative simultaneous determination of Pantoprazole and Domperidone in combined pharmaceutical-dosage forms. The method was based on UV-Spectrophotometric determination of two drugs, using simultaneous equation method. It involves absorbance measurement at 290 nm (λ_{max} of Pantoprazole) and 287 nm (λ_{max} of Domperidone) in MeOH:ACN(60:40v/v). For UV Spectrophotometric method, linearity was obtained in concentration range of 1-15 µg/ml for domperidone and 1-50 µg/ml for Pantoprazole respectively, with regression 0.999 and 0.995 for Domperidone and Pantoprazole respectively. Recovery was in the range of 99 -103%; the value of standard deviation and %R.S.D were found to be < 2 %; shows the high precision of the method., in accordance with ICH guidelines. The method has been successively applied to pharmaceutical formulation and was validated according to ICH guidelines.

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INTRODUCTION

Analytical chemistry may be defined as the science and art of determining the composition of material in terms of elements or compounds contained in it. Analytical chemistry is divided into two branches quantitative and qualitative. Analytical methods developed using sophisticated instruments such as spectrophotometer, HPLC, GC and HPTLC have wide applications in assuring the quality and quantity of raw materials and finished products. The main types of instruments in use for measuring the emission or absorption of radiant energy from substances are called by various names such as Photometer, Colorimeter and Spectrophotometer. Domperidone:5-Chloro-1-[1-[3-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1yl)propyl]piperidin-4-yl]-1,3-Dihydro-2H-benzimidazol-2 onehydrogen (*Z*) butenedioate. It is used as Peripheral dopamine receptor antagonist, antiemetic. Domperidone is also used to prevent stomach problems such as nausea and vomiting associated with certain medications used to treat parkinson's disease. Pantoprazole: Sodium 5-(difluoromethoxy)-2-[(*RS*)-[(3,4-dimethoxypyridin-2-yl)methyl]sulphinyl]benzimidazol-1-idesesquihydrate. It is used as Proton pump inhibitor; treatment of peptic ulcer disease. It helps treat painful symptoms caused by conditions such as gastroesophageal reflux disease(GERD) and it also used used to treat other conditions in which the stomach makes excess acid, such as Zollinger-Ellison syndrome. The specific aim/objective of the research was to develop UV Spectrophotometric method for the simultaneous estimation of Pantoprazole and Domperidone in bulk and pharmaceutical dosage form and validate the proposed method in accordance with ICH guidelines for the intended analytical application.

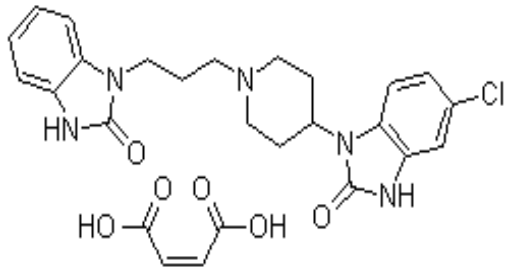


Fig no 1: Structure of Domperidone.

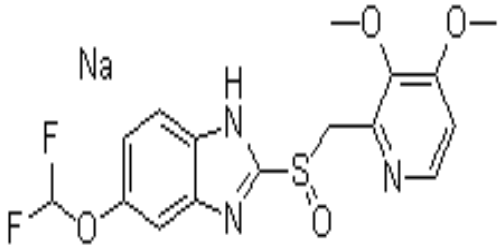


Fig no 2: Structure of Pantoprazole.

METHODOLOGY:

Calibration of UV-Visible Spectrophotometer:

The following measurements considered critical in calibration of a UV spectrophotometer

Calibration of Absorbance scale

Check the absorbance using potassium dichromate solution UV at the wavelength indicated below, which gives for each wavelength the exact value of A (1%, 1cm) and the permitted limits.

Wave length	A(1%,1cm)	Maximum tolerance
235	124.5	122.9-126.2
257	144.0	142.4-145.7
313	48.6	47.0-50.3
350	106.6	104.9-108.2

Detection and Control of Stray light

Stray light may be detected at a given wavelength with suitable filters or solutions; for example, the absorbance of a 1.2% w/v solution of potassium chloride at a path-length of 1cm should be greater than 2.0 at about 200nm when compared with water as reference liquid.

Method Development & Validation of UV-Spectrophotometer

Preparation of standard drugs solutions

Pure drug samples of Domperidone and Pantoprazole were dissolved separately in Methanol: Acetonitrile(60:40 v/v) so as to give several dilutions of standard in the concentration range of 1-15 mcg/ml for Domperidone and 1-50 mcg/ml for Pantoprazole respectively. All dilutions were scanned in the wavelength range of 190-400 nm.

Simultaneous equation method based on the principle that ,the total absorbance of the components in a mixture is the sum of individual absorbance ,two wavelength selected to frame the simultaneous equation method were at 287 and 290 nm for calibration curves, stock solutions of Domperidone and Pantoprazole in the concentration range of 1-15 mcg/ml and 1-50 mcg/ml. The absorbance of domperidone and Pantoprazole were measured at 287 nm and 290 nm, calibration curves were plotted .The absorptivities of both the drugs at both the wavelengths were determined.

PROCEDURE FOR ANALYSIS OF CAPSULE FORMULATION

Twenty capsules were weighed accurately. The average weight was determined and then ground to a fine powder. A quantity equivalent to 10 mg of domperidone and 20 mg of Pantoprazole were transferred into a 100 ml volumetric flask. The contents were ultrasonicated for 10 min with methanol, made to volume and filtered through Whatmann filter paper No.41. The solution was further diluted with methanol to give concentration of 10mcg/ml and 20mcg/ml of Domperidone and Pantoprazole respectively. Absorbances of these solutions were measured at 287 and 290 nm respectively.

U.V. validation

Linearity & Range

The linearity of calibration curves (Absorbance $V_{s.}$ concentration) in pure drug solution was checked over the concentration ranges of about 1-50 µg/ml and 1-15 µg/ml for Pantoprazole and Domperidone. The results were show in the table no-2 .

Accuracy

Accuracy of the method was determined by recovery experiments. To the formulation, the reference standards of the drug were added at the level of 80%, 100%, 120%. The recovery studies were carried out three times and the percentage recovery and percentage relative standard deviation of the recovery were calculated and shown in table no-3 and 4 .

Assay

Twenty capsules were weighed accurately. The average weight was determined and then ground to a fine powder. A quantity equivalent to 10 mg of domperidone and 20 mg of Pantoprazole were transferred into a 100 ml volumetric flask. The contents were ultrasonicated for 10 min with methanol, made to volume and filtered through Whatmann filter paper No.41. The solution was further diluted with methanol to give concentration of 10mcg/ml and 20mcg/ml of Domperidone and Pantoprazole respectively. The results are shown below in table no-4.

Precision

The data for Intraday and Interday precision studies at three different concentrations in the linearityrange. The%RSD values for Intraday and Interday precision were < 2%, indicating that the method was sufficiently precise. The results were shown in the table no-5 and 6 .

LOD & LOQ

The LOD & LOQ were separately determined based on the standard deviation of Y-intercept of the calibration curve. The standard deviation of the Y-intercept and the slope of the calibration curves were used to calculate the LOD and LOQ by using the equations 3.3*std.dev/slope for LOD, 10*std.dev/slope for LOQ. The results were shown in the table no-7 .

RESULTS& DISCUSSION

Results for UV-Spectrophotometer

The absorbance and absorptivities values at the particular wavelength of Pantoprazole and Domperidone can be obtained from the following Table:1

λ_{max} of Pan=290 nm, λ_{max} of Dom=287 nm. Both drugs are soluble in Methanol and Acetonitrile.

Table:1 Absorbance and values at the particular wavelength of Pantoprazole and Domperidone and Capsule.

S.No	Name of Drug	λ_1 at 287 nm	λ_2 at 290 nm
1	Pantoprazole	ax_1=0.03680233	ax_2=0.0371652
2	Domperidone	ay_1=0.02731832	ay_2=0.0257032
3	Capsule	A_1=1.092	A_2=1.084

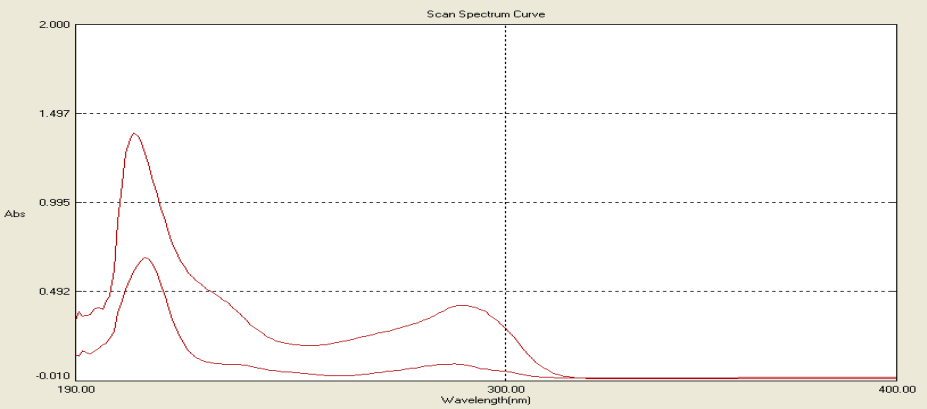


Fig no:1 Overlain Spectra of Pantoprazole& Domperidone.

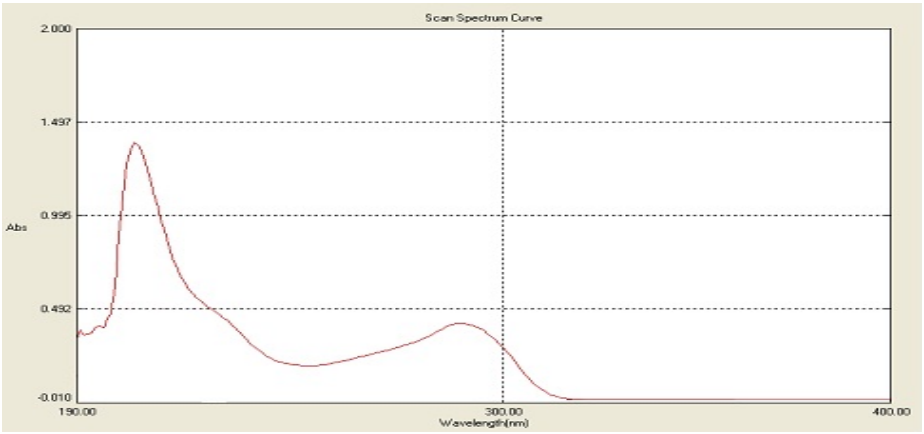


Fig no:2 Spectra of Pantoprazole.

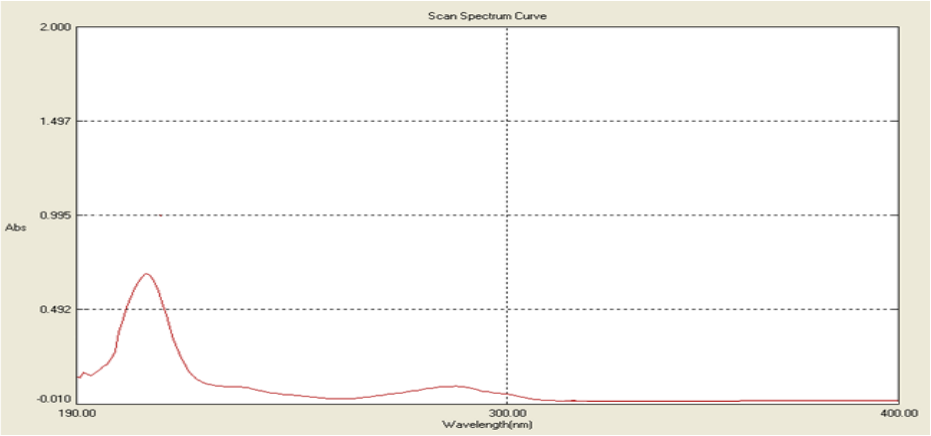


Fig no:3 Spectra of Domperidone.

$C_{x=}$ $A_1*ay_2-A_2*ay_1/ (ax_2*ay_1)-(ax_1*ay_2)$
C_y $= A_2*ax_1-A_1*ax_2/ (ax_2*ay_1)-(ax_1*ay_2)$
Therefore C_x= 20.28 µg/ml, C_y=9.952 µg/ml.

Linearity

Table:2 Linearity Values of Pantoprazole and Domperidone.

Linearity of Pantoprazole **Linearity of Domperidone**

S.No	Concentration	Absorbance	S.No	Concentration	Absorbance
1	10	0.395	1	2	0.054
2	20	0.779	2	4	0.111
3	30	1.085	3	6	0.163
4	40	1.418	4	8	0.219
5	50	1.788	5	10	0.273

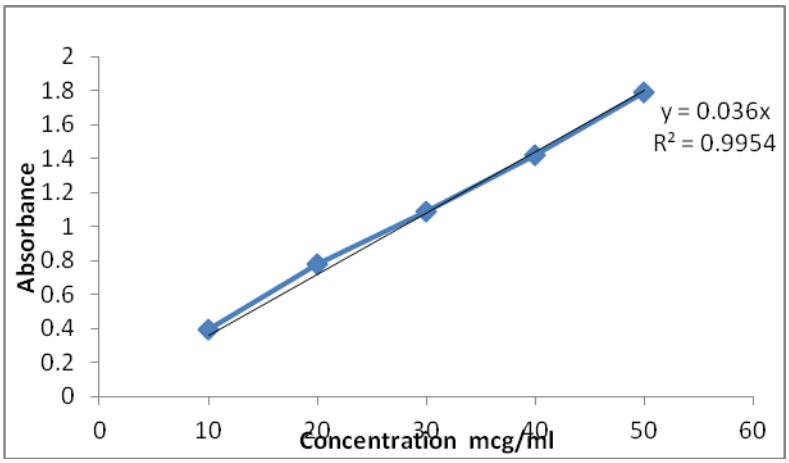


Fig-4 Calibration curve of Pantoprazole at 290 nm.

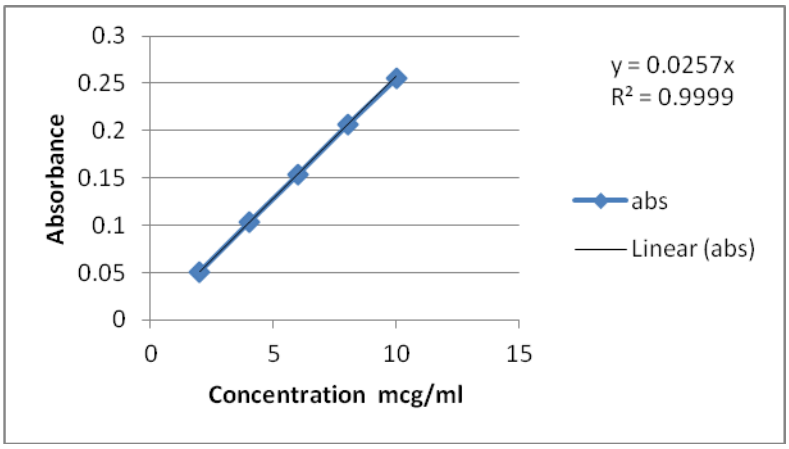


Fig- 5 Calibration curve of Domperidone at 287 nm.

Accuracy:

Table:3 Recovery Reports of Pantoprazole and Domperidone

Drug	QC Conc. (µg/ml)	Amount of Drug added	Amount of Drug found(µg/ml) Mean± S.D	% RSD	% Recovery
		80%	8.83±0.049	0.554	98.56
		100%	10.04±0.028	0.028	100.6
Pan	5	120%	11.1±0.028	0.254	101.7
		80%	9.04±0.014	0.155	100.3
		100%	9.93±0.021	0.213	99.23
Dom	5	120%	10.88±0.014	0.129	99.2

Table: 4 Accuracy values.

Drug	Label claim mg/tablet	Amount added	Amount found	% Recovery	%RSD
Pantoprazole	20	20 mg	20.28 mg	100.4	0.282
Domperidone	10	10 mg	9.95 mg	99.5	0.132

Precision:

Table: 5 Interday studies of Pantoprazole and Domperidone.

DAY	Pantoprazole				Domperidone			
	287 nm		290 nm		287 nm		290 nm	
	Mean	%RSD	Mean	%RSD	Mean	%RSD	Mean	%RSD
1.	0.521	0.221	0.625	0.186	0.393	0.39	0.358	0.967
2.	0.464	0.777	0.561	0.617	0.355	0.281	0.290	0.689

Table:6 Intraday studies of Pantoprazole and Domperidone.

	Pantoprazole				Domperidone			
	287 nm		290 nm		287 nm		290 nm	
	Mean	%RSD	Mean	%RSD	Mean	%RSD	Mean	%RSD
1.	0.521	0.221	0.62	0.186	0.397	0.39	0.358	0.967
2.	0.512	0.406	0.61	0.433	0.375	0.38	0.336	0.595
3.	0.484	0.206	0.584	0.342	0.361	0.319	0.312	0.977

LOD & LOQ

Table:7 LOD & LOQ.

PARAMETER	PANTOPRAZOLE	DOMPERIDONE
LOD	0.264 µg/ml	0.331 µg/ml
LOQ	0.816 µg/ml	1 µg/ml

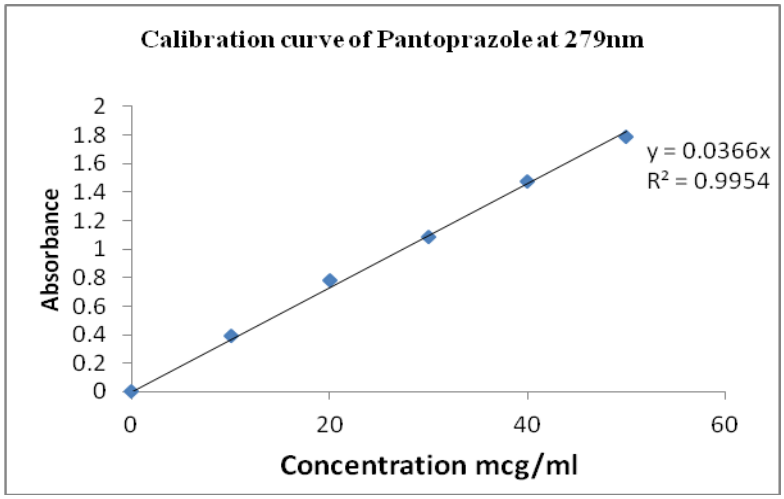
Range:

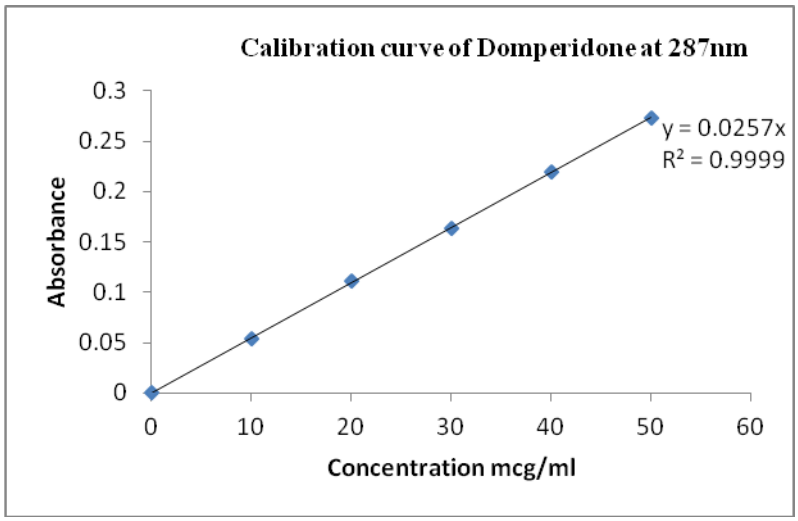
Beers law limit for Pantoprazole = 1-50µg/ml

Beers law limit for Domperidone = 1-15µg/ml

Table:8 Parameters of UV-Spectrophotometer.

Validation Parameters	Pantoprazole	Domperidone
Mobile phase	MeOH:ACN(60:40 v/v)	MeOH:ACN(60:40 v/v)
Detection wavelength	290 nm	287 nm
Beers limit	1-50µg/ml	1-15µg/ml
Linearity	10-50 µg/ml	2-10 µg/ml
R^2	0.995	0.999
LOD	0.264 µg/ml	0.331 µg/ml
LOQ	0.816 µg/ml	1 µg/ml
Precision	% RSD < 2	% RSD < 2
Recovery	98-101%	99-101%





CONCLUSION

The Proposed UV-Spectrophotometric method is suitable technique for simultaneous determination of Pantoprazole and Domperidone in Fixed Dose Combinations (FDCs) without any interferences form each other. All the parameters for both the drugs met the criteria of ICH guidelines for method validation. The UV Spectrophotometric method is rapid, simple and cost effective. The developed method may be recommended for routine and QC analysis of the investigated drugs to provide simple, accurate and reproducible quantitative analysis for the determination of Pantoprazole and Domperidone.

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