Available Online at

http://www.ijcpa.in

April-June 2016

International Journal of CHEMICAL AND PHARMACEUTICAL ANALYSIS

eISSN: 2348-0726 ; pISSN : 2395-2466

Research Article | Volume-3 | Issue-3 | Article ID: 1017

METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF DOMPERIDONE MALEATE IN PHARMACEUTICAL DOSAGE FORM BY UV- SPECTROPHOTOMETRY

Sita Kumari Karanam*, Soudamini Alekhacharan and Venkata Padmini Madem

Department of Pharmaceutical Analysis, Maharajah's College of Pharmacy,
Phool baugh, Vizianangaram, Andhra Pradesh – 535002, India

***Corresponding Author:** Email: sitakaranam@gmail.com*

Received: 19 April 2016 / Revised: 11 May 2016 / Accepted: 21 June 2016 / Available online : 30 June 2016

ABSTRACT

A simple, rapid, specific, accurate and economic UV spectrophotometric method has been developed using methanol as solvent to determine the Domperidone Maleate (DOM) tablet dosage formulations. At a pre-determined λmax of 285.9 nm, it was proved that the developed method obeyed Beer-Lambert's law in the concentration range of 10-60µg/ml having line equation y = 0.040x + 0.365 with correlation coefficient of 0.998. There is no interference from any common pharmaceutical excipients. The precision of method was determined by performing repeatability study, intra-day study and inter-day study. The accuracy of the method was confirmed by recovery studies from tablets at three different levels of standard additions. Results of the analysis were validated statistically and by recovery study. The analytical method was validated for various parameters as per ICH (International Conference on Harmonization) guidelines.

Keywords *– Method Development, Validation, Domperidone maleate (DOM), UV spectrophotometry, Tablet dosage form.*

1. INTRODUCTION

Domperidone is an antiemetic and antinauseant[1] and acts on dopamine receptor system as an antagonist. It is official in EP[2]. Domperidone Maleate (DOM) is Dopamine Antagonist, chemically 5-Chloro-1-[1-[3-(2-oxo-2, 3-dihydro-1H1Hbenzimidazol-1-yl) propyl] piperidin-4-yl]-1,3-dihydro-2H-benzimidazol-2-onehydrogen (Z)- butenedioate. Domperidone does not cross the blood brain barrier and therefore has fewer adverse CNS effects than other dopamine antagonist[3]. DOM has been determined in human plasma, human serum and human milk and rat plasma has been evaluated in coevaporates by HPLC and has been determined, with cinnarizine, in tablets, by HPLC[4]. The overview of Domperidone Maleate was represented (Table-1).

Literature survey revealed that Spectrophotometry[1,5-7], Spectroflourimetry[8] and HPLC[1,9-12] and HPTLC[13-15] and LC-MS[16,17] methods have been developed on single DOM or their combination with other drugs.

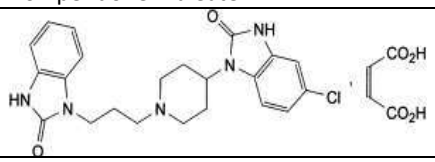
UV-Visible Spectrophotometry is one of the most frequently employed techniques in pharmaceutical analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution. Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the U.V-Visible region. In qualitative analysis, organic compounds can be identified by use of

spectrophotometer, if any recorded data is available, and quantitative spectrophotometric analysis is used to ascertain the quantity of molecular species absorbing the radiation. The wavelength for far UV region is 10-200nm and near UV region is 200-400nm. Spectrophotometric technique is simple, rapid, moderately specific and applicable to small quantities of compounds. The fundamental law that governs the quantitative spectrophotometric analysis is the Beer -Lambert law[18].

The aim and scope of the proposed work in accordance with ICH guideline for the intended analytical application[19] was:

- To develop suitable Spectrophotometric method for assay of Domperidone tablet.
- Perform the validation for the method.

Table 1: Overview of Domperidone Maleate

Feature	Domperidone Maleate
Structure	
IUPAC Name:	5-Chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H1H benzimidazol- 1-yl) propyl] piperidin-4-yl] -1,3- dihydro-2H-benzimidazol-2-onehydrogen (Z)- butenedioate
Category :	Therapeutic Class: Antiemetic Pharmacologic Class: Dopamine Antagonist
Properties Color: Form: Solubility: Melting point:	 White Solid Very slightly soluble in water, sparingly soluble in dimethyl formamide, slightly soluble in methanol, very slightly soluble in alcohol. 240-244ºC
Molecular Formula & Molecular Weight:	$C_{22}H_{24}ClN_5O_2$, 425.91126 g/mol
Mechanism of Action:	Domperidone blocks the action of dopamine. It has strong affinities for the D2 and D3 dopamine receptors which are found in the chemoreceptor trigger zone, located just outside the blood brain barrier, which regulates nausea and vomiting. It facilitates gastric emptying and decreases small bowel transit time.
Pharmacokinetic data: Bioavailability: Protein Binding: Metabolism: Half life: Excretion:	 High 91-93% Hepatic and intestinal (first pass) 7 hrs Breast Milk, Renal.
Trade Name:	Motilium, Ridon, Escacid DXR, Dompan
Drug picture:	
References:	Sohan Chitlange *etal.,* 2012; Siva Kumar ; Shubhangi Pawar *etal.*, 2010.

2. MATERIALS AND METHODS

2.1 Materials

A standard sample of DOM was purchased from Yarrow Chemicals, Mumbai. Tablet formulation DOMSTAL (10 mg of DOM, Manufactured by Torrent Pharmaceutical Ltd., Sikkim), was purchased from local market of Vzm. All chemicals and reagents used are of AR grade and purchased from Lotus Enterprises, Vsp.

2.2 Instrumentation

The Agilent Tech. Cary 60 UV-Vis spectrophotometer was used. The absorption spectra were recorded over the wavelength range 200-400 nm against the solvent blank. Agilent Tech. digital weighing balance was used for weighing samples.

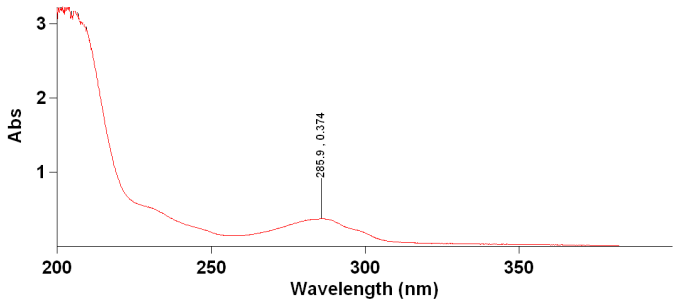


Figure 1: Scan of Domperidone in the range of 200 to 400 nm

2.3 Methods

2.3.1 Selection of solvent

Methanol gave spectra without noise, and as it is economical, it was selected as a solvent for the preparation of solutions.

2.3.2 Selection of analytical wavelength

Sample solution was scanned over the wavelength range of 200 nm to 400 nm. λ max for DOM was found at 285.9 nm. Representative absorption spectrum of DOM is shown in (Figure 2).

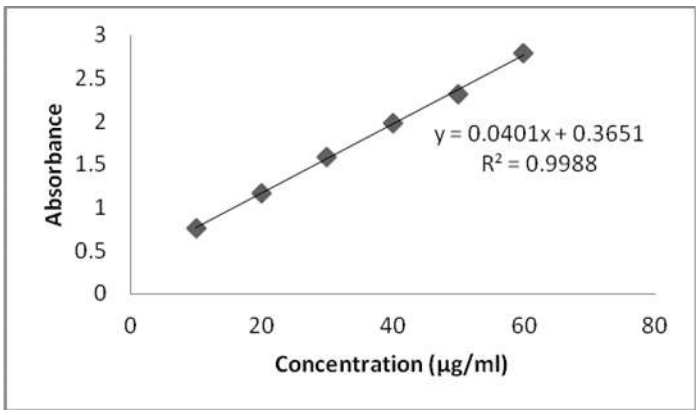


Figure 2: Calibration Curve of Domperidone

2.3.3 Standard solution of Domperidone (100µg/ml)

Accurately about 25mg of the drug was weighed and transferred to 25ml volumetric flask and dissolved in about 20 ml of methanol. The volume was made up to the mark with methanol. 1 ml of this solution was transferred to 10 ml volumetric flask and diluted up to 10 ml with methanol. This solution contained 100 µg of drug per ml of the solution.

2.3.4 Determination of λ max and Calibration curve

1 ml of standard stock solution was pipette out and transferred to a 10 ml volumetric flask. The volume was made up to the mark with methanol. This solution contained 10 µg/ml of the drug. The absorbance of this solution was scanned in the UV range of 200 to 400nm against methanol as blank. The absorbance maximum was found at a wavelength at about 277 nm.

2.3.5 Preparation of Calibration Curve for Domperidone at 285.9nm.

1.0, 2.0, 3.0, 4.0, 4.5 and 5 ml of the standard stock solution are pipette out in to a series of 10 ml volumetric flask. The volumes are made up to the mark with methanol and mixed to obtain solutions in the concentration range of 10,20,30,40 and50 µg/ml of drug.

The absorbance of these resultant solutions were measured at 285.9 nm against methanol as blank and a graph was plotted between absorbance obtained and the concentrations of the solutions. The Lambert-Beer's law was obeyed with the concentration range 10 to 50 µg/ml at 285.9 nm (Figure-2 and Table-2).

Table 2: Data for Calibration Curve of Domperidone

CONCENTRATION	ABSORBANCE
10	0.7624
20	*1.165*
30	1.5864
40	1.9759
50	2.321
60	2.7965

Table 3 shows the optical and regression characteristics of Domperidone. This shows that the method is linear and obeys Beer's law in the concentration range from 10-50 µg/ml, with correlation coefficient 0.998.

Table 3: Optical Parameters of Domperidone

Parameters	Observations
Beer's law limit (µg/ml)	5-30
Regression equation (y = a + bc)	y=0.040x +0.365
Slope (b)	0.080
Intercept (a)	0.365
Correlation coefficient (r2)	0.998

Table 3: Specificity Study for Domperidone

S.No.	Conc. (µg/ml)	Pure drug	Tablet formulation	% Interference
1	10	0.5674	0.5567	25.3
2	10	0.5426	0.5575	22.2
3	10	0.5586	0.5585	24.2
4	10	0.5385	0.5540	21.6
5	10	0.5281	0.5530	20.3
6	10	0.5138	0.5425	18.6
Mean				22.03

2.3.6 Method Validation

Method validation is the process used to confirm that the analytical procedure employed for a specific test is suitable for its intended use. Results from method validation can be used to judge the quality, reliability and consistency of analytical results; it is an integral part of any good analytical practice. The analytical method was validated for various parameters as per ICH (International Conference

on Harmonization) guidelines[20] are Accuracy, Precision, Repeatability, Specificity, Detection Limit, Quantitation Limit, Linearity, and Range.

2.3.6.1 Specificity

About 1 ml of the standard stock solution was taken in six 10 ml volumetric flasks and the volume was made up to the mark with methanol. The absorbance of these solutions were measured and recorded. For specificity determination about 1 ml of the stock solution was taken in six 10 ml volumetric flasks and about 1 ml of a 10 µg/ml solution was added to them and the volume was made up to mark with methanol. The absorbance was measured and recorded.

2.3.6.2 Linearity and Range

The linearity of response was determined in concentration in the working range of 10 to 50 µg/ml of the drug. The calibration curve is plotted between absorbance and concentration, correlation coefficient and a regression line equation for DOM was obtained. Linearity is expressed in terms of correlation coefficient of linear regression line.

2.3.6.3 Accuracy

The accuracy of method developed was determined by a recovery study from marketed formulation at three level of standard addition. Percentage recovery of Domperidone tablets were found out. Recovery between 98%-102% justifies the accuracy of the method. 10µg/ml Domperidone standard solution was spiked with 8, 10 and 12µg/ml sample solution of Domperidone tablets. The absorbance and % recovery result was measured.

2.3.6.4 Precision

a) Repeatability

0.5 ml of the standard stock solution was taken in a 10 ml volumetric flask and the volume was made up to the mark with methanol. This solution contained 5 µg/ml of the dug. The absorbance of this solution was measured six times and recorded.

Variations of results within the same day (intraday), variation of the results between days (interday) were analyzed and its %RSD for each observation was calculated.

b) Intra-day precision

0.5 ml, 1 ml, and 1.5 ml of the standard stock solution was taken in 10 ml volumetric flasks and volume was made up to the mark with methanol to obtain solution of concentration 5.0, 10 and 15 µg/ml. The readings were taken in triplicate for each concentration at 0 hr, 3 hr and 6 hr. within a day and recorded.

c) Inter-day precision

0.5 ml, 1 ml and 1.5 ml of the standard stock solution was taken in 10 ml volumetric flasks and the volume was made up to the mark with methanol to obtain solution of concentrations of 5.0, 10 and 15 µg/ml. The readings were taken in triplicate for each concentration at 0 hr., 24 hr. and 48 hr. intervals and recorded

2.3.6.5 Limit of detection (LOD) and limit of quantification (LOQ)

The sensitivity of the method was determined with respect to limit of detection (LOD) and limit of quantitation (LOQ). LOD and LOQ of Domperidone was determined by using standard deviation of the response and slope approach as defined in International Conference on Harmonization (ICH) guidelines (Pritesh G. Dhartarkar). LOD and LOQ values were calculated using the relation,

$$LOD = 3.3\delta / S$$

$$LOQ = 10\,\delta / S$$

Where, δ= standard deviation of residuals from the curve; S=slope of the curve

2.4 Estimation of Domperidone in tablet dosage forms

The powder of twenty tablets Domstal (10 mg), (Torrent Pharmaceuticals) of the same batch number were mixed and accurately weighed. Accurately about 104.95 mg powder (equivalent to 10 mg of Domperidone) was dissolved in about 60 ml methanol and ultra sonicate up to 10 minutes and filtered through Whatman Filter paper 40 into a 100 ml volumetric flask. The residue was washed with more methanol into the flask. The volume was made up to the mark with methanol. 2.5 ml of the resultant solution was transferred to 25 ml volumetric flask and the volume was made up to the mark with methanol to obtain a solution of 10 µg/ml of the drug. The absorbance of this solution was measured in quadruplet and recorded. The concentration was then determined from the calibration curve.

3. RESULTS AND DISCUSSION

3.1 Method Development and Optimization

The present study was carried out to develop a simple, sensitive, accurate and precise UV- Spectrophotometric method for estimation of DOM in pure and tablet formulation. The overlain spectra of DOM exhibit λ max of 285.9 nm.

3.2 Method Validation

3.2.1 Specificity

The concentrations of the solutions were determined and % interference was calculated. The results are shown in (Table-4). Standard calibration curve for DOM was linear with correlation coefficients (R^2) values in the range of 0.999 at the selected wavelength. It can be concluded from the results that developed method is specific and the % interference was negligible (22.03).

Table 4: Result of Recovery Study of Domperidone Tablets

S.No.	Conc. of reference Std. solution (µg/ml)	Conc. of sample solution added (µg/ml)	Conc. after spiking (µg/ml)	% Recovery
80%- Rec-1	0.8	1	8.42	105
80%- Rec-2	0.8	1	7.72	96.5
80%- Rec-3	0.8	1	6.62	82.7
100%-Rec-1	1	1	10.01	101
100%-Rec-2	1	1	9.18	91.8
100%-Rec-3	1	1	9.515	95.15
120%-Rec-1	1.2	1	10.37	86.4
120%-Rec-2	1.2	1	10.03	83.5
120%-Rec-3	1.2	1	10.03	85.8
Mean ± S.D.	91.98 ± 1.59			
% RSD	1.59			

3.2.2 Linearity and Range

The calibration curve obtained was evaluated by its correlation coefficient. The absorbance of the samples in the range of 10-50µg/mL was linear with a correlation coefficient (R^2) 0.998 (figure 2).

3.2.3 Accuracy

The accuracy of the method was confirmed by recovery studies from tablet at three different levels of standard additions; and % recovery was found to be 91.98 ± 1.59 justifies the accuracy of method. The mean % recovery was found to be 1.59 which was acceptable.

3.2.4 Precision

Keeping the concentration of the drug same, procedure was repeated for 6 times. The calculated RSD for repeatability study is 1.14, which is acceptable and shows good repeatability of method (Table-5).

Table 5: Results of Repeatability Studies for Domperidone

Theoritical Conc. (µg/ml)	Absorbance	Observed Conc. (µg/ml)	Mean Conc. (µg/ml)	SD	RSD
5	0.753	4.85	5.07	0.058	1.14
	0.768	5.03			
	0.775	5.12			
	0.781	5.2			
	0.785	5.25			
	0.767	5.02			

a) Intraday Precision

The precision of method was determined by performing repeatability study, intra-day study and inter-day study. The % RSD of repeatability study was found to be 1.14%. The method was repeated three times in a day (intra-day precision) and the calculated mean RSD was 3.22 shown in (Table-6).

Table 6: Intra-day Precision

Conc. (µg/ml)	Absorbance			Conc. found (µg/ml)			**Mean Conc. (µg/ml) ± SD**	RSD
	1	2	3	1	2	3		
5	0.3550	0.2484	0.2573	1.37	1.45	1.34	1.37±1.28	94.48
10	0.4749	0.4753	0.4724	1.37	1.37	1.34	1.36±0.70	97.8
15	0.6479	0.6503	0.6498	3.52	3.56	3.56	3.54±1.41	99.4
Mean							**3.22**	

b) Interday Precision

Similarly the method was repeated for three different days (inter-day precision) and the calculated mean RSD was 2.49 (Table-7). The readings were taken in triplicate for each concentration at 0 hr., 24 hr. and 48 hr. intervals. The calculated mean RSD was 1.01.

The % RSD values for repeatability, intraday and interday precision data were in range of the specified limit of 1-3%, respectively. Hence, the method was found to be precise in the specified range.

Table 7: Inter-day Precision

Conc. (µg/ml)	Absorbance			Conc. found (µg/ml)			Mean Conc. (µg/ml) ± SD	RSD
	1	2	3	1	2	3		
5	0.2087	0.2216	0.2101	1.95	1.78	1.93	1.88±0.156	98.64
10	0.4821	0.4743	0.4595	1.46	1.36	1.30	2.06±0.42	95.5
15	0.6476	0.6453	0.6507	3.53	3.50	3.57	3.53±2.121	97.4
Mean							2.49	

3.2.5 Limit of detection (LOD) and limit of quantification (LOQ):

The LOD and LOQ were calculated as 4.59 mg/mL and 13.91 mg/mL respectively. Hence the relationship between the concentrations and the absorbances of metronidazole showed linearity (Table -8).

Table 8: LOD and LOQ of DOM

	DOM
LOD	4.59
LOQ	13.91

3.2.6 Estimation of Domperidone in tablet dosage forms:

The proposed method has successfully estimated the amount of Domperidone resulting in mean % assay is 99.56 ± 0.058 (Table-9).

Table 9: Results of Estimation of Domperidone in Vomistop Tablet

Brand	Label claim (mg)	Theoretical conc. (µg/ml)	Calculated conc. (µg/ml)	Amount found (mg/tab)	% Assay	Mean % Assay ± SD
Vomistop	10	10	9.93	0.00993	99.3	99.56 ± 0.058
			9.98	0.00998	99.8	
			9.96	0.00996	99.6	

4. CONCLUSION

The proposed UV spectrophotometric methods are a simple, accurate, precise, rapid and economical and validated for the UV estimation of DOM in tablet dosage form in terms of specificity, linearity, accuracy, precision and repeatability. The proposed methods use low-cost reagents, solvents and instruments that are accessible in laboratories. Hence, these methods can be conveniently adopted for the routine analysis in quality control laboratories.

5. ACKNOWLEDGEMENT

The authors are thankful to Department of Pharmaceutical Analysis, Maharajah's College of Pharmacy for providing facilities to carry out this research work.

6. REFERENCES

1. Kulkarni AS, Balkrishna MV, Method development and validation for the simultaneous determination of Omeprazole and Domperidone in solid dosage form by RP-HPLC, International Journal of Pharmacy and Pharmaceutical Sciences, 2012; 4(5):109-114.
2. Kumar PR, Prakash PB, Krishna MM, Yadav S and Deepthi CA. Simultaneous Estimation of Domperidone and Pantoprazole in Solid Dosage Form by UV Spectroscopy. European Journal of Chemistry, 2006; 3(12): 142-5.
3. Sekhar EC, Kumar RS, Sankar MR and Prasanthi P, Simultaneous Estimation of Naproxen Sodium and Domperidone Maleate in Bulk and Pharmaceutical Dosage Form by Modified RP-HPLC Method, International Journal of Pharmaceutical and Chemical Sciences, 2012; 1(4):1616-1623.
4. Sivakumar T, Manavalan R, and Valliappan K, Development and validation of a reversed-phase hplc method for simultaneous determination of Domperidone and Pantoprazole in pharmaceutical dosage forms, Acta chromatographica, 2007; 18: 130-142.
5. Salem MY, El-Bardicy MG, Mohamed F and SEI-Zanfally E, Simultaneous Determination of Domperidone Maleate and Cinnarizine in a Binary Mixture Using Derivative Ratio Spectrophotometry and Classical Least Squares Calibration, Journal of Pharmaceutical and Biomedical Analysis, 2002; 30:21-33.
6. Kapil K, Naik S, Garima J and Mishra N, Spectrophotometric Method for Simultaneous Estimation of Paracetamol and Domperidone Maleate in Tablet Formulation, Asian Journal of Research in Chemistry, 2009; 2(2):112-114.
7. Sawant R, Bhangale L, Joshi R and Lanke P, Validated Spectrophotometric Methods for Simultaneous Estimation of Paracetamol, Domperidone Maleate and Tramadol Hcl in Pure and Tablet Dosage Form, Journal of Chemical Metrology, 2010; 4(1):21-27.
8. Walash MI, Belal F, El Enany N, Abdelal AA, Second-derivative Synchronous Fluorometric Method for the Simultaneous Determination of Cinnarizine and Domperidone in Pharmaceutical Preparations, Application to Biological Fluids, Journal of Fluoresc, 2008;18(1):61–74.

9. Karanam SK, Alekacharan S and Patnaikuni SSA, RP-HPLC method and validation for the simultaneous estimation of domperidone maleate and pantoprazole in tablet dosage form, International Journal of Pharmaceutical Letters and Reviews,2015; 2(2): 18-23.
10. Varalakshmi M, Ratna JV, Chaitanya K and Israel DS, RP-HPLC Method Development and Validation of Domperidone Maleate, International Journal of Pharmaceutical Research and Development, 2011; 3(4):61-64.
11. Singh RK, Ramakrishna S and Gupta P, RP-HPLC Method Development and Validation for Simultaneous Estimation of Ranitidine Hydrochloride and Domperidone Maleate in Combined Tablet Dosage Form, International Journal of Pharmaceutical Sciences and Research, 2010; 1(8):77-87.
12. Battu PR, Simultaneous HPLC Estimation of Pantoprazole and Domperidone Maleate from Tablets, International Journal of Chem Tech Research, 2009; 1(2):275-277.
13. Susheel JV, Lekha M and Ravi TK, High Performance Thin Layer Chromatographic Estimation of Lansoprazole and Domperidone in Tablets, Indian Journal of Pharmaceutical Sciences,2007; 69(5):684-686.
14. Patel B, Patel M, Patel J and Suhagia B, Simultaneous Determination of Omeprazole and
15. Domperidone in Capsule by RPHPLC and Densitometric HPTLC, Journal of Liquid Chromatography and Related Technologies, 2007; 30(12):1749-1762.
16. Pawar SM, Patil BS and Patil RY, Validated HPTLC Method for Simultaneous Quantitation of Famotidine and Domperidone Maleate in Bulk Drug and Formulation, International Journal of Advances in Pharmaceutical Sciences, 2010;1(1):54-59.
17. Reddy BP, Reddy MS, Development and validation of RP-HPLC for the Rabeprazole sodium in pharmaceutical formulations and Human Plasma, Asian Journal of Research in Chemistry, 2009; 2(1): 70-72.
18. Li Z, Yao J, Zhang Z and Zhang L, Simultaneous Determination of Omeprazole and Domperidone in Dog Plasma by LC–MS Method, Journal of Chromatographic Science, 2009; 47: 881-4.
19. Behera S, Ghanty S, Ahmad F, Santra S, and Banerjee S, UV-Visible Spectrophotometric Method Development and Validation of Assay of Paracetamol Tablet Formulation, J Anal Bioanal Tech, 2012; 3(6):151-156.
20. Chauhan S, Kumar P, Kothiyal P, Validated Method Development for the Estimation of Domperidone by UV- Spectroscopy, International Journal of Pharma Research & Review, 2015; 4(10):1-7.
21. ICH Q2B Validation of Analytical Procedures-Methodology. Consensus Guidelines, ICH Harmonized Tripartite Guidelines, 1996.