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DEVELOPMENT AND VALIDATION OF UV- SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF DOMPERIDONE IN API AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

A rapid, simple, selective, sensitive, precise and specific UV Spectrophotometric method has been developed for the determination of Domperidone in API and pharmaceutical dosage form. Domperidone standard solution was scanned in the UV range (200-400nm) in 1cm quartz cell in a double beam UV Spectrophotometer. The spectrophotometric detection was carried out at an absorption maximum of 288 nm using Methanol as a solvent. The method was validated for specificity, linearity, accuracy, precision, robustness and ruggedness. The detector response for the Domperidone was linear over the selected concentration range 5-25µg /ml with a correlation coefficient of 0.999 and equation for the regression curve was found to be *y=0.0297x+0.115.* The accuracy was between 99-101%. The precision (%RSD) among six samples preparation was 0.308%. The LOD and LOQ are 0.045 and 0.1µg /ml respectively. Statistical analysis proved that the methods are repeatable and specific for the determination of the said drug. These methods can be adopted in the routine assay analysis of Domperidone in API and pharmaceutical dosage form.

KEYWORDS

Domperidone, Methanol and Method Validation.

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INTRODUCTION

Domperidone is a potent dopamine antagonist used for treatment of nausea and vomiting. Domperidone does not cross the blood brain barrier and therefore has fewer adverse CNS effects than other dopamine antagonists. It stimulates gastro-intestinal motility and is used as an antiemetic for the short term treatment of nausea and vomiting of various aetiologies, including that associated with cancer therapy. Domperidone has been determined in human plasma, human serum and human milk, and

rat plasma has been evaluated in co-evaporates by HPLC, and has been determined, with cinnarizine, in tablets, by HPLC[1-3].

Domperidone is (5-chloro-1-{1-[3-(2, 3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl]-4- piperidinyl} benzimidazolin-2-one).

Literature survey revealed that DMP has been estimated with other drugs using UV, HPLC, LCMS, Flourimetry and HPTLC. The present study is to estimate DMP using a simple, sensitive, accurate, precise and more economical UV spectroscopic method[1,2,3,4,7,8].

MATERIAL AND METHODS

Instruments

For weighing, a calibrated weighing balance (Shimadzu) of 1mg sensitivity was used. A Shimadzu UV-visible double beam spectrophotometer- 1800 was used. All the glass wares and were made of borosilicate and were calibrated.

Material

Pure standards of DMP was obtained as a gift sample and its marketed formulation (DOMSTAL Tablets) was purchased from the market. Methanol of analytical grade was used as the solvent. A double-beam shimadzu UV- visible spectrophotometer, 1800 with a pair of 1 cm matched quartz cells were used to measure the absorbance of the solutions.

UV Spectroscopic Method

Solvent Selection

Domperidone is soluble in methanol.

Preparation of Standard Stock Solution

The standard stock solution of Domperidone (DMP) was prepared by transferring accurately weighed 10 mg of Domperidone into 10 ml volumetric flask containing methanol, then volume was made up to the mark by using methanol to give a concentration of 1000µg / ml. From this, 1ml of the solution was transferred to a 10 ml volumetric flask and make up the volume with methanol to give a concentration of each 100µg/ml, which is a standard stock solution and it is further diluted with methanol to get concentration range of 10µg/ml of Domperidone (DMP).

Determination of absorption maxima

The prepared standard solution (10µg/ml) were scanned in the UV-VIS spectrophotometer in the wavelength range of 200-400 nm and an overlain spectrum was recorded. The drug showed Absorption maxima at 288 nm. The absorbance of above solution was measured at the selected wavelength and absorptivity was determined (Table No.1).

Quantitative Analysis of Tablet Dosage Form

20 Tablets of marketed formulation of Domperidone of 10mg (DOMSTAL Tablet) was weighed, their average weights determined. The correct amount of drug powder equivalent to label claim was weighed and transferred to 10 ml volumetric flask, dissolved in methanol and sonicated for 15 min. The volume was then made up to the mark using same solvent, from this 1 ml was taken and diluted to 10 ml with methanol which gives 100µg/ml of DMP. From this 1 ml was taken and diluted to 10 ml with methanol which gives 10µg/ml of DMP. Absorbance of this sample solutions was recorded at 288 nm and then concentration of the drug was calculated and the results are given in Table No.2.

Method Validation

The developed method was validated as per ICH guidelines for the following parameters:

Linearity

From the 'Std Stock DMP' (100µg/ ml), 0.5, 1, 1.5, 2, 2.5 ml for DMP and was transferred in a series of 10 ml volumetric flasks. The volume was made up to the mark with methanol to obtain the concentration of 5, 10, 15, 20, 25µg/ml for DMP. Calibration curves of DMP was constructed by plotting the Absorbance of DMP v/s Conc. of DMP. The correlation coefficient (r^2) of least square linear regression for DMP was calculated.

Range

The Range of the analytical method was decided from the interval between upper and lower level of calibration curve by plotting curve.

Accuracy

Recovery study was carried out by the standard addition method by adding a known amount of DMP to the pre-analyzed sample at three different

concentration levels that is 80%, 100%, 120% of assay concentration and percent recovery were calculated. 1 ml of tablet solution was transferred to 4 different 10 ml volumetric flasks (labeled as blank, 80%, 100%, 120%) separately and 0, 8, 10, 12µg/ml standard solution was added respectively and the volume was made up to the mark with methanol. Absorbance was noted for these samples. Standard deviation and % RSD was calculated. Accuracy is reported as % recovery, which was calculated from the expression as equation given below:

% Recovery = Observed value / True value ×100

Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scattering) between a series of measurements obtained from multiple sampling of the same sample under the prescribed conditions. The precision of the method was determined in terms of repeatability and intra-day and inter-day precisions. Intra-day and inter-day precision (Intermediate Precision)

Intraday precision was determined by analyzing the drugs at concentration (10µg/ml) for the drug and each concentration for three times, on the same day. Inter-day precision was determined similarly, but the analysis being carried out daily, for two consecutive days.

Repeatability

Repeatability of the method was determined by analyzing six samples of same concentrations of the drug (10µg/ml) for DMP. Absorbance of was measured.

Robustness

The robustness of the developed method is its capacity to remain unaffected by small changes in altered conditions. To determine the robustness of the method, the wavelength of analysis was deliberate and the assay was evaluated. The effect of detection wavelength was studied at ±5 nm.

Ruggedness

Ruggedness was determined by carrying out analysis by two different analysts and the respective absorbance was noted and the results were indicated as % RSD.

Limit of Detection

Detection limit was determined based on the standard deviation of absorbance of same concentration that is a standard solution of DMP (10µg/ml) and LOD calculated by LOD = 3.3 (SD/S) Where, SD- standard deviation; S= slope of the curve

Limit of Quantification

Quantification limit was determined based on the standard deviation of peak area of same concentration that is standard solution DMP (10µg/ml) prepared six times and LOQ calculated by LOD = 10(SD/S) Where, SD= standard deviation; S= slope of Curve.

RESULTS AND DISCUSSION

Linearity

The linearity of this method was determined at ranges from 5-25µg/ml for DMP. The regression equation was found to be.

Accuracy

The accuracy of the analytical method for DMP was determined at 80%, 100% and 120% levels of standard solution. Absorbance was measured at 288 nm results were expressed in terms of % recoveries.

Precision

The precision (measurement of intra-day, inter-day, repeatability) results showed good reproducibility with the relative standard deviation (% RSD) below 2.0 %. This indicated that method was highly precise.

Preliminary Analysis of Domperidone

Preliminary analysis of Domperidone such as description, solubility was performed.

Assay of Tablet formulation

Amount of drug present in tablet formulation was calculated using simultaneous equation at 288 nm for DMP, and $y = 0.0297x + 0.115$ for DMP. Amount of Domperidone was found to be 99.06% of label claim. This method can be employed for routine analysis of both the drugs.

Summary and Conclusion

Summary of UV Spectrophotometric Method for Domperidone.

Table No.1: Absorptivity of DMP at 288 nm

S.No	Components (10µg/ml)	Absorptivity at 288 nm
1	DMP	0.419

Table No.2: Result analysis of the tablet Mixture

S.No	Drug	Label Claim (mg / tab.)	Amount found (mg)	% Drug found
1	DMP	10	9.96	99.6

Table No.2: Linearity of Domperidone

Domperidone (DMP)		
S.No	**Concentration (µg/ml)**	**Absorbance**
1	5	0.257
2	10	0.419
3	15	0.560
4	20	0.714
5	25	0.852
6	Regression equation: $y = 0.0297x + 0.115$	
7	$R^2 = 0.999$	

Table No.3: Table for accuracy

S.No	Drug	Amount present (µg/ml)	Amount of standard drug added (µg/ml)	Amount found (µg/ml)	%Recovery
1	DMP	5	80%(8µg/ml)	12.9	99.23
		5	100%(10µg/ml)	14.14	101
		5	120%(12µg/ml)	16.90	99.41

Intra-day Precision

Table No.4: Intra-day precision

S.No	DMP	
	Concentration (µg/ml)	**Absorbance**
1	10	0.419
2	10	0.418
3	10	0.419
4	10	0.418
5	10	0.420
6	10	0.418
7	% RSD	0.200

Inter-day Precision

Table No.5: Inter-day precision

S.No	DMP	
	Concentration (µg/ml)	**Absorbance**
1	10	0.419
2	10	0.421
3	10	0.419
4	10	0.419
5	10	0.419
6	10	0.419
7	% RSD	0.123

Repeatability

Table No.6: Repeatability study

S.No	DMP	
	Concentration (µg/ml)	**Absorbance**
1	10	0.420
2	10	0.419
3	10	0.419
4	10	0.419
5	10	0.420
6	10	0.419
	% RSD	0.308

Limit of Detection

Table No.7: For Limit of Detection

S.No	LOD (µg/ml)	Con.
1	DMP	0.045µg/ml

Limit of Quantification

Table No.8: For Limit of Quantification

S.No	LOQ (µg/ml)	Con.
1	DMP	0.1µg/ml

Robustness

Table No.9: Robustness

S.No	Analyst	Absorbance
		DMP(10 µg/ml)
1	Analyst 1	0.420
2	Analyst2	0.421
3	Analyst3	0.420
4	%RSD	0.137%

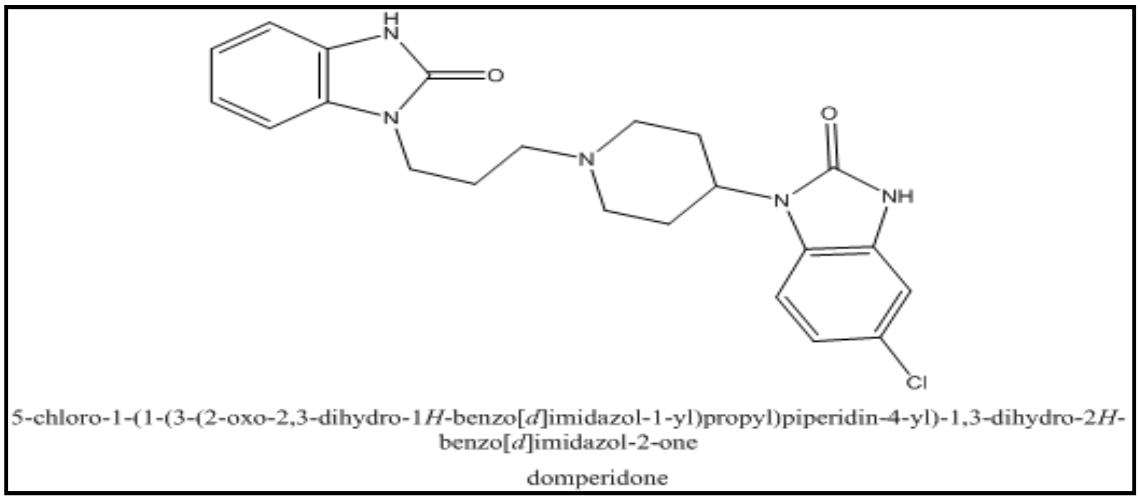
Ruggedness

Table No.10: Ruggedness

S.No	Wavelength	Absorbance
		DMP(10 µg/ml)
1	Wavelength 1	0.422
2	Wavelength 2	0.422
3	Wavelength 3	0.421
4	%RSD	0.13%

Table No.11: For Summary

S.No	Parameters	Values
		DMP
1	Beer's Law limit (µg/ml)	5-25
2	Absorption maxima (nm)	288
3	Standard regression equation	*y = 0.0297x +0.115*
4	Correlation coefficient (R^2)	0.999
5	Accuracy	99-101%
6	Precision (% RSD) Repeatability	0.308
7	LOD (µg/ml)	0.045
8	LOQ (µg/ml)	0.1
9	Robustness (%RSD)	0.137
10	Ruggedness (%RSD)	0.13
11	Assay (%)	99.06



5-chloro-1-(1-(3-(2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)propyl)piperidin-4-yl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one

domperidone

Figure No.1: Structure of Domperidone

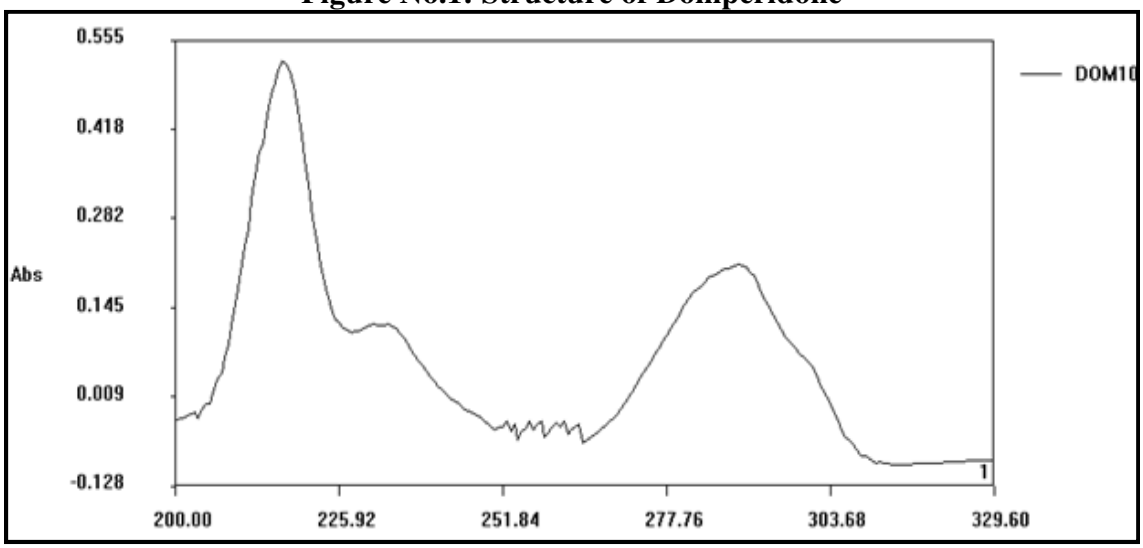


Figure No.2: Spectra showing absorption maxima of DMP at 288 nm

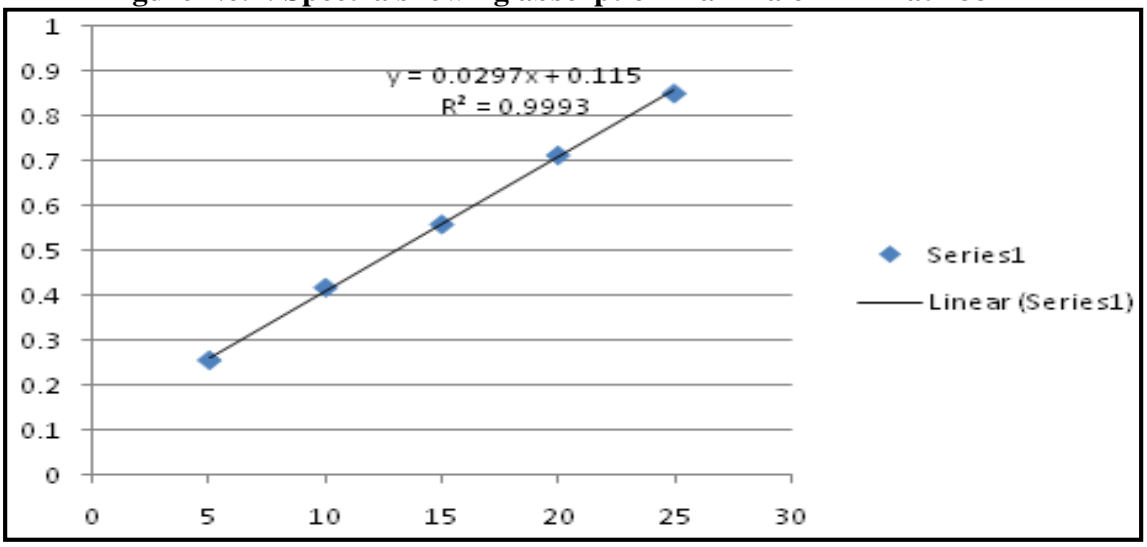


Figure No.3: Linearity of DMP

CONCLUSION

The UV-Spectrophotometric method was developed and it is found to be simple, accurate, precise, highly sensitive, reproducible and inexpensive. The proposed method was found suitable for determination of Domperidone in API and its dosage form without any interference from the excipients. This method can be effectively applied for the routine analysis of Domperidone in API. Its advantages are the low cost of reagents, speed and simplicity of sample treatment, satisfactory precision and accuracy.

ABBREVIATIONS

UV-Ultra Violet
API- Active Pharmaceutical Ingredient
DMP- Domperidone
LOD- Limit of Detection
LOQ- Limit of Quantification

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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