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Validated UV spectrophotometric method for estimation of domperidone for dissolution study

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ABSTRACT

The aim of this research paper was to develop a simple, sensitive, rapid, accurate and economical Ultra Violet spectrophotometric method for the estimation of Domperidone.The study was performed in pH 6.8 phosphate buffer with 0.5 % Sodium Lauryl Sulphate (SLS) and presence of the drug was analysed using UV spectrophotometer. Various analytical parameters such as linearity, range, precision, accuracy, limit of detection (LOD) and limit of quantification (LOQ) were determined according International Conference on Harmonization (ICH) guidelines. Absorbance maximum (λmax) of drug in pH 6.8 phosphate buffer was found to be 284 nm. Beer's law was obeyed over the concentration range of 2 - 10 µg/ml with a correlation coefficient (R^2) value of 0.999. % RSD values below 2 at different concentration levels for Intra and inter-day precision indicated that the proposed spectrophotometric method is highly reproducible. LOD and LOQ were 0.84 and 2.54µg/ml respectively signifying that it can be adopted for routine quality testing. The results of the study demonstrated that the developed method is accurate, precise and reproducible while being simple, cheap and less time consuming and hence can be suitably applied for the analysis of Domperidone in pharmaceutical preparations for dissolution studies.

Keywords: Domperidone, Quantitative determination, UV spectrophotometric method.

INTRODUCTION

Domperidone is described chemically as 5-chloro-1-[1-[3-(2,3-dihydro-2-oxo-1H-benzimidazole-1-yl) propyl]-4-piperidinyl1]-1,3-dihydro-2H-benzimidazole-2-one [1].DOM is a poorly water soluble dopamine D2 antagonist and widely used as an antiemetic. It is a basic, lipophilic BCS class II drug. It possesses very poor oral bioavailability and shows significant first pass metabolism [2] shown in the figure 1.

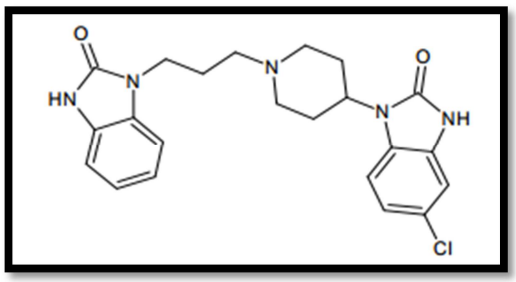

Figure 1: Structure of Domperidone

Several techniques such as HPLC, HPLC with fluorescence detention, LC-MS, capillary electrophoresis, spectrophotometric, titrimetric and flow injection analysis for the estimation of DOM alone and with its major metabolites had been reported. This methods used for the estimation are bit time consuming, tedious and expensive [3, 4]. The aim of the present study is to develop a new simple, rapid, reliable and precise UV spectrophotometric method of DOM for routine analysis from bulk and pharmaceutical formulation and in-vitro dissolution studies.

MATERIALS AND METHODS

Instrument

A doublebeam UV-Visible Spectrophotometer (Lab India 3200) with a matched pair of 1 cm quartz cells were used for experimental purpose.

Materials

Domperidone was procured as gift sample from souvenier chemical, Mumbai, India. Freshly prepared 6.8 pH phosphate buffer and all other chemicals and reagents were of analytical grade.

Preparation of 6.8 pH phosphate buffer solution

Dissolve 28.80 g of disodium hydrogen phosphate and 11.45 g of potassium dihydrogen phosphate in sufficient water to produce 1000 ml. The pH of the buffer solution was adjusted with the help of 1N HCl and 0.1N NaOH [4].

Preparation of DOM Standard Stock Solutions

Standard stock solution of DOM (100 mg) was prepared in 100 ml in phosphate buffer pH 6.8 with 0.05 % w/v SLS to get the final concentration of 1000 µg/ ml [5].

Preparation of DOM Working Solution

Aliquots of stock solution were further diluted with phosphate buffer pH 6.8 with 0.05% SLS solution to get working solution of 2, 4, 6, 8 and 10µg/ml and the working standards were scanned through UV spectroscopy[3].

Determination of λmax

The standard solution of DOM (6 µg/ml) was scanned in the wavelength region of 200-400 nm and the λmax was found to be 284 nm (**Fig.2)** [8].

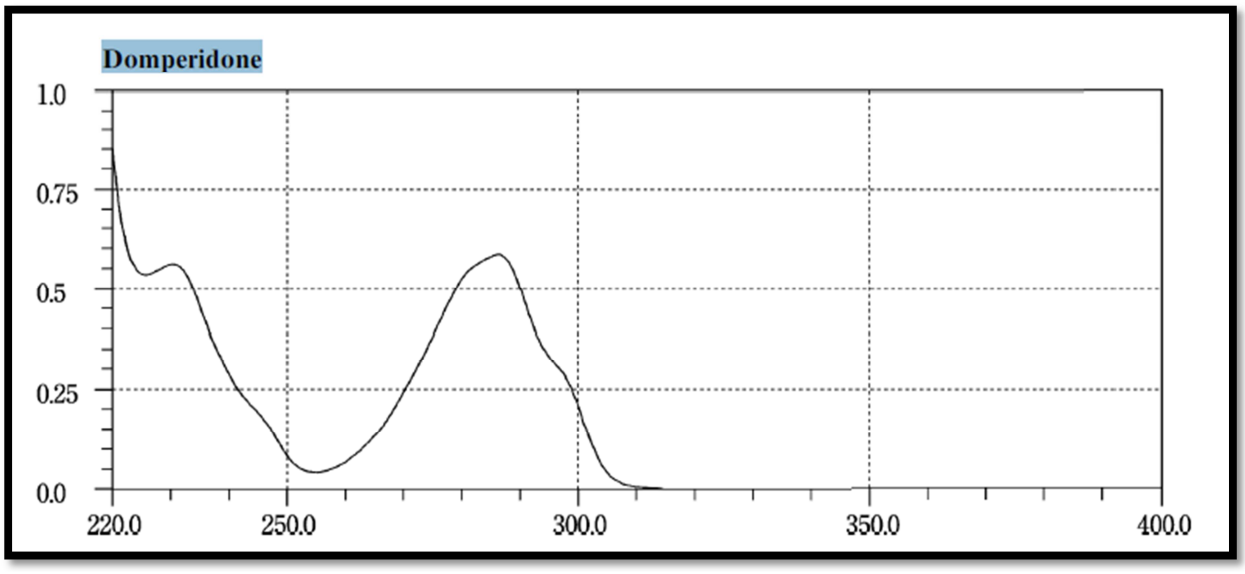

Figure 2: Spectra of Domperidone showing λmax at 284nm

Preparation of calibration curve

Different aliquots were taken from working solution and diluted with phosphate buffer pH 6.8 separately to prepare series of concentrations from 2-10 µg/ml. Absorbance was measured at 284 nm against phosphate buffer pH 6.8 as blank [5]. Finally the calibration curve was plotted between concentration (x-axis) and absorbance (y-axis) shown in (**Fig 3**) [6].

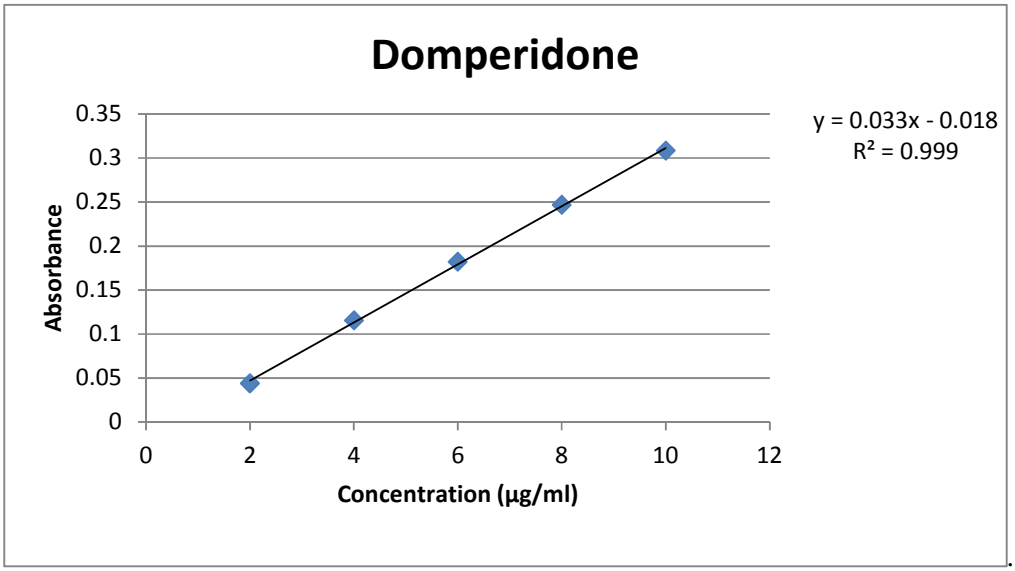

Figure 3: Standard Calibration curve of Domperidone

Validation procedure

1. Linearity or Range

The linearity of the method is its ability to elicit test results that aredirectly proportional to the concentration of the analyte in samples [7]. The prepared aliquots (2-10 µg/ml) were scanned for absorbance at λmax value 284 nm. The absorbance range was found to be 0.0438- 0.3083. These solutions obeyed Beer-Lambert's law in above concentration range with regression of 0.999 [8].

2. Intraday Precision

It is determined by analyzing the drug at a 3 different concentration and each concentration for three times, on a same day and calculated the value of Mean, SD, and %RSD [11, 12]. The % R.S.D. values found to be less than 2, indicating that the proposed method is precise [13].

3. Interday Precision

It is determined similarly, but the analysis being carried out daily for three consecutive days and calculated the value of Mean, SD, and %RSD [10].

4. Repeatability

Repeatability of the method is determined by analyzing the drug at a same concentration for minimum six times and the %RSD was calculated. [12].

5. Recovery Studies

To assess the accuracy of the proposed method, recovery studies were carried out at three different levels. To the pre-analyzed sample solution a known amount standard drug solution was added at a three different level (80%, 100%, and 120%) absorbance recorded. The % recovery was then calculated as [10, 11].

$$\% \text{ Recovery} = \frac{A - B}{C} x100$$

A= total amount of drug estimated

B= amount of drug found on pre-analyzed basis
C= amount of pure drug added to formulation

6. Limit of Detection (LOD)
It is the lowest amount of analyte in a sample that can be detected but not necessarily quantified under the stated experimentalconditions. Limit of detection can be calculated using followingequation as per ICH guidelines. Limit of detection were determined by using the formula based on the SD of response and slope [10-12].

$$\mathrm{LOD} = 3.3 \, \mathrm{x} \frac{\mathrm{S}}{\mathrm{X}}$$

X= slope of line
S= standard deviation

7. Limit of Quantification (LOQ)
It is the lowest concentration of analyte in a sample that can bedetermined with the acceptable precision and accuracy under statedexperimental conditions. Limit of quantification can be calculatedusing following equation as per ICH guidelines [13, 14].

$$\mathrm{LOQ} = 10 \, \mathrm{x} \frac{\mathrm{S}}{\mathrm{X}}$$

X= slope of line
S= standard deviation

8. % RSD
% RSD values were determined by using the formula based on the SD of response and mean of the response. The % R.S.D. values found to be less than 2, indicating that the proposed method is precise [13-18].

$$\%\mathrm{RSD} = \frac{\text{SD of Response}}{\text{Mean of Response}} \mathrm{x}100$$

RESULTS AND DISCUSSION

Linearity or Range
The prepared aliquots (2-10 µg/ml) were scanned for absorbance at λmax value 284 nm. The absorbance range was found to be 0.0319- 0.2106. These solutions obeyed Beer-Lambert's law in above concentration range with regression of 0.993. Limit of detection (LOD) and limit of quantification (LOQ) for the assay were also calculated and shown in the table 2.

Accuracy or % Recovery
The % recovery was found to be in the range of 93.64%, 101.3% and 103.6% and % RSD value 0.793, 0.698 and 0.750 respectively shown in the table 3.

Intraday precision
The % RSD for Intraday precision for the concentration 2µg/ml was found in the timing of 10AM, 1PM and 4PM with the results of 0.492, 0.485 and 0.476 respectively and shown in table 4.

The % RSD for Intraday precision for the concentration 4µg/ml was found in the timing of 10AM, 1PM and 4PM with the results of 0.723, 0.480 and 0.239 respectively and shown in table 4.

The % RSD for Intraday precision for the concentration 6µg/ml was found in the timing of 10AM, 1PM and 4PM with the results of 0.241, 0.080 and 0.161 respectively and shown in table 4.

Interday precision
The % RSD for Interday precision for the concentration 2µg/ml was according to three days with the results of 0.485, 0.569 and 0.476 respectively and shown in table 5.
The % RSD for Interday precision for the concentration 4µg/ml was according to three days with the results of 0.242, 0.396 and 0.996 respectively and shown in table 5.

The % RSD for Interday precision for the concentration 6µg/ml was according to three days with the results of 0.508, 0.161 and 0.089 respectively and shown in table 5.

Repeatability

The repeatability of the proposed method was assessed by analyzing domperidone in concentration as 6 µg/ml in triplicate. Results of repeatability were expressed in the terms of % RSD found to be 0.321 and shown in the table 6.

Table 2: Optical parameters of DOM

S.No	Parameters	In Phosphate Buffer pH 6.8 (0.5 % SLS)
1	Absorbance maximum (λmax) in nm	284
2	Beer's law limit (µg/ml)	2 – 10
3	Slope	0.033
4	Intercept	0.018
5	Correlation coefficient	0.999
6	Mean standard deviation	0.0084
7	LOD (µg/ml)	0.84 µg/ml
8	LOQ (µg/ml)	2.54 µg/ml

Table 3: Recovery Studies

Amount taken	Amount added %	µg/ml	% Recovery	SD	%RSD
6	80	4.8	93.64	0.742	0.793
6	100	6	101.3	0.707	0.698
6	120	7.2	103.6	0.777	0.750

Table 4: Intraday Precision Analysis

Timing	2µg/ml			4µg/ml			6µg/ml		
	Mean	SD	%RSD	Mean	SD	%RSD	Mean	SD	%RSD
10 AM	0.0203	0.0001	0.492	0.0415	0.0003	0.723	0.1243	0.0002	0.241
1 PM	0.0206	0.0001	0.485	0.0416	0.0002	0.480	0.1245	0.0001	0.080
4 PM	0.0210	0.0001	0.476	0.0418	0.0001	0.239	0.1239	0.0002	0.161

Table 5: Interday PrecisionAnalysis

Day	2µg/ml			4µg/ml			6µg/ml		
	Mean	SD	%RSD	Mean	SD	%RSD	Mean	SD	%RSD
1	0.0206	0.0001	0.485	0.0414	0.0001	0.242	0.0984	0.0005	0.508
2	0.0351	0.0002	0.569	0.0504	0.0002	0.396	0.1242	0.0002	0.161
3	0.0210	0.0001	0.476	0.0502	0.0005	0.996	0.1124	0.0001	0.089

Table 6: Repeatability Analysis

Concentration (µg/ml)	Mean	SD	%RSD
6	0.1244	0.0004	0.321

CONCLUSION

The proposed method for the estimation of DOM was found to be simple, sensitive and reliable with goodPrecision and accuracy. The method is specific while estimating the commercial formulations without interferenceof excipients and other additives. Hence this method can be used for the routine analysis of DOM in pure andpharmaceutical formulations.

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