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Research Article

A Simple and Rapid Validated UV Spectrophotometric Method for Estimation of Dapoxetine in Bulk and Tablet Dosage Form

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ABSTRACT

The present study was undertaken to develop a spectrophotometric method for the determination of Dapoxetine in pharmaceutical dosage forms. This paper reports a simple, rapid, accurate and precise UV-Spectrophotometric method for the assay of Dapoxetine in bulk and marketed tablet dosage form has been developed. The validation of the designed method was also carried out in terms of linearity, precision, accuracy, specificity, limit of detection, limit of quantification and by performing recovery study. Beer's law was obeyed in the concentration range of 5-35 µg/ml with a good correlation coefficient (r=0.999). Method is validated as per ICH guidelines and this study is statistically significant as all the statistical parameters are within the acceptance range (% RSD < 2.0 and SD < 2.0) for both accuracy and precision.

INTRODUCTION

Dapoxetine, a drug which is the earliest compound developed particularly for the treatment of premature ejaculation in men [1]. It works by inhibiting the serotonin transporter, increasing serotonin's action at the post synaptic cleft, and as a consequence promoting ejaculatory delay [2]. Chemically Dapoxetine is designated as (S)-N, N-Dimethyl-3-(naphthalen-1-yloxy)-1-phenylpropan-1-amine with an empirical formula of $C_{21}H_{23}NO$ and the molecular weight of 305.41342 g. The structural formula is shown in Fig. 1.

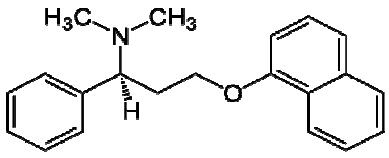

Figure 1: Chemical structure of Dapoxetine

While no official method for the determination of Dapoxetine in oral formulation has been described yet, detailed literature survey of Dapoxetine reveals that column-switching high-performance liquid chromatography is described for the determination of Dapoxetine and its mono- and di-desmethyl metabolites in human plasma [3-4].

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Although various analytical methods have been reported for determination of Dapoxetine in bulk as well as in pharmaceutical formulations, the reported chromatographic methods necessitate sample pretreatment and time-consuming extraction steps prior to analysis of the drug. Furthermore, these methods have need of expensive equipment's and considerably skilled personnel.

Our present study has been designed to describe a simple, accurate, rapid and precise spectrophotometric method for the determination of Dapoxetine in bulk and marketed dosage forms. The method was optimized and validated as per as the International Conference on Harmonization (ICH) guidelines.

MATERIALS AND METHODS

Instruments

A Shimadzu UV-Visible spectrophotometer (SHIMADZU UV-1800 spectrophotometer) with a pair of matched quartz cells was used for all absorbance measurements. Analytical balance was used for weighing and Ultrasonic Bath (POWER SONIC 405, China) used for sonicating the drug and sample solution.

Materials and Reagents

Dapoxetine was obtained as a gift sample from NIPRO JMI Pharma Ltd. (First Japanese Joint

Venture Pharmaceuticals in Bangladesh) and it was used as the reference standard. Tablets of different brands of Dapoxetine were purchased from our local market; each tablet was labeled to contain 30 mg of Dapoxetine. All chemicals and reagents were of analytical or pharmaceutical grade.

Determination of λ_{max}

An ultra violet spectrophotometric scanning (200 nm - 380 nm) was carried out to select the λ_{max} for the detection of Dapoxetine, because every drug should have adequate absorbance in the same solvent for the simultaneous determination.

Preparation of Standard Stock Solution

According to the solubility characteristics of the drug, methanol was selected as the solvent for the analysis of Linagliptin. Weigh accurately about 25 mg of Linagliptin pure drug into a clean and dry 50 ml volumetric flask. Dilute with 25 ml of methanol (used as solvent) and shake well. Then the volume was made up to 50 ml using methanol and mix well. Take 2 ml of this solution into a clean and dry 50 ml volumetric flask and then diluted up to 50 ml using methanol to obtain a solution that has a concentration 20 µg/ml which is standard stock solution.

Preparation of Sample Stock Solution

Twenty tablets were weighed accurately and their average weight was determined and crushed to powder. Then weigh accurately about 65 mg of powder sample (equivalent to 25 mg of Dapoxetine) into a clean and dry 50 ml volumetric flask. Dilute with 25 ml of methanol and the flask was shaken ultrasonically for 10 minutes. Then the volume was made up to 50 ml using methanol and mix well. Filter the solution through Whatman No. 42 filter paper (Whatmann International Limited, Ket, UK). After filtration an aliquot of 2 ml of this solution was transferred into a clean 50 ml volumetric flask and the volume was adjusted up to the mark with methanol. Absorbance of this solution at 292 nm was recorded.

Preparation of Calibration Curve

Standard stock solutions of Dapoxetine were serially diluted with methanol to get varying concentrations of stock solutions. Varying concentration of Linagliptin solutions 5.0, 10.0, 15.0, 20.0, 25.0, 30.0 and 35.0 µg/ml were prepared for construction of calibration curves. Then the contents of each flask were mixed well and immediately transferred to the spectrophotometric cell to record absorbance at its λ_{max} nm.

METHOD VALIDATION

The proposed method has been validated for specificity, linearity, limit of detection, limit of quantification, precision, and accuracy as per ICH guidelines [5-6].

Specificity

A study conducted to establish specificity of the proposed method using UV-Spectrophotometer for the reference standard and quality control samples of Dapoxetine. Both the standard solution and sample solution of Dapoxetine were shown maximum wavelength of absorbance at 292 nm.

Linearity

The linearity of an analytical procedure is its ability of produce results that will directly proportional to the concentration of an analyte in the samples. The linearity was evaluated in the range of Beer's law obeyed concentration range of 5-35 µg/ml of standard stock solutions. The determination was repeated three times at each concentration level. The linearity was evaluated by linear regression analysis, which was calculated by the least square regression method.

Limit of Detection (LOD)

Limit of Detection (LOD) is defined as the lowest concentration of analyte that gives a detectable response. LOD is determined by the analysis of samples with known concentration of analyte and by establishing the minimum level at which the analyte can be reliably detected. LOD was calculated using the following equations [7].

$$\mathbf{LOD = 3.3 \times S_o/b,}$$

Where S_o and b are the standard deviation of the response and the slope of the calibration curve.

Limit of Quantification (LOQ)

Limit of Quantification (LOQ) is defined as the lowest concentration that can be quantified reliably with a specified level of accuracy and precision. LOQ is generally determined by the analysis of samples with known concentrations of analyte and by establishing the minimum level at which the analyte can be quantified with acceptable accuracy and precise. LOQ was calculated using the following equations [7].

$$\mathbf{LOQ = 10 \times S_o /b}$$

Where S_o and b are the standard deviation of the response and the slope of the calibration curve.

Accuracy

The accuracy is the measure of how close the experimental value is to the true value. The recovery study was carried out as 80%, 100% and 120% of the test concentration as ICH Guidelines. The recovery study was performed three times at each level. Accuracy was determined and expressed as percent recovery.

Precision

Method repeatability was determined by six times repetitions of assay procedure. The reproducibility of the proposed method was determined by analyzing tablet at different time intervals on same day and different day in triplicates (Intra-day and Inter-day assay precision). Standard deviation and percent RSD was determined.

Potency Test

The proposed validated method has been applied for the determination of potency of the tested tablets of Dapoxetine.

RESULTS AND DISCUSSION

A simple, rapid and accurate UV spectrophotometric analytical method has been developed and validated for the analysis of Dapoxetine in bulk and pharmaceutical preparations.

Table 1: Absorbance of Dapoxetine solutions of varying concentrations at 292 nm

SN	Dapoxetine	
	Conc. (µg/ml)	Absorbance
1	0	0
2	5	0.114
3	10	0.217
4	15	0.339
5	20	0.449
6	25	0.554
7	30	0.670
8	35	0.798

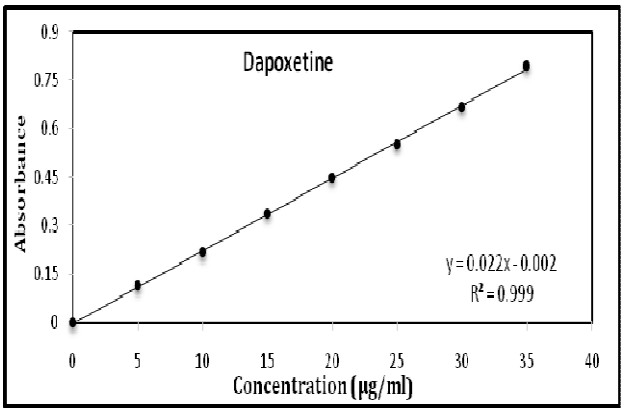

Figure 2: Calibration curve of Dapoxetine

Dapoxetine shows good solubility in methanol. A superior linear relationship was evident between the absorbance and concentration in the range of 5-35 µg/ml (Table 1, Fig. 2) and obeyed the Beer's law. The correlation coefficient was 0.999 indicating good linearity. The representative linear equation was y = 0.022x - 0.002, calculated by the least squares method. The limit of detection (LOD) was found as 0.959µg/ml, while the limit of quantification (LOQ) was 2.906µg/ml (Table 2).

Table 2: Linearity, LOD and LOQ data of Dapoxetine

SN	Parameter	Dapoxetine
1	Wavelength detection (λmax)	292
2	Slope	0.0226
3	Intercept	0.0027
4	Correlation coefficient (r)	0.999
5	Beers law limit	5-35 µg/ml
6	Regression equation (y=mx+c)	y = 0.0226x - 0.0027
7	Limit of detection	0.959 µg/ml
8	Limit of quantification	2.906 µg/ml

This drugs show good regression values at their respective wavelengths and the results of recovery study reveals that any small change in the drug concentration in the solution could be accurately determined by the proposed methods. The results of accuracy, inter-day and intra-day precision were listed in Table 3 and 4 respectively. Precision is validated by studying the repeatability and intermediate precision. Repeatability results indicate the precision under the same operating condition over a short interval of time and inter assay precision. Intermediate precision study expresses within laboratory variation in different days. In both inter-day and intra-day precision study, shows %RSD are not more than 2.0% which indicated good repeatability and intermediate precision (Table 4).

After the validation of the newly developed of this method, the proposed method was applied successfully for the analysis of Dapoxetine in pharmaceutical dosage form (tablets). The potency of marketed formulation was determined by this validated method and the results are presented in Table 5. Percentage estimation of Dapoxetine from tablet dosage form by this method is 97.84% with standard deviation (SD) <2 (Table 5).

Table 3: Recovery study for Dapoxetine (Accuracy)

Drug	Level of Recovery	Sample ID	Theoretical Value (mg)	Actual Value (mg)	% Recovery	Mean ± SD*	% RSD
Dapoxetine	80%	Spl_01	24.146	22.96	95.09	95.93 ± 1.46	1.52
		Spl_02	24.146	22.96	95.09		
		Spl_03	24.146	23.57	97.61		
	100%	Spl_01	30.460	28.93	94.98	95.00 ± 0.33	0.35
		Spl_02	30.460	28.84	94.68		
		Spl_03	30.460	29.04	95.34		
	120%	Spl_01	36.809	36.35	98.75	99.39 ± 1.52	1.53
		Spl_02	36.809	36.18	98.29		
		Spl_03	36.809	37.22	101.12		

*mean of three determinations

Table 4: Result of Precision (intra-day and inter-day precision)

Component	Intra-day precision		Inter-day precision	
	%Amount Found ± SD*	% RSD	%Amount Found ± SD*	% RSD
Dapoxetine	96.84 ± 0.55	0.57	97.62 ± 0.91	0.93

*mean of six determinations

Table 5: Potency determination of the Dapoxetine marketed dosage form

Dosage form	SL No.	Sample Code	Label claim(mg)	Amount found (mg)	Potency (%)	Mean ± SD
Tablet	1	DAPO-1	30	29.5	98.33	97.84 ± 0.942
	2	DAPO-2	30	28.98	96.5	
	3	DAPO-3	30	29.37	97.9	
	4	DAPO-4	30	29.59	98.63	

CONCLUSION

This study reveals that, the proposed method was found to be simple, accurate and rapid for the routine determination of Dapoxetine in bulk drug and pharmaceutical dosage forms. The method showed high sensitivity, acceptable linearity and accuracy. Furthermore, the method uses simple reagents with minimum steps and time for sample preparation, which allow it to be useful for routine analyses and quality-control assay of Dapoxetine in pharmaceutical preparations.

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