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SIMPLE VALIDATED UV-SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF DAPOXETINE

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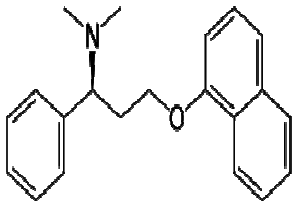
ABSTRACT

A simple,sensitive,cost effective, reproducible and accurate UV-spectrophotometric method was developed in ultraviolet region for the estimation of Dapoxetine in pure drug, pharmaceutical formulation. Linear response obtained was in the concentration range of 10-50 µg/ml with correlation coefficient of 0.9997 in solvent. Excellent recovery proved that method was sufficiently accurate. There is no interference from any common pharmaceutical additives and diluents. Results of the analysis were validated by recovery studies according to ICH Q2(R1) guidelines.

KEY WORDS: Dapoxetine, Spectrophotometry , Validaton.

1.INTRODUCTION

Chemically Dapoxetine is (*S*)-*N,N*-[dimethyl-3-(naphthalen-1-yloxy)-1-phenylpropan-1-amine] hydrochloride. Its empirical formula is $C_{21}H_{23}NO$.Dapoxetine is a white colored Powder with molecular mass of 305.413 g/mol. It is partially soluble in water and greatly soluble in methanol. It is a short-acting selective reuptake inhibitor (Goodman and Gillman) and the only drug with regulatory approval for the treatment of premature ejaculation in men (Feige,2011; wikepedia,2010).Analysis is an important component in the formulation development of any drug molecule. A suitable and validated method has to be available for the analysis of drug(s) in bulk, in drug delivery systems. A literature survey revealed that only a few HPLC (Hamilton and Cornpropst,2002) methods are available for the estimation ofDapoxetine. The authors now propose a new validated, sensitive and reproducible UV-Spectrophotometric method for the determination of Dapoxetine and the Tablet dosage forms was also observed. The information about spectrophotometric methods of Dapoxetine were not reported in literature. An attempt has been made to develop simple, sensitive, and economical method in UV region with greater precision and accuracy for the estimation of Dapoxetine in pure drug and tablet formulation.



Chemical structure of Dapoxetine

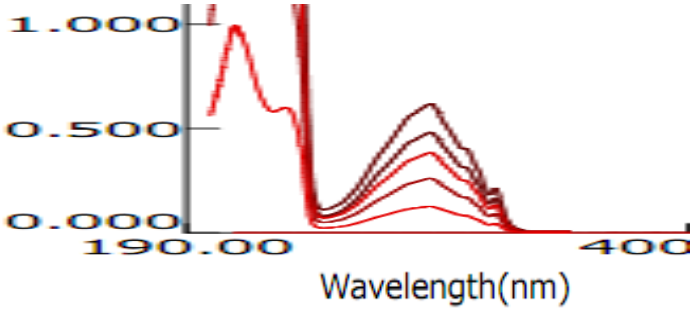


Fig.1.Overlain spectra of Dapoxetine in Methanol:Water(80:20)

2.MATERIALS AND METHOD

Instrumentation,Reagents&Chemicals: Instruments used were, UV-Visible spectrometer**,** model T-60U- PG Instruments with 8mm matched pair of quartz cell and spectral band width of ±2nm and SHIMADZU ELB300 ANALYTICAL BALANCE. Dapoxetine pure drug (99.99%) was obtained as a gift sample from Emcure pharmaceuticals, Pune. All chemicals and reagents used were of analytical grade.Formulation used for studies was developed by Emcure pharmaceuticals with brand name Sustinex.

Selection of solvent: The ideal property of a solvent should be that the drug should be completely soluble in the solvent used. The drug should be stable in the solvent used and should be economical and volatile. Taking above factors in to consideration the suitable sovent selected Was methanol.

Selection of Method and Wavelength: For estimation of Dapoxetine single wavelength spectrophotometric method employing 292.2 nm analytical wave length were used.

Preparation of Standard solutions: Accurately weighed 10mg of Dapoxetine transferred in to a 100ml volumetric flask and dissolved in 20 ml of methanol. It was then sonicated for 10 minutes and made up to the mark with distilled water to give a stock solution having 100 µg/ml concentration. For calibration curve, serial dilutions were made for Dapoxetine in the range of 10, 20, 30, 40, 50µg/ml concentrations were prepared by diluting the stock solution with

methanol:water (80:20). The absorbance values of above solutions were measured as blank and calibration curve was prepared. It obeyed beer's law in these concentration ranges.

Sample preparation for tablet analysis: To determine the content of Dapoxetine in conventional tablets (label claim: 30 mg Dapoxetine per tablet), 20 tablets were weighed, their mean weight was determined and they were finely powdered and powder equivalent to 10 mg of Dapoxetine was weighed and transferred in to a 100ml volumetric flask containing 20 ml Methanol, sonicated for 10 min and the resulting sample solution was then filtered through Whatmann filter paper (No. 14). The filterate was further diluted with distilled water to obtain the final concentration of 100µg/ml. Appropriate dilution(30µg/ml) of Dapoxetine were prepared, the absorbance at wavelength 292.2nm was measured. From calibration curve the final drug concentration in tablet was calculated.

EXPERIMENTAL:

Preparation of calibration curve: Standard stock solution was suitably diluted with solvent to obtain concentrations ranging from 5-50 µg/ml. Absorbance of these solutions were measured at 292.2 nm (λmax Dapoxetine) using UV, calibration curve was obtained by plotting graph between concentration and absorbance shown in figure 1.

Linearity: Linearity was obtained between5-50µg/ml concentration. Graph was plotted for concentration and absorbance. The equation of calibration curve obtained was Y=0.01225x+0.0101, the correlation coefficient (R^2) was 0.9997 shown in fig.2

Limit Of Detection (LOD) and Limit Of Quantification (LOQ): The LOD and LOQ of Dapoxetine were determined by using standard deviation of response and slope approach as defined by ICH guidelines. The LOD and LOQ were found to be 0.524and 1.59 respectively.

Precision: Precision was calculated for intraday and inter-day of pure drug, the data shows that the method is sufficiently precise shown in table 5 & 6.

Accuracy: To determine the accuracy of the method recovery was performed by standard addition method. To pre-analyzed sample known amount of standard Dapoxetine was spiked in different concentrations. The recovery was performed at three levels 50%, 100%,150% of standard Dapoxetine, solutions were analyzed and percentage recovery was calculated from calibration curve shown in table3.

Stability: The standard stock solution of Dapoxetine 30 µg/ml in Methanol was subjected to heat at 40^0C,50^0C for 10 minutes then diluted up to the mark and absorbance were measured. The absorbance of initial and after heating are obtained the same. Hence concluded the drug is stable in Methanol.

3.RESULTS AND DISCUSSION

Attempt has been made to develop rapid sensitive, economic, precise and accurate analytical method for Dapoxetine in pure and pharmaceutical dosage form. The proposed method is based on UV spectrophotometric absorption in UV region using methanol and water as solvent, maximum absorbance was found to be at 292.2nm. LOD and LOQ were found to be 0.524 and 1.59 respectively. Beer's law was obeyed in concentrations ranging from 10-50µg/ml,. The correlation co-efficient values were above 0.9997 which shows that absorbance was linear with concentration. The optical characteristics such as Beer's law limits correlation co-efficient, slope, intercept and molar absorptivity were calculated. To study interference of various excipients recovery was done for formulation. It showed that there is no interference of excipients on the pure drug. The percentage label claim present in tablet formulation was confirmed by repeated analysis of formulation. It was found to be 99.46%.Precision of the method was confirmed by Intraday and inter-day analysis, % RSD values were found to be less than2. From all the validation parameters, the developed method was found to be simple, economical, precise and accurate. Hence proposed method could be effectively applied for analysis of Dapoxetine in bulk and formulated tablet dosage form.

4.CONCLUSION

A spectrophotometric method for quantifying Dapoxetine in pure and tablet has been developed and validated .The method is selective, precise, accurate and linear over the concentration range studied. The method is simple and suitable for the determination of Dapoxetine in formulation, without interference from excipients or from common degradation products, suggesting its application in IPQC and pharmacokinetic studies.

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Table 1: Validation Parameters

S.No.	Parameter	Result
1.	Absorption maxima (λmax) (nm)	292.2nm
2.	Linearity range (µg/ml)	5-50 µg/ml
3.	Standard regression equation	Y=0.01225x+0.0101
4.	Correlation coefficient (r^2)	0.99977
5.	Molar absorptivity	11620

Table2: Calibration data for Analysis of Dapoxetine in methanol:water(80:20) at $\lambda_{292.2}$

Conc µg/ml)	Avg Absorbance
10	0.128
20	0.260
30	0.381
40	0.497
50	0.622

Table3: Recovery data of Dapoxetine in methanol : water (80:20)

Ingredient	Amount of drug from formulation	Amount of standard added	Percentage added	Amount recovered	% recovery
Dapoxetine	30µg	5 µg	50	34.92 µg	99.77
-do-	30 µg	10 µg	100	40.24 µg	100.6
-do-	30 µg	15 µg	150	54.66 µg	99.38

Table 4: Results of samples (Assay)

Sample	Label	Amount Found	% label claim
Dapoxetine	30	29.84	99.46

Table 5: Intraday precision of Dapoxetine in methanol:water(80:20)

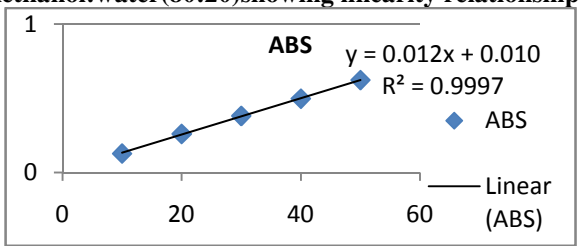
Parameter	% Recovery Estimated (Mean±RSD)*		
	30 (µg/ml)	30(µg/ml)	30(µg/ml)
Morning	99.89± 0.38	99.65 ± 0.93	99.48 ± 0.90
Afternoon	99.96± 0.80	99.98 ± 1.10	100.05 ± 0.23
Evening	99.21 ± 0.84	99.76 ± 0.46	99.72 ± 0.21

* n=3 (Average of 3 determinations)

Table 7: Inter-day precision of Dapoxetine in methanol:water(80:20)

Parameter	% Recovery Estimated (Mean±RSD)*		
	30 (µg/ml)	30(µg/ml)	30(µg/ml)
Day -1	99.68± 0.67	100.24 ± 0.21	99.09 ± 0.74
Day -2	100.05± 0.18	99.04 ± 0.96	100.42 ± 0.16
Day -3	99.28 ± 0.94	99.78 ± 0.72	98.96 ± 0.96

Fig.2: Calibration Curve of Dapoxetine in methanol:water(80:20)showing linearity relationship



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