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Application of validated Derivative Spectrophotometric method for estimation of Duloxetine in tablets

KEYWORDS: Duloxetine, zero order, first order derivative spectrophotometry, validation

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ABSTRACT *Two simple, sensitive, precise and economical UV- spectrophotometric methods have been developed for the determination of Duloxetine in tablet formulation. Method A is simple and direct UV spectrophotometric method and is based on determination of Duloxetine in methanol at 290nm. Method B is first order derivative spectrophotometric method and involved estimation of Duloxetine in methanol using the first-order derivative technique at 274 nm as maxima and 300 nm as minima. Linearity was obtained in the concentration range of 9- 15 µg/ml. These methods were validated as per ICH guidelines and are successfully applied to pharmaceutical formulations because no interferences from tablet excipients were found. The proposed methods were found to be simple, sensitive, accurate, precise, rapid and economical for the routine quality control application of Duloxetine in pharmaceutical formulations.*

INTRODUCTION

Duloxetine (fig.1) is chemically as, N-methyl-3-(1-napthyloxy)-3-(thiophen-2-yl)-propan-1-amine. It belongs to the class narcoleptics. Duloxetine hydrochloride is a newer selective serotonin and nor epinephrine reuptake inhibitor used for major depressive disorders. It has been approved for the treatment of major depressive disorder and for the diabetic peripheral neuropathic pain. Duloxetine it is effective for major depressive disorder and generalized anxiety disorder.

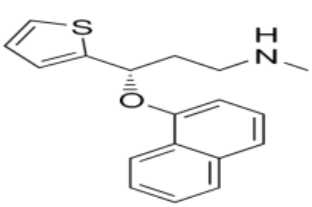

Figure – 1 Duloxetine

Duloxetine is not official in any pharmacopoeia. In Literature, several UV Spectrophotometric methods [1-9], Spectroflorimetric method [10], RP-HPLC [11-13] methods for estimation of Duloxetine are present. Till date there is no derivative spectrophotometric method was reported. Hence an attempt has been made to develop novel derivative spectrophotometric method for its estimation in bulk and pharmaceutical formulation with good precision, accuracy, linearity, reproducibility.

MATERIALS AND METHODS

Apparatus

A Lab India model 3000 double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Win system software.

Reagents and Materials

Duloxetine was supplied by Aurobindo Pharma Ltd, Hyderabad, India as a gift sample. The commercially available tablets of Duloxetine were procured from local market labeled to contain 30 mg Duloxetine t. Methanol (AR Grade, S. D. Fine Chemicals LtD., Mumbai, India) and Whatman filter paper no. 41 (Whatman International Ltd., England) were used in the study.

Preparation of Standard Stock Solution

10 mg of Duloxetine was accurately weighed and transfer in 100 ml volumetric flask and add about 70 ml of methanol, shaken and sonicate till dissolved and volume was made up to the mark with methanol and mixed well. Pipette out 1.2 ml of Duloxetine stock solution into 10 ml volumetric flask and make up to the mark with methanol to produce 12 µg/ml of Duloxetine solution.

Preparation of Sample Solution

Twenty tablets were weighed and powdered. The quantity of the powder equivalent to 10 mg of Duloxetine was transferred to a 100 ml volumetric flask, ultrasonicated for 30 minutes with methanol to dissolve the drug as completely as possible. Further diluted and make up the volume using methanol. The solution was filtered through a Whatman filter paper. Pipette out 0.4ml of resulting solution was diluted to 10 ml with diluent.

DEVELOPMENT OF THE METHODS

Method A: Zero Order Spectroscopic Method

The solutions were scanned in the range from 400-200 nm, and the peak was observed and gives maximum absorbance at 290 nm (fig-3). So, the wavelength selected for the analysis of the drug was 290 nm. The drug followed the Beer's-Lamberts law in the range of 9-15 µg/ml.

Method B: First Order Derivative Spectroscopic Method

The standard drug solution was diluted so as to get the final concentration in the range of 9-15 µg/ml and scanned in the first order derivative spectra. The first order derivative spectra showed a maxima and minima at 274 and 300 nm respectively (fig-3) The amplitude of absorbance was measured at 274 nm (peak maxima) and at 300 nm (peak minima) and was plotted against concentration to give calibration curve, and regression equation was calculated.

VALIDATION OF THE PROPOSED METHODS

Linearity

Calibration curves for Duloxetine were plotted over a concentration range of 9 – 15 µg/ml for both the methods. Accurately measured standard working solutions of Duloxetine (9.0, 10.5, 12.0, 13.5 and 15 ml) were transferred to a series of 10 ml volumetric flasks and diluted up to the mark by methanol. Absorbance was measured at a wavelength 290 nm and was plotted absorbance versus concentration to give calibration curve for method A and from this curve regression equation was calculated. First derivative curves of different concentration solutions were obtained, which shows maxima at 274 nm and minima at 300 nm. The calibration curve of amplitude against concentration of the drug showed linearity

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for method B.

Accuracy (% Recovery)
The accuracy of the method was performed by calculating recovery of Duloxetine by the standard addition method. Known amounts of standard solutions of Duloxetine were added at 50, 100 and 150% levels to pre quantified sample solutions of Duloxetine. At each level of the amount 3 determinations were performed. Calculate the amount found and amount added for Duloxetine and calculate the individual recovery and mean recovery values.

Method Precision
The precision of the instrument was checked by repeated scanning and measurement of the absorbance of solutions (n = 5) of Duloxetine without changing the parameters for the methods. The repeatability was expressed in terms of relative standard deviation. The %RSD was found to be within the specified limits.

Intermediate Precision
The intraday and inter day precision of the proposed method was performed by analyzing the corresponding responses 3 times on the same day and on 3 different day with same dimensions. The results were reported in terms of relative standard deviation.

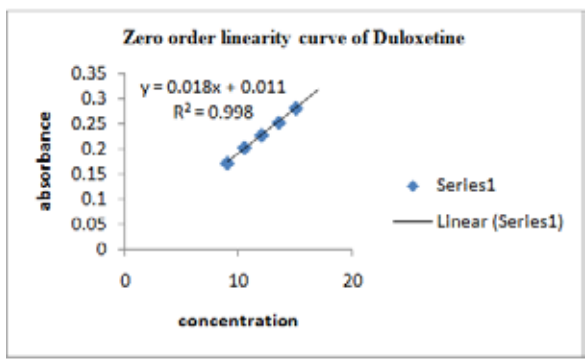
Limit of Detection and Limit of Quantification
LOD and LOQ were calculated from the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the five replicate determinations of same concentration (12 µg/ml of Duloxetine), standard deviation (SD) of the responses was calculated. From these values LOD and LOQ were determined on the basis of standard deviation and slope of the regression equation.

$LOD = 3.3 \times \sigma/S$ $LOQ = 10 \times \sigma/S$

σ = the standard deviation of the response and S = slope of the calibration curve

Estimation of Duloxetine in Pharmaceutical Formulation
Pharmaceutical formulation of Duloxetine was purchased from local pharmacy. Sample solutions were prepared as described earlier. Then this solution was analyzed by two methods. The nominal content of the tablets was determined either from the calibration curve or using the regression equation.

RESULTS AND DISCUSSION
Method A is simple UV spectrophotometric method. In this method the simple UV spectrum of Duloxetine in methanol was obtained which exhibits absorption maxima at 290 nm (Fig-3). Method B is the first derivative spectrophotometric method. Maxima occur at 274 nm and minima at 300 nm (Fig- 3). The calibration curves were linear in concentration range of 9 – 15 µg/ml. The low percentages of RSD values of inter day and intraday for both methods, reveals that the proposed methods are precise. The LOD and LOQ values show that proposed method is sensitive. The % mean recoveries for both methods were found to be 99.8% shows that the methods are accurate. The methods were successfully used to determine the amounts of Duloxetine present in tablets. The results obtained are in good agreement with the corresponding labeled amount. The % assay was found to be 100.2% and 100% for proposed methods. No interference of the excipients with the absorbance appeared. Characteristic parameters and summary of validation parameters for the two methods are given in Table 4. The proposed methods were found to be, sensitive, rapid, accurate, precise and for the routine analysis of Duloxetine in pharmaceutical formulations. By observing the validation parameters, the methods were found to be simple, sensitive, accurate, precise and economic than earlier reported methods. Hence the methods can be employed for the routine analysis of Duloxetine in tablet formulations.



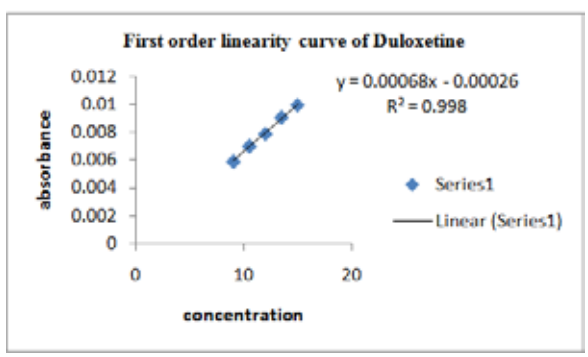


Figure-2 linearity curve of Duloxetine

Table: 1 Results of Intra and Inter Day Precision

parameters	Intraday precision		Inter day precision	
	S.D	%RSD	S.D	%RSD
Zero derivative	0.0033	1.62	0.0011	0.55
First derivative	0.00005	0.62	0.000049	0.60

Table: 2 Assay Results for Determination of Duloxetine in Pharmaceutical Formulation

Parameters	label claim in mg	Amount found in mg	Drug content
Zero order	30	30.06	100.2%
First order	30	30.00	100.0%

Table: 3 Results of Accuracy

Accuracy level	Absorbance		Amount added		Amount found		% recovery		Mean recovery	
	Zero	First	Zero	First	Zero	First	Zero	First	Zero	First
50%	0.112	0.004	5.0	5.0	4.99	4.99	99.8	99.8	99.8%	99.8%
100%	0.224	0.008	10.0	10.0	9.98	9.98	99.8	99.8		
150%	0.337	0.012	15.0	15.0	15.0	14.9	100	99.8		

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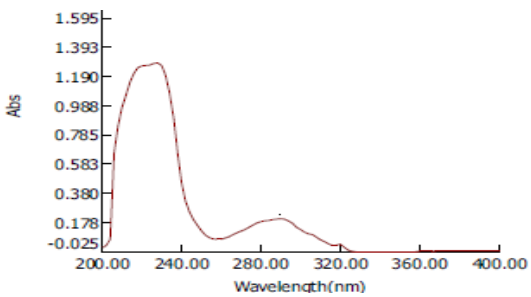
Table: 4 Regression Analysis Data and Summary of Validation Parameters for the Proposed Methods

Paramer	Zero order	First order
Absorption maxima and minima (nm)	290	274 & 300
Beer's-Lamberts range (µg/ml)	9-15	9-15
Regression equation y=mx+c	Y = 0.018x + 0.011	Y = 0.00068x -0.00026
Slope(m)	0.018	0.00068
Intercept(c)	0.011	-0.00026
Correlation coefficient (r2)	0.998	0.998
Mean Recovery %	99.8	99.8
Precision (% RSD)	1.62	0.62
Intermediate precision	0.55	0.60
LOD (µ g/ml)	0.2	0.23
LOQ (µ g/ml)	0.611	0.72



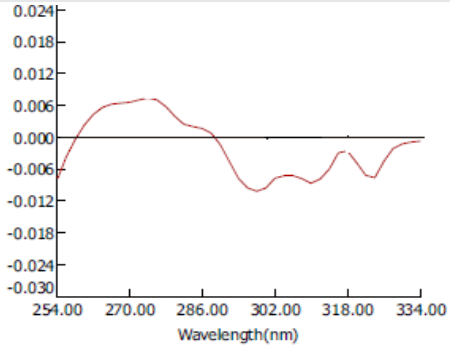


Figure-3 zero and first order derivative spectrums of Duloxetine

CONCLUSION

The proposed first order derivative spectrophotometric method for estimation of Duloxetine in their tablet dosage form is novel, accurate, precise, and reproducible and also shows good linearity than earlier reported methods. Moreover the method is simple, rapid, and economic and does not involve the use of complex instrument such as HPLC, which is expensive in both the hardware and chromatographic reagents hence can be employed for routine analysis in quality control laboratories.

REFERENCE

1. Kishore Methuku, et. al, Method Development and Validation of Duloxetine Hydrochloride in bulk and formulation using UV spectrophotometric method, Journal of Pharmaceutical and Scientific Innovation, 1(3), 81-86, 2012. | 2. Hemant Kumar T, et.al, Estimation of Duloxetine Hydrochloride by Visible Spectrophotometric Method, International Journal of Research in Pharmaceutical and Biomedical Sciences, 3 (1), 2012. | 3. Kamila MM, et.al, validated UV spectrophotometric method for determination of Duloxetine hydrochloride, Pharmazie, 62(6), 414-5, 2007. | 4. R. Vijay Amirtha Raj, et.al, A Validated UV Spectrophotometric Determination of an Antidepressant Drug – Duloxetine Hydrochloride From Capsule Formulations, International Journal of Pharma and Bio Sciences, 2(1), 716-720, 2011. | 5. Mohammad Yunoos, et.al, Simple UV Spectrophotometric Determination of Duloxetine Hydrochloride in Bulk and in Pharmaceutical Formulations, E-Journal of Chemistry, 7(3), 785-788, 2010. | 6. Kiran Aarelly, et.al, Method Development and Validation of Duloxetine Hydrochloride in Bulk and Formulation Using UV Spectrophotometric Method, IJPI's Journal of Analytical Chemistry, 2(10), 1-9, 2012. | 7. Amirtha Raj, R. Vijay, et.al, A Validated UV Spectrophotometric Determination of An Antidepressant Drug -- Duloxetine Hydrochloride From Capsule Formulations, International Journal of Pharma & Bio Sciences, 2(1), P-716, 2011. | 8. N. Tamilselvi, et.al, UV spectrophotometric estimation of Duloxetine hydrochloride in tablet dosage form, Research Journal of Pharmacy and Technology, 5 (3), p-365, 2012 | 9. T. Srinivasa Reddy, et.al, visible spectrophotometric methods for the determination of duloxitine hydrochloride in bulk and dosage forms, Der Pharma Chemica, 4(6), 2427-2433, 2012. | 10. SL Prabhu, S Shahnawaz, et.al, Spectrofluorimetric method for determination of Duloxetine hydrochloride in bulk and pharmaceutical dosage forms, Indian Journal of Pharmaceutical Sciences, 70(4), 502-503, 2008. | 11. Ch Narasimharaju Bhimanadhuni, et.al, Development and validation of RP-HPLC method for determination of Duloxetine hydrochloride in bulk and dosage form, International Current Pharmaceutical Journal, 1(5), 98-102, 2012. | 12. Usmangani K. Chhalotiya, et.al, Development and Validation of A Stability-Indicating Rp-Hplc Method For Duloxetine Hydrochloride in its Bulk and Tablet Dosage Form, Scientia Pharmaceutica, 78, 857-868, 2010. | 13. Narasimharao R, et.al, Method Development and Validation of Duloxetine Hydrochloride by RP HPLC, International Journal of Research in Pharmaceutical and Biomedical Sciences, 2 (2), 1335-1340, 2011.