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A validated UV spectrophotometric method for determination of duloxetine hydrochloride

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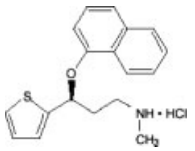
A simple, sensitive and accurate UV spectrophotometric method was developed for the assay of duloxetine hydrochloride in raw material and capsules. Validation of the method yielded good results concerning range, linearity, precision and accuracy. The absorbance was measured at 290 nm for duloxetine capsule solution. The linearity range was found to be 5–50 μg/mL for the drug. It was found that the excipients in the commercial formulation did not interfere with the methods.

1. Introduction

Duloxetine hydrochloride is an antidepressant drug recently approved by US Food and Drug Administration (FDA) for the treatment of major depressive disorder (MDD), pain related to diabetic peripheral neuropathy and stress urinary incontinence (SUI). It is a relatively balanced and potent inhibitor of 5-hydroxytryptamine (5-HT) and norepinephrine (NE) reuptake with weak effects on dopamine reuptake (Tran et al. 2003). Known also as LY248686 it is chemically (+)-(*S*)-*N*-methyl-γ-(1-naphthalenyloxy)-2-thiophenepropanamine hydrochloride (Budavari 2001) and not yet official in any pharmacopoeia. A literature survey has not revealed any UV spectrophotometric method for the determination of the drug, where as methods were reported for the estimation of the drug by HPLC along with its intermediates produced during its synthesis (Soni et al. 2005), for the separation of the drug from structurally-related impurities (Olsen and Argentine 1996) and in human plasma (Johnson et al. 1996).



Duloxetine hydrochloride (CAS number 136434-34-9)

In the present study, a simple, economical, precise and accurate analytical method for the estimation of duloxetine hydrochloride in pure form and in solid dosage forms was developed. The results of the analysis were validated by statistical methods and recovery studies.

2. Investigations, results and discussion

Duloxetine hydrochloride was analyzed by a UV spectrophotometric method both as a raw material and as a pharmaceutical capsule formulation. The linear regression equation

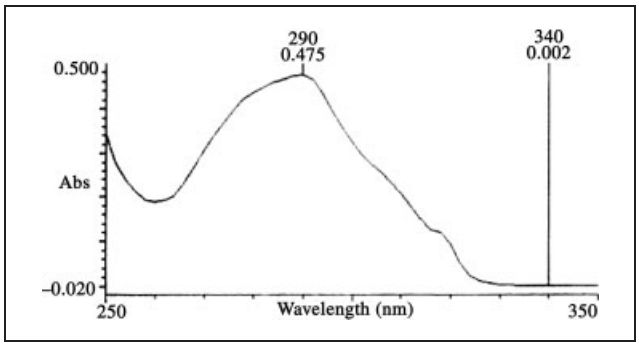


Fig.: UV spectra of duloxetine hydrochloride measured in bidistilled water

Table 1: Analysis of duloxetine hydrochloride capsules (20 mg)

Sl. No	A*	%Analysis ± S.D.	SEM	% C.V.
1	0.288			
2	0.281			
3	0.282	98.913 ± 1.055	0.471886	1.067
4	0.284			
5	0.281			
6	0.280			

* Absorbance – Average of three determinations, S.D.: Standard deviation, SEM: Standard error of mean, C.V.: Coefficient of variance

Table 2: Recovery studies for duloxetine hydrochloride capsules

Sl. No.	Spiked amount (μg/mL)	Recovery amount (μg)	Recovery (%)	Recovery (%) ± S.D.
1	15	15.123	100.824	
2	20	20.123	100.618	
3	25	24.747	98.989	100.265 ± 0.745
4	30	30.069	100.233	
5	35	35.231	100.660	

Table 3: ANOVA of intra- and inter-day assay of duloxetine hydrochloride capsules

					F at level 1%	F at level 5%
Source of variation	SS	df	MS	F_{stat}*	1%	5%
Rows	0.43606667	3	0.1453556	0.20677528	9.78	4.76
Columns	1.08455	2	0.542275	0.77141231	10.92	5.14
Error	4.21778333	6	0.7029639			
Total	5.7384	11				

* $F_{stat} < F$ at level 1% and 5% in both cases

was calculated to be $Y = 0.0186X + 0.0067$ where X and Y are concentration in μg/mL and absorbance respectively.

A standard calibration curve of the drug was constructed by plotting absorbance versus concentration. The UV absorption spectrum (Fig.) was monitored at 290 nm. Agreement with Beer's law was evident from the concentration range of the final dilution of 5–50 μg/mL. The correlation coefficient was obtained as 0.9994 indicating very good linearity. The experimental results obtained for the determination of duloxetine hydrochloride capsules are shown in Table 1. The method had excellent reproducibility for standard solution of 100 μg/mL. The average purity was reached 100.88%

The detailed accuracy is shown in Table 2. In this test the observed concentrations of duloxetine hydrochloride reference substance in the capsule were not significantly different from the stated concentrations by Student's t test, $P = 0.05\%$ (100.27%, $n = 5$).

No interfering intensity was found in the UV spectra due to the capsule excipients. Duloxetine hydrochloride was shown to be stable during all procedure.

3. Experimental

3.1. Chemicals

Duloxetine hydrochloride reference substance was the kind gift from Sun Pharmaceutical Industries (Goa, India). Capsules of brand Duzela®20 (Sun Pharmaceutical Industries, Dadra, India) containing 20 mg of duloxetine hydrochloride were procured from a local pharmacy. Bidistilled water was used as the solvent for the experiment.

3.2. Equipment

A double beam UV-VIS spectrophotometer (UV-2450, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe was employed with spectral bandwidth of 1nm and wavelength accuracy of ± 0.3 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (Precisa 310M, Switzerland).

3.3. Standard solution

The standard solution of duloxetine hydrochloride was prepared by accurately weighing 10 mg of the drug diluted in a 100 mL volumetric flask with distilled water to give a range of solutions with final concentrations of 5–50 μg/mL. The absorbance of each solution was determined at 290 nm.

3.4. Sample preparation

For the analysis of the dosage form, twenty capsules of duloxetine hydrochloride (20 mg) were ground to fine powder and mixed thoroughly. Powder equivalent to 10 mg of the drug was transferred to a 100 ml volumetric flask and dissolved in about 40 ml distilled water by shaking on a rotary flask shaker for one hour. The solution was filtered through Whatman filter paper (No. 41). The filter paper was washed with the blank. The washings were added to the filtrate and the final volume was made up to 100 mL with the blank. After suitable dilution, the absorbance of final sample corresponding to 15 μg/mL was recorded against the blank at 290 nm. All the determination was conducted in triplicate.

The data were analyzed by linear simple regression by the least-squares method. The recoveries were determined by adding known amounts of duloxetine hydrochloride reference substance (0, 50, 100, 150 and 200 μg) to the samples at beginning of the process. A recovery exercise was then performed.

The precision and accuracy of the assay as well as linearity of the calibration curve were determined for intra- and inter-day on three different days. The precision was expressed as the percent coefficient of variation of each curve. The statistical data were calculated by ANOVA (Table 3).

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