Asian Journal of Chemistry Vol. 21, No. 8 (2009), 5908-5912

Spectrophotometric Estimation of Venlafaxine Hydrochloride

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Two rapid, simple, precise and economical methods *viz.*, linear regression equation and standard absorptivity were developed and validated for estimation of venlafaxine hydrochloride in capsule dosage form. The estimation of venlafaxine hydrochloride was carried out at 274 nm. Beer-Lamberts law was obeyed in the concentration range of 50-250 µg/mL and standard absorptivity A (1 %, 1 cm) was found to be 38.794 dl g^{-1} cm^{-1}. The molar extinction coefficient (ε) for the drug was found to be 1214.267 mol^{-1} cm^{-1}. Both methods were validated for linearity, accuracy, precision and robustness. The numerical value for all validation parameters lies within the acceptable limits.

Key Words: Venlafaxine hydrochloride, UV Spectrophotometry, Linear regression equation, Standard absorptivity.

INTRODUCTION

Venlafaxine chemically, (RS)-1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]-cyclohexanol hydrochloride or (±)-1-[a[a-(dimethylamino)methyl]-*p*-methoxybenzyl] cyclohexanol hydrochloride (Fig. 1), is a bicyclic antidepressant and is usually categorized as a serotonin-norepinephrine reuptake inhibitor (SNRI), but it has been referred to as a serotonin-norepinephrine-dopamine reuptake inhibitor[1]. It works by blocking the transporter "reuptake" proteins for key neurotransmitters affecting mood, thereby leaving more active neurotransmitters in the synapse. The biopharmaceutical classification system (BCS) teaches that the two main indicators of drug bioavailability are the aqueous solubility and the ability of the drug molecules to permeate biologic membranes[2]. Automated and miniaturized methods for determination of solubility of solid compounds have been developed[3,4].

Aqueous drug solubility can be estimated from easily obtainable properties, such as the melting point, the octanol-water partition coefficient, the hydrogen-bonding capacity of the molecule and its nonpolar surface area[3,5-7]. Determining the aqueous solubility of a compound is an essential parameter in drug discovery. Poor water solubility can interfere with *in vitro* testing, giving rise to inaccurate and

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irreproducible data. Compounds with low aqueous solubility tend to be highly bound to plasma proteins with poor systemic tissue distribution and increased potential of CYP-mediated drug inhibition[8]. Gastrointestinal stability of venlafaxine was evaluated *in vitro* in simulated gastric (SGF) and intestinal (SIF) fluids using a stability indicating HPLC method[9]. Venlafaxine hydrochloride was estimated in tablets and capsules by RP-HPLC in the range of 99.02-101.68 %[10]. It was also estimated by formation of blue coloured chromogen of venlafaxine with felin Ciocalteu reagent in presence of alkali, *i.e.* the estimation was based on the colorimetric reaction in between venlafaxine and felin Ciocalteu reagent[11]. Thus literature review revealed that there is no spectrophotometric method for estimation of the venlafaxine without treating with any reagent. Present work is aimed to develop and validate direct spectrophotometric methods which are simple, accurate, precise, rapid, reproducible and economic.

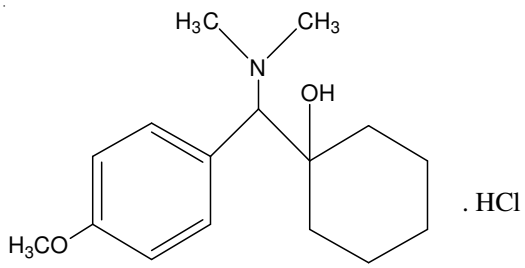

Fig. 1. Structure of venlafaxine hydrochloride

EXPERIMENTAL

UV 1601 series (Shimadzu), UV-Vis double beam spectrophotometer was used. Venlafaxine hydrochloride was gift sample from Alembic Limited, Vadodara.

Standard solution and calibration curve: The standard solution (1000 µg/mL) of venlafaxine hydrochloride drug was prepared in distilled water. The standard solution (1000 µg/mL) was diluted with distilled water, to obtain various dilutions (50, 100, 150, 200 and 250 µg/mL) (Figs. 2 and 3). All the solutions of drug were scanned between 230 nm and 400 nm. The λ_{max} for venlafaxine hydrochloride was found at 274 nm.

Standard absortivity method: Five dilutions were prepared in triplicate and the absorbances were observed at 274 nm. From these observations the standard absorptivity A (1%, 1cm) and molar extinction coefficient were calculated (Table-1).

Validation of method: As per ICH guidelines[12,13], six dilutions in three replicate were used to validate both methods for linearity, accuracy (by recovery studies-standard addition to pre-analyzed samples), repeatability (within day), intermediate precision (days, analyst and instrument variation) and robustness and statistical parameters were calculated for them (Table-2).

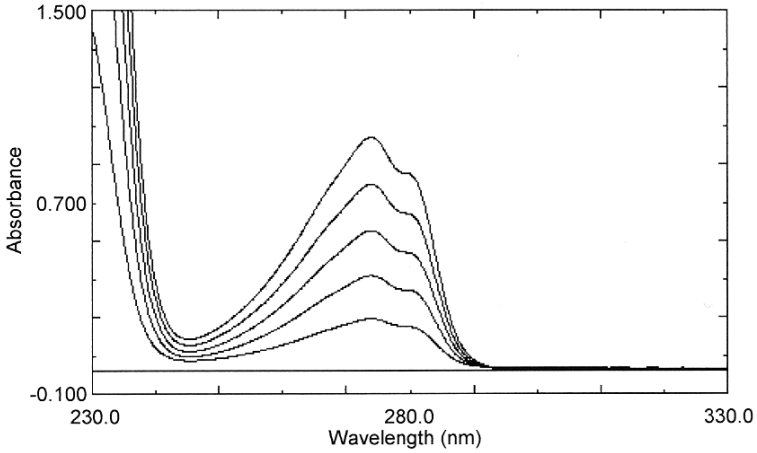

Fig. 2. Gaussian spectra of venlafaxine hydrochloride

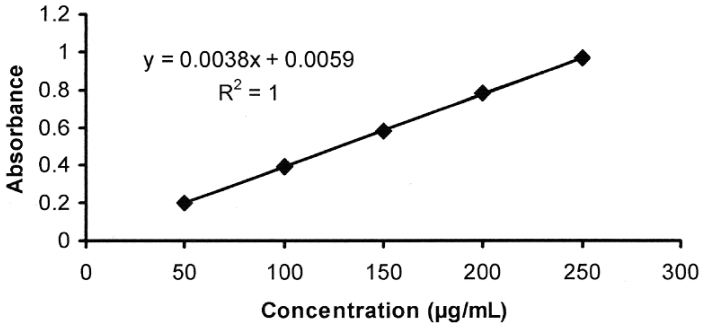

Fig. 3. Calibration curve for venlafaxine hydrochloride

TABLE-1
STANDARD ABSORPTIVITY (A) (1 %, 1 cm) AND
MOLAR EXTINCTION COEFFICIENT (ε)

Concentration (µg/mL)	Absorbance at 274 nm			Standard absorptivity A (1 %, 1 cm) = A/bc)		
	I	II	III	I	II	III
50	0.1973	0.1935	0.1898	39.46	38.70	37.96
100	0.3917	0.3823	0.3948	39.17	38.23	39.48
150	0.5828	0.5623	0.5735	38.85	37.49	38.23
200	0.7766	0.7689	0.7825	38.83	38.45	39.16
250	0.9670	0.9890	0.9925	38.68	39.56	39.70
	A (1 %, 1 cm)* in dl g^{-1} cm^{-1}			38.794		
	ε** in mol^{-1} cm^{-1}			1214.267		

*Mean of 15 above standard absorbtivities determination.
**Molar extinction coefficient ε = A (1 %, 1 cm) × Molecular weight/10.

TABLE-2
RESULTS OF VALIDATION PARAMETERS

Validation parameter	% Found* (mean)	SD	CV	SEx	SEσ
Linear regression equation method					
Accuracy	100.23	0.23	0.229	0.054	0.038
Precision	100.56	0.45	0.447	0.106	0.075
I. Repeatability	99.98	0.26	0.260	0.061	0.043
II. Intermediate precision					
a. Days	99.78	0.28	0.281	0.066	0.047
b. Analysts	99.89	0.29	0.290	0.068	0.048
c. Instruments	100.09	0.48	0.479	0.113	0.081
Robustness	99.52	0.25	0.251	0.059	0.042
Standard absortivity method					
Accuracy	100.58	0.46	0.457	0.108	0.077
Precision	99.64	0.24	0.241	0.057	0.041
I. Repeatability	99.73	0.56	0.562	0.132	0.093
II. Intermediate precision					
a. Days	100.34	0.65	0.648	0.153	0.108
b. Analysts	99.67	0.48	0.482	0.113	0.082
c. Instruments	99.12	0.36	0.363	0.085	0.064
Robustness	99.81	0.56	0.561	0.132	0.093

*Mean of six dilutions in three replicates, SD = Standard deviation, CV = Coefficient of variance, SEx = Standard error of mean and SEσ = Standard error of standard deviation.

Quantitative estimation: Powder equivalent to 75 mg was taken from powder of 20 capsules (strength 75 mg) and dissolved in 100 mL distilled water. Three different dilutions were prepared from stock solution, which were analyzed by linear regression equation (LRE) method and standard absorptivity (SA) method (Table-3).

TABLE-3
RESULTS OF CAPSULE ESTIMATION

Concentration	% Found by LRE method			% Found by SA method		
(μg/mL) →	100	150	200	100	150	200
Batch ↓						
I	101.700	99.930	100.600	101.200	100.400	99.350
II	102.100	100.300	101.400	101.500	100.800	100.200
III	100.900	99.600	101.200	100.800	99.700	99.950
IV	101.200	100.700	101.500	102.000	99.900	100.030
V	102.400	100.200	100.900	101.600	101.100	99.700
VI	100.000	99.130	100.900	100.400	98.700	99.700
Mean	101.38	99.980	101.080	101.250	100.100	99.820
SD	0.875	0.555	0.343	0.579	0.865	0.301
CV	0.863	0.555	0.339	0.571	0.864	0.302
SEx	0.357	0.226	0.140	0.236	0.353	0.123
SEσ	0.253	0.160	0.099	0.167	0.250	0.087

LRE = Linear regression equation method and SA = Standard absorptivity method.

RESULTS AND DISCUSSION

Venlafaxine hydrochloride is highly water soluble, which give good shape of Gaussian spectra (Fig. 2) against water as a blank. Both methods, linear regression equation and standard absorptivity for the estimation of venlafaxine hydrochloride in capsule dosage form were found to be simple, accurate, reproducible and economical. These methods were very much economical as solvent is water. Beer-Lambert's law was obeyed in the concentration range of 50-250 µg/mL. Both methods were validated for validation parameters with the acceptable values of the coefficient of variation. The values of standard deviation, RSD and all other statistical data for the validated parameters were found to be satisfactory and therefore the methods may be used for routine analysis.

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(*Received*: 12 July 2008; *Accepted*: 19 May 2009) AJC-7557