Development and Validation of Spectrophotometric Method for Determination of Venlafaxine Hydrochloride

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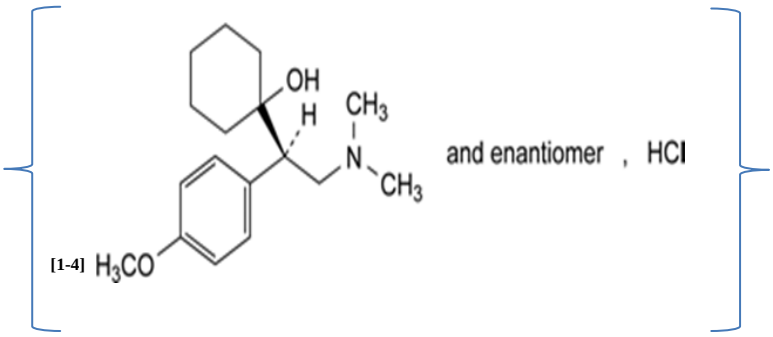
Abstract:

In these studies describes a simple, accurate, precise and cost effective UV-visible spectrophotometric method for the estimation of Venlafaxine hydrochloride in bulk and pharmaceutical formulations. The method is based on the measurement of absorbance of Venlafaxine hydrochloride solution in 0.1N NaOH at 223nm in the wavelength range of 200-400nm. The method obeys Beer's Lambert's law in the selected concentration range 5-25 µg/ml in selected media. The slope, intercept and correlation coefficient were also calculated. Results of percentage recovery study shows that the method was not affected by the presence of common excipients in tablets. The parameters like linearity, precision, accuracy, sensitivity study i.e. Limit of detection and limit of quantitation were studied according to International Conference on Harmonization (ICH) guidelines. The developed method was validated in terms of accuracy, precision, linearity, limit of detection and limit of quantitation which proves suitability of proposed method for routine estimation of venlafaxine hydrochloride in bulk and pharmaceutical formulations.

Keywords: UV-visible spectrophotometer, Method development, Venlafaxine hydrochloride.

Introduction:-

Venlafaxine Hydrochloride is an established anti-depressant drug. Chemically it is known as [2-(Dimethyl amino)-1-(4-methoxyphenyl) ethyl] cyclohexanol hydrochloride with molecular weight 313.9. Freely soluble in water and elimination half-life of 4-5 hrs. [1, 2, 3.4] Venlafaxine hydrochloride is a third generation antidepressant. It inhibits the reuptake of serotonin, nor epinephrine and to a lesser extent dopamine. It lacks monoamine oxidase activity and more importantly, the adverse effect profile of tricyclic antidepressants. Venlafaxine has no affinity for brain muscarinic, cholinergic, histaminergic or adrenergic receptors.[5.6] Literature survey revealed that most of the HPLC methods used hyphenated techniques with detectors such as mass-spectrometry, flourimetry, Electrospray mass spectrometric techniques all these methods have high sensitivity, but most of them highly expensive and are not easily available in quality control laboratories.[7,8] So author's objective is to develop accurate, simple, UV spectrophotometric method which is free from extraction techniques, and shorter time and highly sensitive technique.



Materials:-

Venlafaxine hydrochloride was received as a gift sample from Cipla Ltd., Mumbai, India. All analytical grade chemicals and solvents were supplied by S.D. Fine Chemicals, Mumbai, India. Distilled water was used to prepare all solution. Freshly prepared solutions were always employed.

Instruments:-

Jasco V – 630 UV/VISIBLE spectrophotometer with data processing system was used. The sample solution were recorded in 1 cm matched quartz cells was used for spectral an absorbance measurements. Shimadzu AY - 220 electronic balance was used for weighing the sample.

Standard Solution:-

Selection of common solvent:-

0.1 N NaOH was selected as a common solvent for developing spectral characteristics of drug. The selection was made after using different acids and bases and their different normalities.

Preparation of standard drug solution:-

Standard stock solution containing Venlafaxine hydrochloride was prepared by dissolving 10 mg of venlafaxine hydrochloride separately in 5 ml of 0.1 N NaOH sonicated for 5 min. and then final volume of the solutions was made up to 10 ml with same solvents to get stock solution containing 1000 ppm

Selection of λ max: -

The standard stock solution was further diluted with 0.1N NaOH to get a 10 µg/mL of concentration (1 mL to 100 mL). The solution was scanned between 200 and 400 nm using 0.1N NaOH as blank. From the spectrum obtained, 223 nm was selected as λmax for the analysis of venlafaxine hydrochloride.

Standard stock solution was further diluted to obtain 5-25 µg/ml with 0.1N NaOH. Calibration curve was plotted in the concentration range of 5-25 µg/ml of venlafaxine hydrochloride using 0.1N NaOH as blank.

Validation of the Proposed Method [9, 10]

The proposed method was validated according to the International Conference on Harmonization (ICH) guidelines.

Linearity (calibration curve):

The developed method validated as per ICH guidelines. The plot of absorbance verses concentration is shown in fig1for 0.1N NaOH. It can be seen that plots are linear in the concentration range 5-25 µg/ml with correlation coefficients (r^2) of

Precision (repeatability):

Intraday and interday precision was determined by measurement of the absorbance for three times on same day and on three different days. The relative standard deviation for replicates of sample solution was less than 2% which meet the acceptance criteria for established method.

Accuracy (recovery study)

Recovery study was carried out by adding a known quantity of pure drug to the preanalysed formulations and the proposed method was followed. From the amount of drug found, percentage recovery was calculated as per ICH guidelines.

Sensitivity:

Sensitivity study was carried out where limit of detection (LOD) and limit of quantification (LOQ) were determined using following equation.

$$\mathbf{LOD = 3.3^* \sigma / S} \qquad \mathbf{LOD = 10^* \sigma / S}$$

Where, σ = standard deviation of the response

s = slope of calibration curve

Result and Discussion

The maximum absorption for venlafaxine hydrochloride in 0.1N NaOH was observed at 223nm. The high values of correlation coefficient in 0.1N NaOH indicate linearity for venlafaxine hydrochloride in 0.1N NaOH. Beer's law was obeyed for 0.1N NaOH in the range of 5-25 µg/ml the accuracy of method was determined by calculating mean percentage recovery and % relative error. The percentage recovery ranges from 99 µg/ml and % relative errors was within 2% in 0.1N NaOH and are presented in table 4. Precision was calculated as repeatability, inter and intraday variation for venlafaxine hydrochloride, percentage RSD was found to be less than 1. The repeatability data are presented in table 2 and table 3. LOD was found to be 0.9587 µg/ml for detection of venlafaxine hydrochloride in 0.1N NaOH. LOQ was found be 0.2905 µg/ml in 0.1N NaOH. The proposed method was found to be simple, accurate, precise and rapid for the routine determination of venlafaxine hydrochloride in bulk and combined dosage form.

Conclusion:-

Simple spectrophotometric method for determination of venlafaxine hydrochloride have been developed and validated as per ICH guidelines. The proposed method is found to be simple, rapid, sensitive, accurate and reproducible also can be used for the routine quality control analysis of venlafaxine hydrochloride in bulk and pharmaceutical formulations.

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Table No.1 Optical Parameters for Determination of Venlafaxine Hydrochloride

Sr.no	Data	Results
1	Wavelength [nm]	223nm
2	Slope	0.034
3	Correlation coefficient	0.996
4	Intercept	0.0218
5	LOD (mcg/ml)	0.9587
6	LOQ(mcg/ml)	0.2905

Precision:

Table no.2: Intraday Variability

Conc. (mcg/ml)	Absorbance			Mean	Standard Deviation[±]	%RSD
	Trial I	Trial II	Trial III			
5	**0.0750**	**0.0779**	**0.0712**	**0.0747**	**0.00036**	**0.35**
10	**0.1651**	**0.1670**	**0.1681**	**0.1667**	**0.0015**	**0.89**
15	**0.2247**	**0.2267**	**0.2272**	**0.2262**	**0.0013**	**0.5747**
20	**0.3301**	**0.3314**	**0.3318**	**0.3311**	**0.00086**	**0.2597**
25	**0.4520**	**0.4525**	**0.4540**	**0.4528**	**0.00026**	**0.057**

Table no.3: Interday Variability

Conc. (mcg/ml)	Absorbance			Mean	Standard Deviation [±]	%RSD
	Trial I	Trial II	Trial III			
5	**0.1612**	**0.1620**	**0.1630**	**0.1620**	**0.00089**	**0.5493**
10	**0.2234**	**0.2240**	**0.2245**	**0.2239**	**0.00055**	**0.2456**
15	**0.3510**	**0.3540**	**0.3550**	**0.3533**	**0.0017**	**0.4811**
20	**0.4101**	**0.4120**	**0.4130**	**0.4117**	**0.0014**	**0.3400**
25	**0.4820**	**0.4831**	**0.4837**	**0.4829**	**0.00083**	**0.1718**

Table no.4: Result of Assay

Formulation	Label claim	% amount found	%C.V
Ventab	**37.5mg**	**99%**	**0.078**

Table no.5: Recovery Study

Amount of drug taken from tablets (mg)	Amount of standard drug added (mg)	Total amount recovered/mg	%recovery	Standard deviation [±]	%RSD
10	**5**	**14.70**	**98%**	**0.0025**	**0.7921**
10	**10**	**19.76**	**98.8%**	**0.00017**	**0.3253**
10	**15**	**24.54**	**98.16%**	**0.00007**	**0.0083**

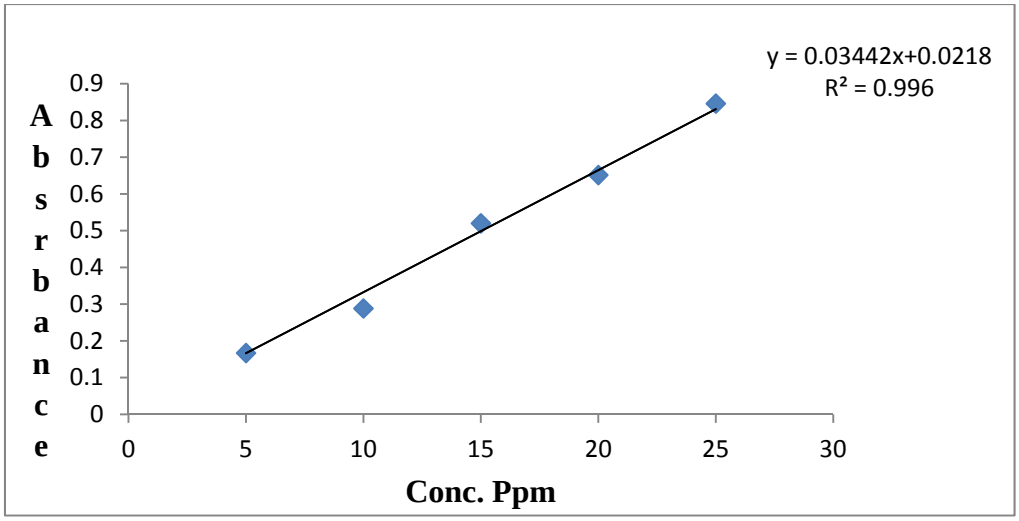

Fig.1 Calibration Curve of Venlafaxine Hydrochloride in 0.1N NaOH