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SPECTROPHOTOMETRIC ESTIMATION OF MIRTAZAPINE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

Three simple, precise and economical UV spectrophotometric methods have been developed for the estimation of Mirtazapine in bulk and pharmaceutical formulations. Chemically, mirtazapine is tetracyclic piperazinoazepine derivative used as antidepressant agent. Mirtazapine has absorbance maxima at 316.0 nm in zero order spectrum method (Method A), in the first order derivative spectra, showed sharp peak at 300.0 nm when n = 1 (Method B). Method C has based on calculation of area under curve (AUC) for analysis of Mirtazapine in the wavelength range of 330.0 nm – 300.0 nm. The drug followed the Beer-Lambert's law in the concentration range of 5-50 µg/ml. Results of the analysis were validated statistically and by recovery studies and were found to be satisfactory.

KEYWORDS : *Mirtazapine (MP); Ultraviolet spectrophotometry; Zero order spectrum; First order derivative spectroscopy and Area under curve (AUC).*

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INTRODUCTION

Mirtazapine is an antidepressant agent belonging to a chemical class, tetracyclic piperazinoazepine derivative.[1] Chemically, it is 1,2,3,4,10,14b-hexahydro-2-methylpyrazino-2,1-a-pyrido-2,3-c-benzazepine.[2] It enhances central noradrenergic and serotonergic activity by blocking α_2 receptors and selectively antagonizing $5HT_2$ and $5HT_3$ receptors.[2-3] It is classified as a noradrenergic and specific serotonergic antidepressant. Mirtazapine has been used successfully in the treatment of mild to severe depression. It is official in U. S. P.[1] It is also listed in The Merck Index[2] and Martindale, The Extra Pharmacopoeia[3]. Literature survey reveals that HPLC[4-9] and HPTLC[10] methods for determination of MP are reported. Hence the objective of the work is to develop new UV spectrophotometric methods for estimation of mirtazapine in bulk and pharmaceutical formulations with good accuracy, simplicity, precision and economy.

MATERIALS AND METHODS

Instrument

A Shimadzu UV/VIS double beam spectrophotometer model 1700 consists of matched quartz cell corresponding to 1 cm pathlength and spectral bandwidth of 2 nm.

Materials

Standard gift sample of Mirtazapine was procured from Lupin Pharma. Ltd., Pune. Tablets of MP were procured from marketed commercial brand i.e. Mirtaz (15 mg)

Solvent used

Hydrochloric acid (0.1N) was used as a solvent in the study.

Stock solution

Accurately about 10 mg of the pure drug was weighed and dissolved in 25 ml 0.1 N HCL and the volume was made up to 100 ml with 0.1 N HCL to give standard stock solution (100 µg/ml).

Method A: Aliquots of standard stock solution were pipetted out and suitably diluted with 0.1 N HCL to get the final concentration of 5, 10, 15, 20---- to 50 µg/ml of standard solutions. The solutions were scanned in the spectrum mode from 400 nm to 200 nm wavelength range and the zero order derivative spectra were obtained (Fig.1). The maximum absorbance of MP was observed at 316.0 nm. The drug followed the Beer-Lambert's law in the concentration range of 5-50 µg/ml. The calibration curve was plotted as absorbance against concentration of MP. The coefficient of correlation (r), slope and intercept values of this method are given in Table I. The concentrations of sample solutions were determined from calibration curve.

Method B: The first order derivative spectra at n=1 showed a sharp peak at 300.0 nm (Fig. 2). The absorbance difference at n=1 ($dA/d\lambda$) was calculated by the inbuilt software of the instrument which was directly proportional to the concentration of the standard solution. The standard drug solutions were scanned in the first order derivative spectra. A calibration curve was plotted taking the absorbance difference ($dA/d\lambda$) against the concentration of MP. The coefficient of correlation (r), slope and intercept values of this method are given in Table I. The method was applied for determination of concentration of sample solution.

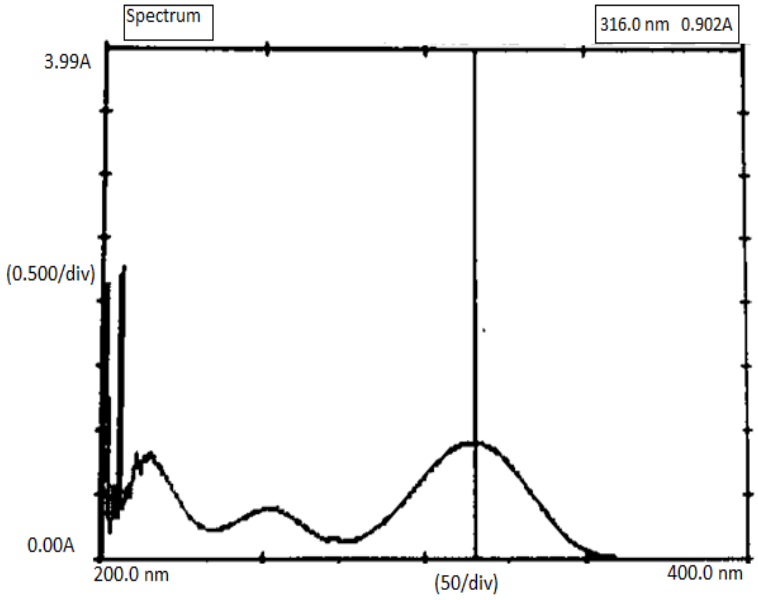

Fig. 1: zero order spectrum of Mirtazapine.

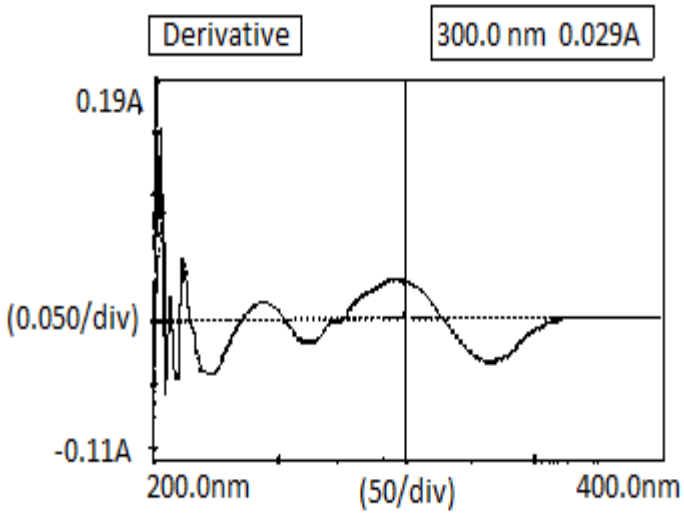

Fig. 2: First order derivative spectrum of Mirtazapine.

Table I: Optical characteristics and other parameters.

Parameters	Method A	Method B	Method C
λ-max (nm)	316.0	300.0	300-330
Beer-Lambert's range (µg/ml)	5-50	5-50	550
Coefficient of correlation (r^2)	0.9995	0.9994	0.9988
Regression equation Y = mx + c			
• Slope (m)	0.0312	0.0010	0.251
• Intercept (c)	0.000	0.000	-0.050
LOD	0.0509	0.0736	0.0474
LOQ	0.2662	0.3870	0.2529

Where, x is concentration in µg/ml and Y is absorbance unit.
A is Zero order derivative spectrum method with n = 0.
B is First order Derivative spectrum method with n = 1
C is the AUC method.

Method C: The AUC (Area under curve) method involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelengths λ1 and λ2. Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which the area has to be calculated. This wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. Suitable dilutions of standard stock solution (100µg/ml) of MP were prepared and scanned in the spectrum mode from the wavelength range 400 nm to 200 nm (Fig. 3). The wavelength range for MP was selected from 330.0 nm to 300.0 nm and measured AUC for each dilutions of MP. The calibration curve was plotted as AUC against concentration of MP. The method was checked by analyzing the samples with known concentration. As the results obtained were satisfactory low, the method was applied for pharmaceutical formulations.

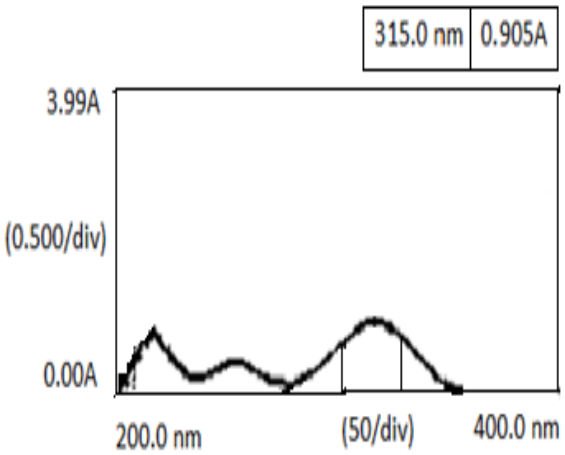

Fig. 3: Wavelength range selected for AUC method of Mirtazapine.

Analysis of tablet formulation

For estimation of Mirtazapine in tablet formulation by all the methods, twenty tablets were weighed and triturated to the fine powder. Tablet powder equivalent to 10 mg of MP was weighed and dissolved in 25 ml 0.1 N HCL. It was kept for ultrasonication for 45 min. Finally, the volume was made up to the mark with 0.1 N HCL.; it was filtered through Whatman filter paper no. 41 to get tablet stock solution of concentration 100 µg/ml. Various dilutions of tablet stock solution were prepared and analyzed for six times by all three methods and concentrations of MP in tablet formulation T1 were calculated by all three methods (Table II). All these methods were validated according to ICH guidelines[6]. Recovery studies were carried out at three different levels i.e. 80 %, 100 % and 120 % by adding the pure drug (8 mg, 10 mg and 12 mg respectively) to previously analyzed tablet powder sample (10 mg) as per ICH guidelines[11,12] and percentage recovery was calculated as shown in Table III. All the methods A, B and C were validated for linearity, accuracy and specificity.

Table II: Estimation of Mirtazapine in tablet formulation

Method	Tablet formulation	Label claim(mg)	Amount found	% Mean*	S.D.	R.S.D.	S.E.
A	T_1	15	14.99	99.95	0.722	0.723	0.323
B	T_1	15	15.01	100.10	0.467	0.473	0.190
C	T_1	15	14.97	99.84	0.255	0.256	0.104

Where, T1 (Mirtaz) is brand of tablet formulation. * Mean of six estimations (n=6).*

Table III: **Recovery study data**

Method	Tablet	Level of recovery (%)	Amount present (mg/tab)	Amount of drug added(mg)	Amount recovered (mg)*	% recovery*	S.D.	R.S.D.	S.E.
A	T1	80	10	8	17.89	99.42	0.250	0.252	0.144
		100	10	10	19.91	99.55	0.150	0.150	0.086
		120	10	12	21.86	99.40	0.165	0.165	0.108
B	T1	80	10	8	17.98	99.88	0.077	0.078	0.031
		100	10	10	19.92	99.60	0.031	0.032	0.012
		120	10	12	21.94	99.72	0.048	0.046	0.019
C	T1	80	10	8	17.88	99.33	0.246	0.247	0.100
		100	10	10	19.90	99.50	0.252	0.250	0.102
		120	10	12	21.90	99.54	0.262	0.261	0.106

** Mean of six estimations (n=6).*

RESULTS AND DISCUSSION

All methods A, B and C for the estimation of Mirtazapine in tablet dosage from were found to be simple, accurate, precise, specific and reproducible. Beer-Lambert's law was obeyed in the concentration range of 5-50 µg/ml. The values of standard deviation were satisfactory low and the recovery studies were close to 100 %. MP showed a broad spectrum, the derivative spectroscopy method applied has the advantage that it locates the hidden peaks in the normal spectrum when the spectrum is not sharp and it also eliminates the interference caused by the excipients present in the formulation. The AUC method has advantage that it is applicable to be drug which shows the broad spectra without a sharp peak. Hence these methods can be useful in the routine analysis of MP in bulk drug and formulations.

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