New Simple UV Spectrophotometric Method for Determination of Mirtazapine in Bulk and pharmaceutical dosage forms

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ABSTRACT

Mirtazapine is chemically a tetratetracyclic (pyridodibenzazepine) derivative which is classified as a noradrenergic and specific serotonergic antidepressant (NaSSA). Mirtazapine acts as an antagonist at central pre-synaptic α2-receptors, inhibiting negative feedback to the presynaptic nerve and causing an increase in NE release. It is also used for the treatment of Posttraumatic stress disorder. In present work, simple, sensitive, accurate and economical spectroscopic method has been developed for the estimation of mirtazapine in bulk and its pharmaceutical dosage forms. An absorption maximum was found to be at 232nm with the solvent system phosphate buffer (pH 6.8). The drug follows beer's law in the range of 5-30µg/ml with correlation coefficient of 0.999. The percentage recovery of mirtazapine ranged from 99.57-100.26% in pharmaceutical dosage form. Results of the analysis were validated for accuracy, precision, LOD, LOQ and were found to be satisfactory. The proposed method is simple, rapid and suitable for the routine quality control analysis.

Key words: Mirtazapine, UV-Spectrophotometry, Tablets, Estimation.

INTRODUCTION

Mirtazapine chemically, (±)-2-methyl-1,2,3,4,10,14b-hexahydropyrazino[2,1-a]Pyrido [2, 3-c][2] benzazepine. The prevailing theory is that antidepressants increase the concentration of one or more brain chemicals (neurotransmitters) that nerves in the brain use to communicate with one another. The neurotransmitters affected by antidepressants are norepinephrine, serotonin, and dopamine. Blockade of heteroreceptors, α2-receptors contained in serotenergic neurons, enhances the release of 5-HT, increasing the interactions between 5-HT and 5-HT_1 receptors and contributing to the anxiolytic effects of mirtazapine. A survey of literature states that there were no specified reported data on UV method for the estimation of mirtazapine. An absorbance was found to be 232nm and the spectrum was scanned for the drug dissolved in phosphate buffer (pH 6.8).

MATERIALS AND METHODS

Mirtazapine tablets were purchased from sun Pharma, Sikkim. All the reagents and chemicals used were AR grade. Spectrophotometer used was double beam UV-Visible Spectrophotometer with 10mm matched quartz cell Model-UV-1700 PHARMASPEC. Make shimadzu, Japan and Analytical balance: shimadzu, Japan AX 200.

Tablets MIRTAZ – 30 (Sun pharmaceutical industries Ltd. Sikkim), NASDEP-30 (Concern pharma private Ltd. Punjab).

METHOD DEVELOPMENT

Preparation of standard stock solution

Mirtazapine (10mg) was accurately weighed and transferred to a 100ml volumetric flask. It was first dissolved in 25ml of phosphate buffer (pH 6.8) and sonicated for about 10-15 min., then finally made up to the volume with phosphate buffer (pH 6.8) (100µg/ml).

Preparation of calibration curve

From the standard stock solution fresh aliquots were pipetted out and suitably diluted with phosphate buffer (pH 6.8) to get final concentration in the range of 5-30µg/ml. The solutions were scanned under spectrum mode for 200-400nm wavelength range and a sharp peak was obtained at 232nm (Fig-1). A calibration curve was plotted taking an absorbance on y-axis against concentration of standard solution on x-axis (Fig-2). The method was applied for known sample solution and was found to be satisfactory for the analysis of tablet dosage forms.

Optical characteristics

The optical characteristics such as beer's law limit, molar extinction coefficient, % RSD were calculated. Regression characteristics like slope intercept, correlation coefficient, LOD, LOQ, standard deviation were calculated (Table-1).

ASSAY OF MIRTAZAPINE TABLETS

For the analysis of the dosage form 20 tablets of mirtazapine of various brands were weighed. Powder equivalent to 10mg of mirtazapine was taken in to a 100ml volumetric flask. The formulation first dissolved in 25ml of phosphate buffer (pH 6.8) and sonicated for about 10-15 min. finally made up the volume with phosphate buffer (pH 6.8). The solution was filtered and final dilution of the sample (10µg/ml) was prepared and measured the absorbance against blank at 232 nm. The amount of mirtazapine was computed by using the equation referring to the calibration curve (Table-2).

METHOD VALIDATION

The method was validated for different parameters like linearity, Accuracy and Precision.

Linearity

Fresh aliquots were prepared from the stock solution (100µg/ml) ranging from 5-30µg/ml. The samples were scanned in UV-Visible spectrophotometer using phosphate buffer (pH 6.8) as blank. It was found that the selected drug shows linearity between 5-30µg/ml (Table-3).

Accuracy

Accuracy of the method confirmed by studying recovery at 3 different concentrations 50, 75 and 100µg/ml of these expected, in accordance with ICH guidelines, by replicate analysis(n=6). Standard drug solution was added to a pre analyzed sample solution and percentage drug content was measured. The results from study of accuracy were reported (Table 3). % Recovery = [(ct-cu)/ca] ×100. Where ct is conc. of the analyte found; cu is the total conc. of the analyte present in formulation; and ca is the conc. of the pure analyte added to the formulation (Table-4).

Precision

Precision (intra-day precision) of the method was evaluated by carrying out the six independent test samples of mirtazapine. The intermediate precision (inter-day precision) of the method was also evaluated using two different analyst, and different days in the same laboratory. The percent relative standard deviation (%RSD) values obtained by two analysts were found to be good (Table-5).

RESULTS AND DISCUSSION

From the optical characteristics (Table-1) of the proposed method, mirtazapine was shown its maximum wavelength at 232nm in the solvent methanol with a good correlation coefficient 0.999. The percentage purity and relative standard deviation from the assay of the tablet dosage forms (Table-2) were found to be within the limits and from linearity data (Table-3) it was found to be that mirtazapine obeys beer's law in the range of 5-30µg/ml. The accuracy data of the drug (Table-4) was shown good % Recovery and % RSD with the range of 99.57-100.26 and respectively. The inter-day and intra-day (Table-5) precision values were found to be 0.65 and 0.92 respectively, which indicates that the proposed method is accurate and also reveals that there is no interference of the commonly used excipients and additives in the formulation.

CONCLUSION

The proposed method for the estimation of mirtazapine was found to be simple, sensitive and reliable with good precision and accuracy. The method is specific while estimating the commercial formulations without interference of excipients and other additives. Hence this method can be used for the routine analysis of mirtazapine in pure and pharmaceutical formulations.

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Table 1: Optical characteristics and precision of the proposed method

Parameter	Value
Absorption maxima(nm)	232 nm
Beer's law limit (µg/ml)	0.999
Regression equation (Y=mX+c)	Y=0.029x+0.013
Slope (m)	0.029
Intercept (c)	0.013
Standard Deviation	0.001
LOD(µg/ml)	0.00113
LOQ(µg/ml)	0.00344

Table 2: Assay of mirtazapine tablets

Dosage form	Label claim(mg/tab)	Amount found*±SD	% Purity of the tablet±%RSD
MIRTAZ	30	30.29±0.083	100.95±0.295
NASDEP	15	14.96±0.055	100.14±0.438
NASDEP	30	30.13±0.060	100.20±0.135
NASDEP	45	45.26±0.235	100.64±0.451

*An average of three samples of each concentration

Table 3: Accuracy data of the drug

Sample ID	Concentration(µg/ml)		%Recovery±SD	%RSD
	Pure drug	Formulation		
50%	5	6	99.57±0.306	0.308
75%	7.5	8.5	100.26±0.326	0.324
100%	10	11	100.19±0.261	0.26

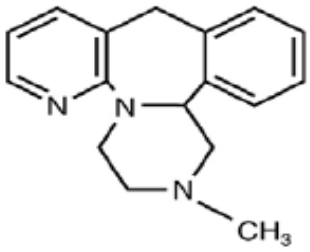
*An average of three samples of each concentration

Table 4: Linearity of mirtazapine in working standard

S.NO	Concentration(µg/ml)	Absorbance
1	5	0.154
2	10	0.308
3	15	0.462
4	20	0.599
5	25	0.732
6	30	0.895

Table 5: Precision of the mirtazapine working standards

Sample no	Analyst -1 (intra-day precision)	Analyst -1 (intra-day precision)
1	0.224	0.214
2	0.226	0.214
3	0.227	0.215
4	0.225	0.215
5	0.224	0.215
6	0.223	0.220
Mean	0.225	0.2155
S.D	0.001	0.002
%RSD	0.65	0.92



Structure of Mirtazapine

Fig.1: Spectrum of mirtazapine in phosphate buffer (pH 6.8)

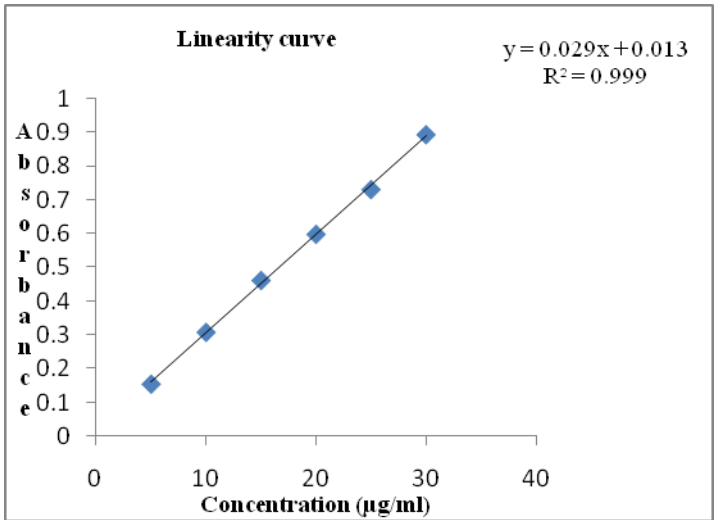


Fig.2: Calibration curve for mirtazapine

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