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DEVELOPMENT OF A VALIDATED UV SPECTROPHOTOMETRIC METHOD FOR THE QUANTITATIVE ESTIMATION OF ASENAPINE MALEATE IN BULK DRUG

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ABSTRACT

A simple, accurate, sensitive, precise and economical spectrophotometric method has been developed for the determination of Asenapine maleate in bulk drug form. Measurementof ultraviolet absorption at 220nm. The proposed method was validated statistically. The developed method obeyed Beer's law in the concentration range of 2-10 µg/mL.The limit of detection (LOD) and limit of quantitation (LOQ) for estimation of Asenapine maleate were 0.20381µg/mL and 0.61761µg/mL respectively. The recovery was in the range of 98.8687 to 101.1068 percentages.The method was validated for several parameters like accuracy, precision as per ICH guidelinesThe values of relative standard deviation and % recovery were found to be satisfactory, indicating that the proposed method is precise and accurate and hence can be used for the routine analysis.

KEY WORDS: Asenapine maleate, UV Spectroscopy, Validation, Assay.

1. INTRODUCTION

Asenapine maleate (3a*RS*,12b*RS*)-*rel*-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1*H*-dibenz[2,3:6,7]oxepino4,5-c]pyrrole maleate(Fig.1) is an orally administered anti-psychotic agent used in the treatment of bipolar disorder and maniac conditions. Asenapine maleate is an atypical antipsychotic drug developed for the treatment of schizophrenia and acute mania associated with bipolar disorder. Asenapine maleate shows high affinity for numerous receptors like serotonin, adrenergic, dopamine, histamine. Asenapine behaves as a partial agonist at the 5-HT_{1A}receptors. At all other targets Asenapine is an antagonist. Literature survey reveals that few analytical methods were reported for the determination of Asenapine maleate and its related substances in biological fluids like plasma, blood, urine and pharmaceutical preparations by spectrophotometry (Halima , 2012), RP-HPLC (Joan Ruan,2001) (Aneesh and rajasekaran, 2012), LC-MS (Theode Boer, 2012). Infactone UV method has been developed yet. Keeping in view of these we have decided to develop a UV spectrophotometric method for the estimation of Asenapinemaliate. The objective of the present work was to develop a simple, sensitive, precise and accurate UV spectrophotometric method for the determination of Asenapine maleate in bulk and formulations as per ICH Guidelines.

2. MATERIALS AND METHODS

UV-Visible Spectrophotometer (Systronics model 2203). The UV-VIS spectrophotometer achieves a resolution of 1 nm with matched quartz cells of 1 cm path length.Asenapine maleate working standard manufactured by LEE Pharma Ltd., Hyderabad, Andhra Pradesh, India. Analytical grade Methanol, Distilled water.

Preparation of standard drug solutions:10mg of Asenapine maleatepure drug was accurately weighed, transferred into a 100ml volumetric flask containing 50 ml ofmethanol and sonicated for about 10 minutes. The volume was made up to the mark with distilled waterto get the stock solution (100µg/ml). This solution was further diluted with the same to get the working standard solution.

Preparation of Calibration curve: Aliquots of standard drug (0.2 ml to 1.0 ml, 100 µg/ml) solution in methanol and distilled water (50:50 %v/v) weretransferred into a series of 10 ml volumetric flasks and the solution was made up to 10ml with methanol and water (50:50, %v/v). After setting the instrument for its spectral properties the solutions were scanned in the wavelength ranging from 210nm-370nm. The wavelength of maximum absorption for Asenapine maleate was found at 220nm. Calibration curve was prepared by plotting concentration of Asenapine maleate on x-axis and their respective absorbances on y-axis.

Procedure for assay of pharmaceutical formulations: Accurately weigh the quantity of drug powder equivalent to 50mg of Asenapine maleate and transferred into a 100ml volumetric flask containing 50 ml of methanol and distilled water (50:50 %v/v). The solution was sonicated for extracting the drug for about 15minutes, filtered through a cotton wool and the filtrate was made up to volume with methanol and distilled water (50:50% v/v). Transfer 0.1ml of the filtered sample solution to 10ml volumetric flask and made up to volume with distilled water. The absorbance of the resulting solution was measured at 220 nm and the amount of Asenapine maleate was computed from its calibration plot.

Validation of the developed method:

Precision: Precision was determined by intra-day and inter-day study. Precision of the method was evaluated by carrying out the assay and analyzing corresponding responses 6 times on the same day and on different days for the sample solution. The percent relative standard deviation (% RSD) was calculated.

Accuracy (Recovery studies): Accuracy studies were performed at three different levels (80%, 100% and 120%) and the samples were analyzed in triplicate by the proposed method. Known amount of standard Asenapine maleate at 80%, 100% and 120% of predetermined sample was added to a pre quantified tablet sample.

Limit of detection and Limit of quantitation: Limit of Detection and Limit of Quantitation were calculated using following formula LOD=3.3(SD)/S and LOQ= 10 (SD)/S, where SD=standard deviation of response (absorbance) and S= slope of the calibration.

3. RESULTS AND DISCUSSION

The proposed method obeyed Beer's law in the concentration range of 2-10 µg/ml. The optical characteristics and the data concerning to proposed method is represented in Table 1. The limit of detection and limit of quantitation for estimation of Asenapine maleate were 0.20381µg/mL and 0.61761µg/mL respectively. Precision study was performed and represented in Table 2. Recovery studies were carried out for the developed method by addition of known amount of standard drug solution of Asenapine maleate to pre-analyzedbulk sample solution at three different concentration levels. The resulting solutions were analyzed by the proposed methods. The recovery (Table 3) was in the range of 98.8687 to 101.1068 percentages. The assay results were tabulated in Table 4.

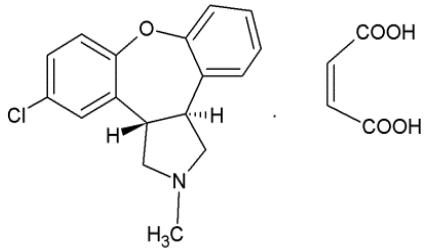


Figure.1.Chemical structure of Asenapine maleate

Table.1.Optical characteristics, regression data of the proposed method

Parameter	Result
λ_{max}(nm)	220
Beer'slawlimits(µg/ml)	2-10
Detectionlimits(µg/ml)	0.203811559
Quantitationlimits(µg/ml)	0.617610785
Sandell's sensitivity (µg/cm^2/0.001absorbance unit)	0.0365
Regression equation(Y=a+bc):Slope(b)	0.0273
Standard deviation of slope(S_b)	0.000201525
Intercept(a)	-0.0003
Standard deviation of intercept(S_a)	0.001220293
Standard error of estimation (S_e)	0.001686077
Correlation coefficient (r)	0.9997
%Relative standard deviation*	1.423

***Averageofsix determinations.**

Table.2.Results of precision study

Precision*	Intra-day	Inter-day
Mean % recovery	100.708	100.586
SD	0.973	1.036
%RSD	0.966	1.030

***average of 6 determinations**

Table.3.Results of accuracy study

Accuracy*	Mean % recovery ± SD	%RSD
80%	97.259 ± 0.847	0.871
100%	99.987 ± 1.119	1.119
120%	99.666 ± 0.666	0.668

***average of 3 determinations**

Table 4: Assay results

Formulation	Amount taken	Amount found	Mean % recovery ± SD	% RSD
Asenapine maleate**(**LEE Pharma Ltd., Hyderabad**)**	250 mg (equivalent)	251.466 mg	100.586 ± 0.775	0.777

Figure.2.UV spectrum of Asenapine maleate

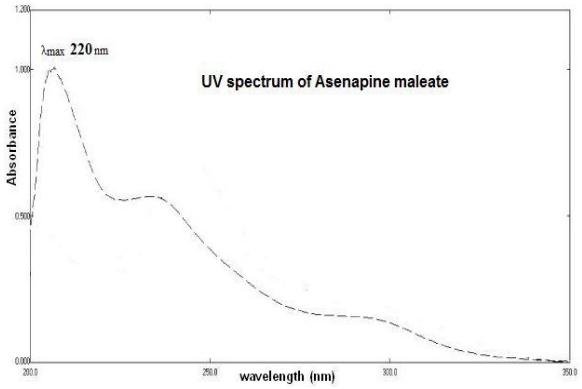
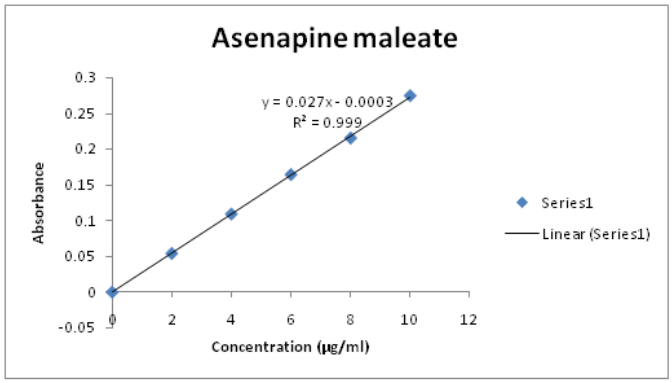


Figure.3.Calibration curve of Asenapine maleate by UV method



4. CONCLUSION

The present study demonstrated an UV spectrophotometric method for the estimation of Asenapine maleate available as bulk form. From the above experimental data results and parameters, the developed method has advantages like the time taken for preparation of standard and sample solutions is less and hence suitable for the analysis ofAsenapine maleate raw material and its pharmaceutical dosage form. In fact statistical analysis of the results shows that the developed method for Asenapine maleate had good precision and accurate and also simple, and cost effective and it can be effectively applied for routine analysis in bulk drug and pharmaceutical formulations.

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