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R E S E A R C H A R T I C L E

Analytical method development and validation for the estimation of asenapine maleate in pure and its solid dosage form by UV-spectrophotometric method

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A B S T R A C T

A simple, economical, rapid, accurate, precise spectrophotometric method has been developed and validated according to ICH Q2 (R1) for the antipsychotic agent, Asenapine Maleate as active pharmaceutical ingredient (API). The U.V absorption maxima of Asenapine maleate was found to be at 275 nm wavelength using 0.1%IPA as a solvent. Linearity range was found to be 5-25µg/ml, with the correlation coefficient being more than 0.999. The relative standard deviation was found to be 0.001. The percentage recovery was within the range of 98% -102%, indicating the significant interference from the other ingredients in the formulation. The method can be applied for the routine analysis of Asenapine Maleate in pharmaceutical preparation.

Keywords: Asenapine Maleate, 0.1%IPA, UV Spectrophotometry and Validation.

A R T I C L E I N F O

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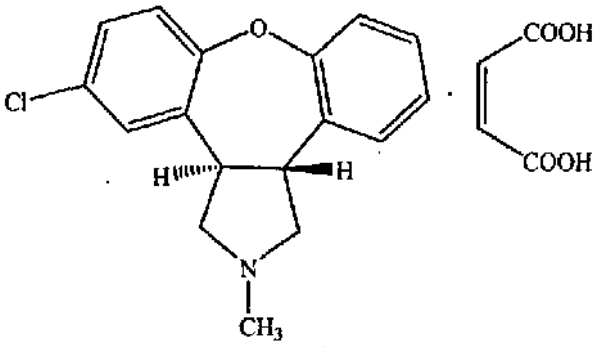
C O N T E N T S

1. Introduction

Asenapine Maleate [1-2] is chemically 5-chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz(2,3-6,7)oxepino(4,5-c) pyrrole, Soluble in **w**ater 0.0312mg/ml and in different pH, Phosphate buffer pH 6.8 &7.4 Borate buffer pH 9.2. It is an Antipsychotic agent. The MOA of Asenapine Maleate as with other drug having efficacy in schizophrenia and bipolar disorders is unknown. It has been suggested that the efficacy of Asenapine Maleate in schizophrenia is mediated througha combination of antagonist activity at D2 and 5HT2A receptors H1Antagonism. Absorption of drugs from

the oral cavity into the mucosal tissue is typically a fast Reach equilibrium with drug in solution in the oral cavity. Direct glucoronidation by UGT1A4 and oxidative metabolisom by cytochrome P450 isoemzyme (predominantly CYT1A2) are the primary metabolic Pathways for Asenapine Maleate. Mean total excretion onbasis of percent recovery total radioactive dosewas 90% with 50%appearing in urine and 40%excreted in feces, asenapine itself was detected only in feces. Asenapine Maleate is a novel drug in acute schizophrenia and for manic/mixed episodes of bipolar disorders. Literature review [3-8] revealed that HPLC, HPTLC, LC-MS and two UV methods were reported for the estimation of Asenapine Maleate in Pharmaceutical dosage forms. So, an attempt is made in this project to develop a simple, cost effective, accurate, precise and sensitive UV- Spectrophotometric method for the estimation of the drug in bulk and its tablet dosage form.



Structure of Asenapine Maleate

2. Materials and Methods

Drug Sample	Asenapine Maleate was obtained as a gift sample from Natco labs, HYD.
Formulation Used	Asenapt containing 10mg of AsenapineMaleatewas purchased from the local pharmacy
Solvent Used	0.1 % Isopropyl Alcohol

Methodology

Selection of Solvent: The solubility of Asenapine Maleate was determined in a variety of solvents as per Indian Pharmacopoeia standards. Solubility test was carried out in different polar and non-polar solvents from the solubility studies,0.1% IPA was selected as suitable solvent for proposed method.

Preparation of Standard Stock Solution:

Standard stock solution was prepared by dissolving accurately 10mg of Asenapine Maleate in 0.1%IPA and the volume was made up to 10ml in volumetric flask (1^0 stock solution, 1000µg/ml).

Preparation of sample solution:

10 mg of Asenapine Maleate tablet powder was weighed equivalantly and transferred into 10 ml standard volumetric flask. The content was dissolved in 0.1%IPA. This solution was filtered through Whatsmann filter paper number 40.

Determination of Absorbance Maxima:

One ml of 1^0 stock solution was diluted to 10 ml with 0.1%IPA(2^0 stock solution, 100µg/ml).1 ml of 2^0 stock solution was taken in 10 ml standard volumetric flask dilute to 10 ml with 0.1%IPA to get the concentration of 10µg/ml. The absorbance of resulting solution was measured against respective blank solution (0.1%IPA) in the UV region of 200-400 nm, which shows maximum absorbance at 275 nm.

Determination of concentration range:

For preparation of different concentrations, aliquots of stock solution of suitable concentrations of Asenapine Maleate were transferred into a series of 10 ml standard flasks and volumes were made upto mark with 0.1%IPA 5 different concentrations were prepared in the range of 5-25µg/ml and the absorbances were measured at 275 nm against solvent (0.1%IPA) blank. The obtained absorbance values are plotted against the concentrations of Asenapine Maleate to get the calibration graph.

Precision:

The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple samplings of homogenous samples.

Intraday and inter day precision:

A variation of results within the same day (intra – day), variation of results between days (inter- day) was analyzed. Intra – day precision was determined by analyzing Asenapine Maleate (15 ug/ml) for six time in the same day at 275 nm. Inter – day precision was determined by analyzing the drug daily twice for three days at 275 nm.

Recovery studies:

To study the accuracy, powder of Asenapine Maleate was taken, and used to carry out the analysis. Recovery studies were carried out by addition of standard drug solution (50%, 100% and 150%) to the sample at 3 different concentration levels. Aliquots of 1.5 ml of sample drug solution of 100 mg/ml were pipette in to each of three 10ml volumetric flasks (15 ug/ml), to all the 3 volumetric flask 0.75ml (7.5 ug/ml), 1.5ml (15 ug/ml) and 2.25 ml (22.5 ug/ml) of standard solution of 100mg/ml was added respectively, the volume was made up to 10.0ml with 0.1%IPA solution and the absorbance was measured at 275nm against 0.1%IPA as blank. The percentage recovery was determined by using the formula.

$$\text{Percentage Recovery} = \text{Amount of drug recovered} / \text{Amount of drug added} \times 100$$

Limit of Detection (LOD) and Limit of Quantification (LOQ):

Preparation of calibration curve from the serial dilutions of standard was repeated for three times. The limit of detection and limit of quantification was calculated by using the average value of slope and standard deviation of intercept.

3. Results and Discussion

Asenapine Maleate was procured from Natco labs, Hyderabad and melting point was recorded to check the identification of the drug, the solubility of asenapine was determined in a variety of solvent ranging from non-polar to polar using essentially a method of scheftr and higuchi.

The drug was found to be very soluble in 0.1%IPA. The absorbance maximum was recorded at wavelength of 275nm. Beers law range was confirmed by linear curve of Asenapine Maleate. From the above studies the optical characteristics such as linearity range (5-25), correlation coefficient (0.999), slope (0.032) and intercept (0.010) were calculated and results were found to be satisfactory. The amount of Asenapine Maleate Present in table formulation (Asenapt10mg) was found.

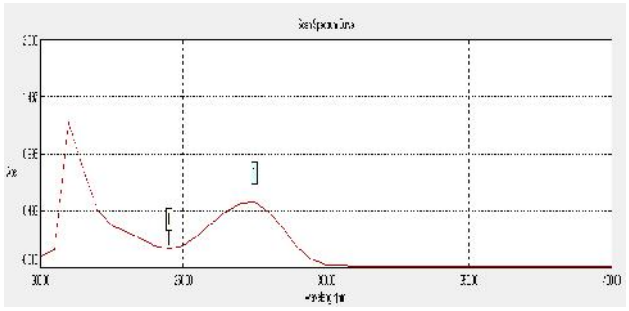


Figure 1: Ultra violet absorption Spectrum of Asenapine Maleate

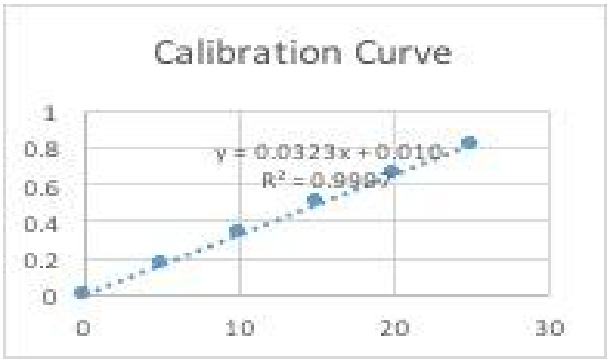


Figure 2: Calibration curve of Asenapine maleate

The precision of the method was confirmed by intraday and interday precision. The percentage of RSD values was found to be 1.29 and 0.86 for intraday and interday analysis. The accuracy was confirmed by recovery studies by adding known amount of pure drug to the previously analyzed formulation and the mixture was analyzed and the percentage recovery was found to be 96.86 – 99.32. The amount of drug recovered from the formulation was very close to the expected value and the % RSD value also very low (0.5743). This indicated that the method was very accurate. The limit of detection and limit of quantification was calculated by using the average value of slope and standard deviation of intercept.

Table 1: Optical Characteristics of Asenapine Maleate

Parameters	Value
λ max (nm)	275
Beers Law limit(µg / ml)	5-25
Correlation coefficient (r2)	0.999
Regression equation (Y)	Y=0.032(X)+0.010
Slope(m)	0.032
Intercept(c)	0.010
LOD(µg / ml)	0.093

Table 2: Assay of Asenapine Maleate

S.No	Lable claim	Amount found	Percentage
1	**10 mg**	**10.06 mg**	**100.66 %**

Table 3: LOD & LOQ

S.No	Validation parameter	Concentration (µg/ml)
1	LOD	0.093
2	LOQ	0.31

4. Conclusion

Estimation of Asenapine Maleate was achieved by UV method. After considering the solubility and stability, 0.1%IPA was selected as solvent. Asenapine Maleate 10µg/ml solution was prepared and scanned in the uv-region from the spectra 275nm was selected as an analyzing wavelength. Calibration curve was plotted by using concentration Vs absorbance. From the calibration curve it was found that Asenapine Maleate obeys beer's law in the range of 5-25µg/ml, correlation coefficient (0.999), slope (0.032) and intercept (0.010), LOD (0.093 µg/ml) and LOQ (0.186449191 µg/ml) were calculated. The precision of the method was studied by making repeated analysis. The percentage of Asenapine Maleate in formulation was found to be 100.66%. The recovery studies were also carried out to ensure the accuracy of the method by adding known concentration of pure drug to a pre analyzed formulation. All the above parameters combined with simplicity and ease of operation ensure that the application of proposed method for estimation of Asenapine Maleate was found to be useful with high accuracy, precision. It can be used for routine analysis of Asenapine Maleate in bulk and pharmaceutical preparation.

Table 4: Inter day Precision of Asenapine Maleate

S.No.	Amount (µg/ml)	Amount Found(µg/ml)	% Recovery	% Average	S.D	%RSD
1	15	15	100			
2		14.9	99.3			
3		14.7	98			
4		15	100	99.88	0.1936	1.29
5		15	100			
6		15.3	102			

Table 5: Intraday Precision of Asenapine Maleate

S.No.	Amount (µg/ml)	Amount Found(µg/ml)	% Recovery	Average %	S.D	%RSD
1	15	15.1	100.6			
2		15.1	100.6			
3		15.1	100.6			
4		14.8	98.6	100.05	0.130	0.86
5		14.9	99.3			
6		15.1	100.6			

Table 6: Recovery studies for the Asenapine Maleate

S .No	% Added	Amount (µg/ml)	Amount Added (µg/ml)	Amount found	Amount recovered	% recovery	SD	% RSD
1	50%	15.1	7.5	7.52	100.26	99.01%	1.263	1.27
2			7.5	7.33	97.73			
3			7.5	7.43	99.06			
4	100%		15	14.49	96.6	96.86%	0.303	0.312
5			15	14.58	97.2			
6			15	14.52	96.8			
7	150%		22.5	22.34	99.5	99.32%	0.141	0.141
8			22.5	22.33	99.24			
9			22.5	22.36	99.37			

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