IJPSR (2016), Vol. 7, Issue 7 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 23 February, 2016; received in revised form, 17 March, 2016; accepted, 04 May, 2016; published 01 July, 2016

UV SPECTROPHOTOMETRIC AND RP-HPLC ESTIMATION OF DRUG ASENAPINE IN TABLET DOSAGE FORM

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Keywords:

Asenapine, Simultaneous estimation, UV-spectrophotometry, RP-HPLC, Recovery study

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ABSTRACT: Asenapine in Tablet dosage form is used as antipsychotic agent. Literature revealed that there is no single method for the simultaneous estimation of this drug in tablet dosage form, which prompted us to develop a simple, rapid, accurate, economical and sensitive UV spectrophotometric and RP-HPLC methods. The simultaneous estimation of UV method is based on the principle of additivity of absorbance, for the determination of Asenapine in tablet formulation. The absorption maximum of the drug was found to be 270.0 nm in methanol. For RP-HPLC mobile phase is a mixture of acetonitrile and 0.1 M phosphate buffer (pH = 3.2) in the ratio of 65:35 v/v and detection wavelength is 270 nm. The accuracy and reproducibility of the proposed method was statistically validated by recovery studies.

INTRODUCTION: Asenapine (ASP) [1] is antipsychotic agent whose IUPAC name is (3aRS,12bRS)-rel-5-Chloro-2,3,3a,12b-tetrahydro-2-methyl-1H-dibenz[2,3:6,7]oxepino[4,5-c]pyrrole. There are some repeated methods for estimation of ASP. Literature survey revealed that Liquid Chromatography–Tandem Mass Spectrometry method have been reported for the estimation of ASP [2] and Formulation Development and Evaluation of Sublingual Film of Asenapine [3] However, no method is reported for the simultaneous estimation of this drug in tablet formulation.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.7(7).3080-84

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.7 (7).3080-84

This prompted us to develop simple, rapid, accurate, economical and sensitive UV spectrophotometric and RP-HPLC methods. The developed method was validated using ICH guidelines for validation [4].

MATERIALS AND METHODS: Shimadzu 1700 UV/Vis spectrophotometer with matched cuvettes and Shimadzu ULFC HPLC system with C_{18} column(100 mm × 4.6 mm, 3.5 µ) equipped with UV visible detector SPD-M20A were used for the experimental work. The chemicals used were of analytical grade. Commercially available tablets (Asenapt 10® and Sublingual Tablet Saphris®) of ASP were procured from the local pharmacy. Standard ASP was received as gift sample from Lundbeck Pvt. Ltd., London.

UV Estimation of ASP:

Standard stock solution of ASP was prepared by dissolving 25.0 mg of standard ASP in methanol

and the volume adjusted to 50.0 ml. Standard solution (25 µg/ml and 10 µg/ml) ASP was further prepared by diluting 2.5 ml and 1.0 ml of stock solution of drug to 50.0 ml in volumetric flask with the methanol.

Spectra of standard solutions of ASP was obtained and scanned between 200- 400 nm (**Fig. 1**). ASP exhibited absorption maxima at 270.0 nm. Calibration curve for drug was prepared in the concentration range of 1.0-90.0µg/ml at corresponding wavelength. Amount of drug was determined using eqn. as C = A / a, where, C = concentration of ASP in g/100 ml, A = absorbance of laboratory mixture at 270.0 nm, a = absorptivity of ASP at 270.0 nm. Percent estimation = (C×D)/W×100, where, C = concentration of ASP in g/100 ml, D= dilution factor and W= weight of drug in the laboratory mixture.

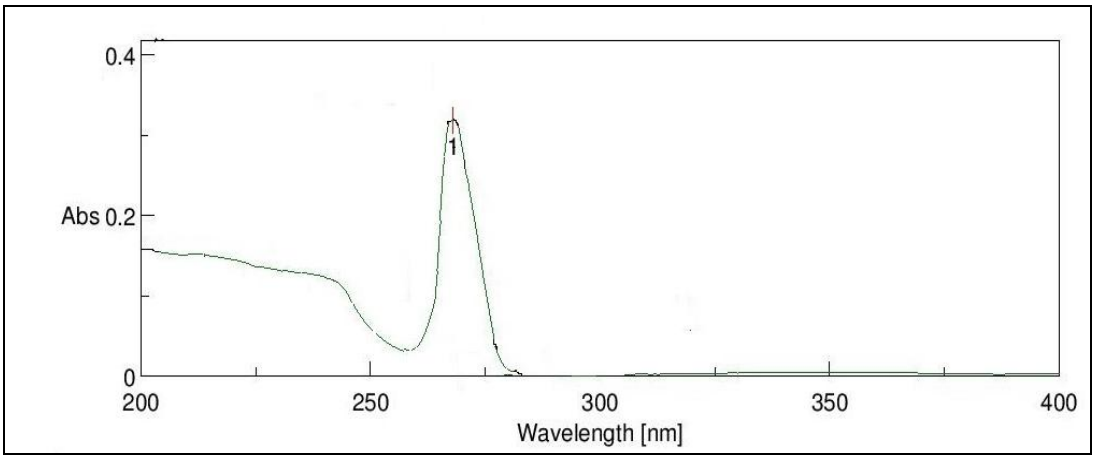

FIG. 1: SPECTRA OF ASENAPINE, SOLVENT METHANOL AND λ_{max} 270.0 nm

Marketed tablets Asenapt 10 and Sublingual tablet Saphris (Sun Pharma Pvt. Ltd., India) were used for the estimation of ASP. Twenty tablets were weighed and crushed to a fine powder. Powder equivalent to 25 mg of ASP (tablet contains 10 mg ASP) was dissolved in the solvent and volume was made up to 50 ml. Insoluble excipients were separated by filtration. The filtrate was further diluted to get final concentration of the drug in the linearity range. Absorbance was noted at the selected wavelength and percent label claim was determined by using the eqn. percent label claim= (C×D×W)/(Wm×L)×100 where, C = concentration of ASP in g/100 ml, W= average weight of tablet, Wm= weight of sample taken and L= label claim of sample taken.

For specificity study weigh tablet powder equivalent to 25.0 mg of ASP in four different volumetric flasks. The samples were exposed to stress conditions for 24 h. First flask at 50°C sample with 1 ml 0.1 M NaOH (Alkali), second flask at 50°C sample with 1 ml 0.1 M HCl (Acid), third flask at 50°C sample with 1 ml 3% H_2O_2 (Oxide) and fourth flask at 50°C only sample (Heat). After 24 h the flasks were cooled to room temperature and diluted with methanol upto 50.0 ml. Prepare 10 µg/ml concentration of each sample solution and analyzed.

RP-HPLC Estimation of ASP:

Preparation of mobile phase: The mobile phase used was a mixture of acetonitrile and 0.1 M phosphate buffer (pH = 3.2) in the ratio of 65:35 v/v and was filtered before use through membrane filter paper (0.4 µ). The elution was carried out at the flow rate of 1 ml/min. Detection was carried out at 270 nm at ambient temperature.

Preparation of standard stock solution:

Standard stock solution of the drug was prepared by dissolving 25 mg of ASP in mobile phase and volume was made up to 50 ml with the same solvent (500 µg/ml).

Preparation of working solution:

Working standard solution was prepared by diluting 2.5 ml of the standard stock solutions to 50 ml with mobile phase (25µg/ml).

Standard calibration curve: Chromatogram of standard solution of ASP was obtained and scanned between 200-400nm (**Fig. 2**) for RP-HPLC method. Various dilutions were prepared by taking 10-50µg/ml ASP solutions. Twenty microliters of the solution from the flasks was injected. Calibration curve was constructed by plotting peak areas against the corresponding drug concentrations.

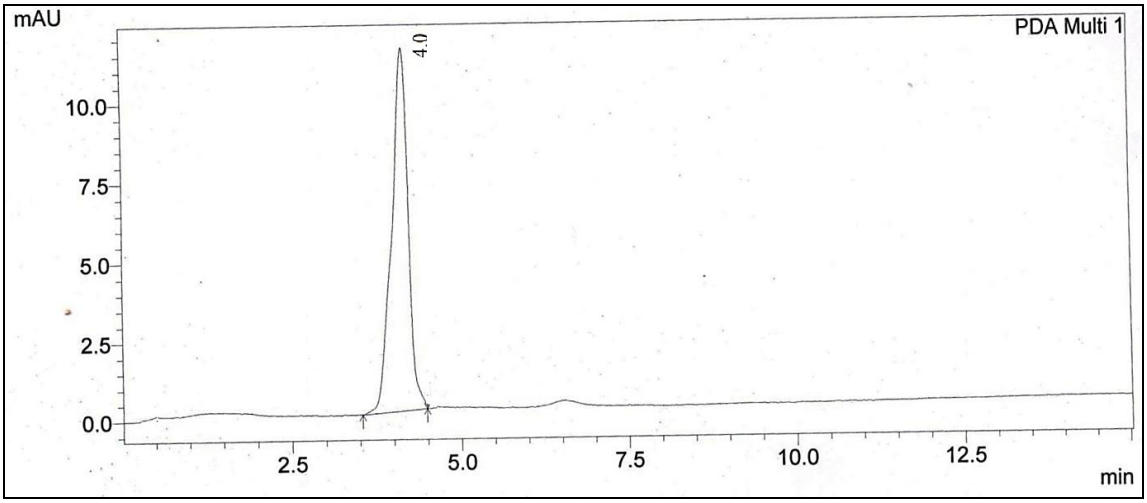

FIG. 2: CHROMATOGRAM OF ASENAPINE. RETENTION TIME IS 4.0 MIN

Estimation of drug in commercial tablet formulation: For the estimation of drug from commercial formulation, twenty tablets, each containing 10 mg of ASP, was weighed and finely powdered. Accurately weighed tablet powder (25 mg) was suspended in the mobile phase and shaken for 15 min. The volume was made up to 50 ml with mobile phase and filtered through Whatman filter paper. Aliquot portion of this solution was diluted to produce 10µg/ml ASP and filtered through membrane filter paper (0.4 µ). Equal volumes of 20µl of standard and sample solutions were injected separately after the equilibrium of stationary phase and area under the curve noted. Amount of the drug in the tablet formulation was calculated using formula $(A_U \times W_S \times W_{AV} \times 100) / (A_S \times L_C \times W_T)$ where, A_U = area of unknown sample, W_S = weight of standard (mg), W_{AV} = average weight of tablet (mg), A_S = area of standard, L_C = labelled claim (mg/tablet), W_T = weight of sample (mg).

For specificity study same procedure was followed mentioned above in UV spectrophotometry method.

RESULTS AND DISCUSSION:

Reproducibility, repeatability and accuracy of the proposed methods by UV Spectrophotometry and RP-HPLC were found to be satisfactory which is evident from the low values of standard deviation (SD), relative standard deviation (RSD) and standard error (SE). Results for UV visible spectrophotometric method was discuss in **Table 1, 2** and **3.** Results for RP-HPLC method was discuss in **Table 4, 5, 6** and **7**.

The accuracy and reproducibility of the proposed methods were confirmed by recovery experiment, performed by adding known amount of the drug to the preanalyzed formulation and reanalyzing the mixture by proposed methods. Percent recovery obtained indicates non–interference from the excipients used in the formulation. Thus, the methods developed in the present investigation are found to be simple, sensitive, accurate and precise and can be successfully applied for the estimation of Asenapine in tablets.

TABLE 1: RESULTS OF STATISTICAL DATA OF MARKETED FORMULATION BY UV SPECTROPHOTOMETRIC METHOD

Tablet brand	Tablet component	Label claim(mg/tab)	SD	RSD	SE
Asenapt 10	Asenapine	10	0.1738	0.0017	0.0777
Saphris	Asenapine	10	0.6909	0.0069	0.3089

TABLE 2: RESULTS OF DRUG RECOVERY STUDY BY UV SPECTROPHOTOMETRIC METHOD

Tablet brand	Amount of pure drug added (µg/ml)	RSD	SE
Asenapt 10	2	98.16	0.5013
		98.17	
		98.26	
	4	97.20	
		97.21	
		97.36	
	6	98.56	
		98.05	
		98.06	
Saphris	5	95.28	1.0411
		95.29	
		95.19	
	10	97.91	
		97.35	
		97.55	
	15	96.77	
		96.85	
		96.52	

TABLE 3: RESULTS OF SPECIFICITY STUDY BY UV SPECTROPHOTOMETRIC METHOD

Tablet brand	Sample	% Label Claim
Asenapt 10	Alkali	94.91
	Acid	95.00
	Oxide	94.99
	Heat	94.92
Saphris	Alkali	95.28
	Acid	94.57
	Oxide	95.19
	Heat	95.30

TABLE 4: SYSTEM SUITABILITY PARAMETERS FOR RP-HPLC METHOD

Retention Time (min)	SD	RSD	SE
3.99	0.946	1.576	224152

TABLE 5: RESULTS OF STATISTICAL DATA OF MARKETED FORMULATION BY RP-HPLC METHOD

Tablet brand	Tablet component	Label claim (mg/tab)	SD	RSD	SE
Asenapt 10	Asenapine	10	0.6245	0.0063	0.2792
Saphris	Asenapine	10	0.5023	0.0050	0.2246

TABLE 6: RESULTS OF DRUG RECOVERY STUDY BY RP-HPLC METHOD

Tablet brand	Amount of pure drug added (µg/ml)	% RSD	SE
Asenapt 10	10	97.15	0.6731
		97.21	
		97.14	
	15	96.21	
		96.67	
		96.72	
	20	98.13	
		98.09	
		97.90	
Saphris	10	97.86	0.3944
		97.40	
		97.80	

	15	98.24
		98.24
		98.28
	20	98.53
		98.50
		98.57

TABLE 7: RESULTS OF SPECIFICITY STUDY BY RP-HPLC METHOD

Tablet brand	Sample	% Label Claim
Asenapt 10	Alkali	95.55
	Acid	96.25
	Oxide	95.90
	Heat	96.59
Saphris	Alkali	96.90
	Acid	97.44
	Oxide	96.36
	Heat	97.17

CONCLUSION: The present study proposed an UV Spectrophotometry and RP-HPLC methods to determine ASP from tablet dosage form. The values of percent recovery and standard deviation indicate that the methods are accurate, reproducible and precise.

ACKNOWLEDGEMENTS: The author wishes to thanks Head of the Department, Department of Pharmaceutical Sciences, RTM Nagpur University, Nagpur for providing necessary facilities. Also, thanks to Lundbeck Pvt. Ltd., London for providing the authentic sample of drug.

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How to cite this article:
Borkar AA and Gaikwad NJ: UV Spectrophotometric and RP-HPLC Estimation of Drug Asenapine in Tablet Dosage Form. Int J Pharm Sci Res 2016; 7(7): 3080-84.doi: 10.13040/IJPSR.0975-8232.7(7).3080-84.