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Development of UV-Spectrophotometric Methods for Analysis of Safinamide Mesylate in Bulk and Tablets

Authors: - Manoj V. Girase[1], Amod S. Patil[2], Bhushan J. Mali*[3], Nitin G. Haswani[2], Bhupendra L. Deore[4]

[1]Department of Pharmacognosy, R. C. Patel Institute of Pharmaceutical Education & Research, Shirpur, Dist: Dhule (MS) India 425 405

[2]Department of Pharmaceutical Chemistry, R. C. Patel Institute of Pharmaceutical Education & Research, Shirpur, Dist: Dhule (MS) India 425 405

3 Department of Pharmaceutical Chemistry, Gangamai College of Pharmacy, Nagaon, Dhule (MS) 424005

4 Department of Quality Assurance, A. R. A. College of Pharmacy, Nagaon, Dhule (MS) 424005

/* Address for Correspondence

Dr. Bhushan J. Mali

Associate Professor, Department of Pharmaceutical Chemistry,

Gangamai College of Pharmacy, Nagaon, Dhule (MS) 424005

Email: bjm3006@gmail.com

Abstract:

Aim: To develop and validate UV- Spectrophotometric methods for the estimation of Safinamide mesylate in bulk and tablets.

Method and materials: In methanol, Safinamide mesylate showed maximum absorption at wavelength 226 nm. In Method A (Zero order spectroscopy) estimation of Safinamide mesylate was performed at 226 nm while in Method B, the zero order derivative spectrum was derivatized into first order derivative spectrum (scaling factor 2) and maximum amplitude at 235 nm was selected for analysis and in Method C, Area under curve of zero order spectrum of Safinamide mesylate was selected in the wavelength range of 227.60-242.20 nm.

Results: The drug was found to obey Beer- Lambert's law in the concentration range of 4 - 24 µg/mL for all three methods. The correlation coefficients were found to be 0.9997, 0.9999 and 0.9997 in Method A, B and C, respectively.

Conclusion: All the methods were validated with respect to accuracy, precision and ruggedness. The mean % recoveries were found satisfactory for all three methods. Thus proposed methods have been successfully applied for the estimation of Safinamide mesylate in bulk and tablet dosage form.

Keywords: Safinamide mesylate, UV spectroscopy, Derivative spectroscopy, Area under curve.

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Introduction:

Safinamide mesylate (SAF) is an orally available derivative from chemical class of α – amino amides, with multiple mechanisms of action involving inhibition of MAO-B and Dopamine reuptake used in the treatment of epilepsy and Parkinson's disease. Chemically, Safinamide mesylate is, (*S*)-(+)-2-[4-(3-fluorobenzyloxybenzylamino) propanamide] methanesulfonate (1:1 salt). The chemical structure is shown in Figure 1. [1, 2]

Literature survey revealed a validated chiral liquid chromatographic method for the enantiomeric separation of Safinamide mesylate [3] and bioassay of Safinamide mesylate in biological fluids of humans and various animal species [4]. HPTLC method for determination of Safinamide mesylate in bulk and in tablets has been reported [5]

To our knowledge so far no Spectrophotometric methods are available for analysis of SAF. Hence an attempt has been made to develop new simple and economical UV-Spectrophotometric methods for its estimation in pharmaceutical formulation with good accuracy, precision and economy so as to utilizes it in routine analysis of the drug. The proposed methods were validated as per the International Conference on Harmonization (ICH) guidelines. [6]

Materials and Methods:

Chemicals and Reagents:

Safinamide mesylate was kindly gifted from Alkem Pharmaceuticals, Mumbai (Maharashtra), India. Safinamide mesylate tablets were obtained from commercial sources within their shelf life period. The solvent Methanol used is of HPLC grade.

Instrumentation:

Shimadzu UV-2450 double beam spectrophotometer (Japan) with 1 cm path length supported by Shimadzu UV-Probe software, version 2.21 with 1 cm matched quartz cells having the silicon photodiode detector was used for all spectrophotometric estimations. Weighing balance used was Shimadzu AUX-120 (Japan).

Experimental:

Preparation of standard stock solution:

An accurately weighed quantity of 10 mg SAF was transferred to 100 ml volumetric flasks, dissolved in methanol and volume was made up to mark with the same solvent to obtain a working standard having concentration 100 µg/mL.

Study of linearity curves:

Method A (Zero - order spectrometry):

Series dilutions of standard solutions were prepared in 10 ml volumetric flasks with methanol to get the concentration ranging from 4 - 24 µg/mL. The above solutions were scanned over the range of 400 – 200 nm. The λ max was found to be 226 nm (Figure 2a). The calibration curve was constructed by plotting concentration against absorbance at 226 nm.

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Method B (First - order derivative spectrometry):

The above mentioned zero-order spectrums were derivatized to get first-order derivative spectra (Figure 2b). The dA / dλ of the corresponding maximum amplitude at 235 nm were measured. The calibration curve was constructed by plotting concentration against amplitude.

Method C (Zero order UV- Spectrometry Area under Curve):

The AUC method involves the measurement of area (Figure 2c) with respect to the selected wavelength region (227.60 - 242.20 nm). The calibration curve was constructed by plotting concentration against AUC.

Analysis of tablet formulation:

Twenty tablets were accurately weighed and powered and the quantity equivalent to 10 mg of SAF was transferred to a 100 ml volumetric flask and volume make up to 50 ml with methanol and sonicated for 20 min. The solution was filtered through Whatmann filter paper no. 41 and the residue was washed thoroughly with methanol. The filtrate and the washings were combined in a 100 ml volumetric flask and diluted to the mark with methanol. From this solution 1.2 mL was transferred to 10 mL volumetric flask and diluted up to mark with the methanol. The resulting solution was analyzed by UV Spectrophotometer.

Method Validation:

Accuracy (Recovery Studies):

To the pre-analyzed sample solutions, a known amount of standard stock solution was added at different levels i.e. 80, 100 and 120 %. The solutions were reanalyzed by proposed methods.

Precision:

Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 8, 12 and 16 µg/mL of SAF solutions for three times in the same day. Inter-day precision was determined by analyzing the 8, 12 and 16 µg/mL of SAF solutions daily for three days.

Ruggedness:

Ruggedness of the proposed method was determined by analysis of aliquots from homogenous slot of 12 µg/mL solution by two analyst using same operational and environmental conditions.

RESULTS AND DISCUSSION:

Safinamide mesylate was found to be soluble in methanol and hence The drug was found to obey Beer- Lambert's law in the concentration range of 4-24 µg/mL for all three methods. The optical characteristics of methods are shown in table 1.

Analysis of tablet formulation:

Amount found was found to be 100.12-101.60% with % RSD less than 2, so it was concluded that this method was specific for determination of SAF from pharmaceutical formulation.

Validation:

Accuracy:

The proposed methods when used for extraction and subsequent estimation of drug from tablet dosage form, after adding a known amount of standard stock solution at different levels i.e. 80,

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100 and 120 % to the pre-analyzed sample solutions, afforded a good recovery with % RSD less than 2 % indicating that the methods are more accurate. The results of recovery are shown in Table 2.

Precision:

The % RSD values in precision study were found to be less than 2 % indicating that the methods are more precise. The results depicted revealed high precision of the methods are presented in Table 3.

Ruggedness:

The % RSD values of ruggedness study were found to be less than 2 % indicating that the methods are rugged. The results are shown in Table 4.

Conclusion:

The literature survey promoted us to develop UV spectrophotometric methods on SAF as no analytical method was reported for it. All three methods were developed and validated as per ICH guidelines and the methods were found to simple, precise, accurate and reproducible and can be used for determination of SAF in tablets. Moreover, proposed methods also indicate no interference of excipients when applied to tablet dosage form. Future plan includes development of same drug either in alone or in combination by more sophisticated techniques.

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Figures

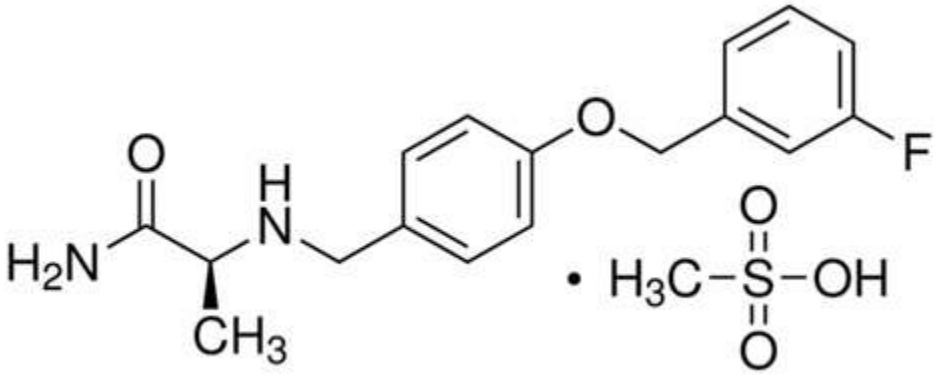

Figure 1. Chemical Structure of Safinamide Mesylate

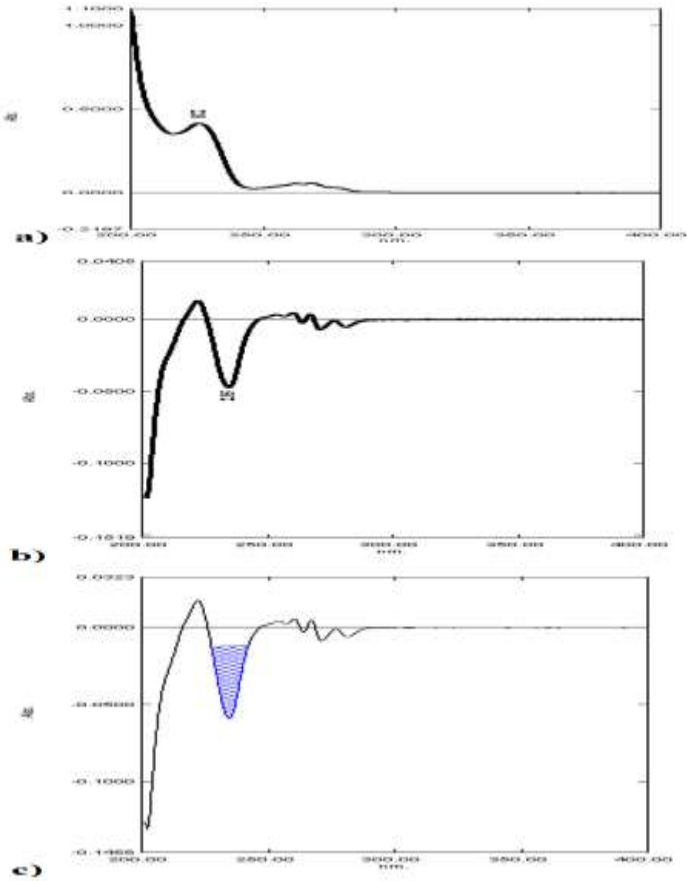

Figure 2. a) Zero order spectrum of SAF at 226nm b) First Order Derivative Spectrum of SAF at 235 nm c) UV-Spectrum of SAF showing AUC

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Table 1. Optical characteristics and statistical data of the regression equations

Parameters	Method A	Method B	Method C
Wavelength	226 nm	235 nm	227.60 - 242.20 nm
Linearity range	4 - 24 nm	4 - 24 nm	4 - 24 nm
Regression equation	Y = 0.0395 X + 0.0304	Y = 0.0036 X + 0.0009	Y = 0.0247 X + 0.0052
Coefficient of correlation	r^{2-}= 0.999	r^{2-}= 0.999	r^2 = 0.999

Table 2: Results of Recovery Studies

Methods	Initial amount of drug [µg/mL]	Excess drug added to the analyte [µg/mL]	% Recovery*	% RSD
A	8	6.4 (80%)	99.92	1.04
		8 (100%)	99.97	1.01
		9.6 (120%)	100.89	0.94
B	8	6.4 (80%)	100.26	1.29
		8 (100%)	100.46	1.05
		9.6 (120%)	100.79	1.00
C	8	6.4 (80%)	99.92	0.41
		8 (100%)	100.25	0.84
		9.6 (120%)	99.73	0.30

***mean of three estimations at each level**

Table 3: Results of Precision Studies

Methods	Conc. (µg/mL)	Intraday Amount found (%)		Interday Amount found (%)	
		Mean	%R.S.D*	Mean	%R.S.D*
A	8	100.39	0.73	100.39	0.44
	12	100.19	0.30	99.94	0.24
	16	100.63	0.17	99.88	0.82
B	8	100.26	0.85	99.88	0.49
	12	101.05	0.49	100.42	0.92
	16	99.89	0.18	100.05	0.48
C	8	99.59	0.28	99.50	0.33
	12	100.23	0.12	100.25	0.16

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	16	99.96	0.13	99.96	0.18

***mean of three estimations at each level**

Table 4: Results of Ruggedness Studies

Methods	Amount taken (µg/mL)	Analyst-1 Amount found (%)		Analyst-2 Amount found (%)	
		Mean ± S.D.	%R.S.D*	Mean ± S.D.	%R.S.D*
A	12	101.32 ± 0.41	0.40	100.58 ± 0.73	0.73
B	12	101.35 ± 0.95	0.94	100.61 ± 0.98	0.98
C	12	100.33 ± 0.63	0.63	100.01 ± 0.81	0.81

***mean of three estimations at each level**