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RESEARCH ARTICLE

Novel Spectrophotometric Methods for the Quantitative Analysis of Rufinamide in Pharmaceutical Dosage Forms

M. MATHRUSRI ANNAPURNA*, G.SIVARAMA KRISHNA, B.PADMAKAR and B.SATYA KIRAN

Department of Pharmaceutical Analysis & Quality Assurance,
GITAM Institute of Pharmacy, GITAM University, Visakhapatnam, India
mathrusri2000@yahoo.com

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Abstract: Two simple, rapid and sensitive spectrophotometric methods were developed for the determination of rufinamide in pharmaceutical formulations in phosphate buffer pH 8.0 and borate buffer pH 9.0. Beer's law was obeyed in a concentration range of 0.5-30 µg/mL in phosphate buffer pH 8.0 and borate buffer pH 9.0 respectively with correlation coefficient of r^2 =0.999 in both the methods. The linear regression equations are found to be y=0.0867x + 0.0241 and y = 0.0898x + 0.0345 in phosphate and borate buffer respectively. The % RSD for intra-day and inter-day precision studies were found to be 0.32 and 0.67 in phosphate buffer pH 8.0 and 0.28 and 0.59 in borate buffer pH 9.0 respectively which is less than 2.0 indicating that the methods are precise. The % RSD in accuracy studies was also found to be less than 2.0. The proposed methods are suitable for the determination of rufinamide in pharmaceutical formulations. No interferences were observed from the excipients in the formulations. The methods were validated according to ICH guidelines.

Keywords: Rufinamide, Pharmaceutical formulations, Validation

Introduction

Rufinamide (RFM) is an antiepileptic drug approved by the US Food and Drug Administration as adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in children 4 years and older and adults. Lennox-Gastaut syndrome consists of a variety of treatment-resistant seizures and is most common among paediatric patients[1] RFM is chemically known as 1- [(2, 6-difluorophenyl) methyl]-1*H*-1,2,3-triazole-4 carboxamide with molecular formula $C_{10}H_8F_2N_4O$ and molecular weight 238.19 g/mol as shown in Figure 1.

The mechanism of action of RFM is unknown but it is presumed to involve stabilization of the sodium channel inactive state, effectively keeping the ion channels closed. It is believed to prolong the refractory period of voltage-dependent sodium channels, making neurons less likely to fire[2]. Very few methods are reported in the literature regarding the

clinical studies and no stability indicating method is available in the official compendia using HPLC for analysing RFM in dosage forms. Analytical methods for RFM from pharmaceutical dosage form should be developed and validated. To date, all analytical methods described in literature for the determination of RFM in biological fluids involve liquid chromatography[3-7] and liquid chromatography–mass spectrometry methods[8-9].

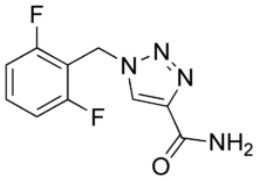

Figure 1. Chemical structure of rufinamide

Experimental

A double beam UV-Vis spectrophotometer (UV-1800, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe was employed with spectral bandwidth of 1nm and wavelength accuracy of ±0.3 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (Denver, Germany). For scanning, the wavelength range selected was from 400 nm to 200 nm with medium scanning speed. All experiments were performed at room temperature (25±1) °C.

Reagents and chemicals

Rufinamide standard (purity ≥ 98.0%) was obtained from Eisai Pharmaceuticals (Visakhapatnam, India). Rufinamide is available commercially with brand names ^{Pr}BANZEL™® and BANZEL® (containing 100, 200 and 400 mg of the drug content) respectively and were procured from the local market.

Preparation of stock and sample solution

The standard solution of rufinamide was prepared by dissolving accurately about 25 mg of the rufinamide with acetonitrile in a 25 mL volumetric flask.

Preparation of phosphate buffer (0.02 M) pH 8.0

50 mL of 0.2 M potassium di hydrogen phosphate was mixed with 46.8 mL of 0.2 M sodium hydroxide and sufficient water to make up to volume in a 500 volumetric flask.

Preparation of borate buffer (pH 9.0)

6.2 g of Boric acid was dissolved in 500 mL of water and pH was adjusted to 9.0 with 1.0 M sodium hydroxide and diluted with water in a 1000 mL volumetric flask. The stock solution was further diluted with phosphate buffer pH 8.0 and borate buffer pH 9.0 for method A and method B (0.5-30 µg/mL) to obtain required sample solutions.

Procedure

Method A

The drug solution was scanned (200-400 nm) against reagent blank (phosphate buffer pH 8.0) and the absorption spectrum (Figure 2) was recorded. The absorption maximum (λ_{max}) was observed at 206 nm. A series of solutions (0.5-30 µg/mL) were prepared and the absorbance of these solutions was recorded at that λ_{max}.

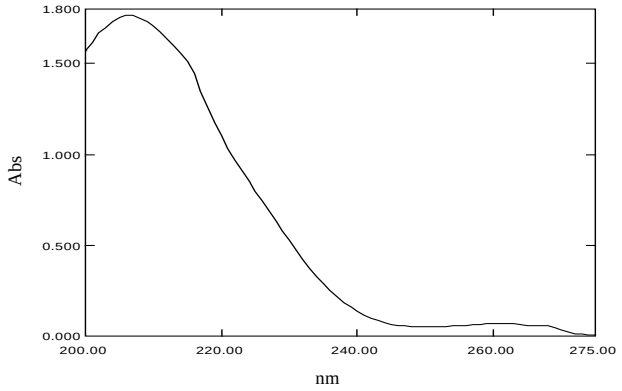

Figure 2. Absorption spectrum of rufinamide (20 µg/mL) in phosphate buffer (pH 8.0)

A graph was plotted by taking the concentration of the solutions on the x-axis and the corresponding absorbance values on the y-axis (Figure 3).

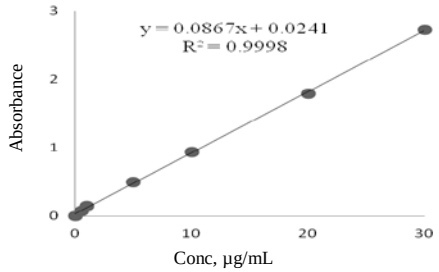

Figure 3. Calibration curve of rufinamide (Phosphate buffer pH 8.0)

Method B

The drug solution was scanned (200-400 nm) against reagent blank (borate buffer pH 9.0) and the absorption spectrum was recorded (Figure 4). A series of solutions (0.5-30 µg/mL) were prepared and the absorbance of these solutions was recorded at that λ_{max}.

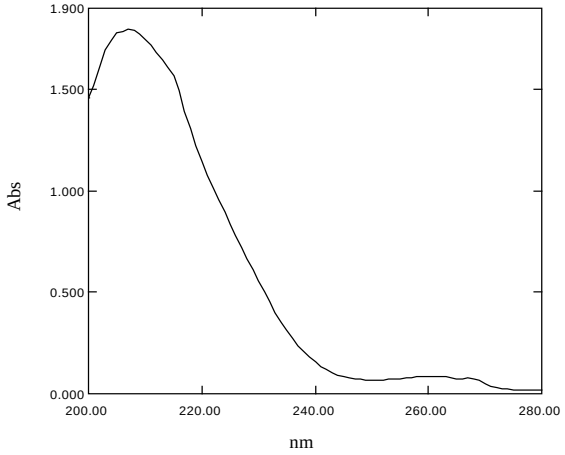

Figure 4. Absorption spectrum of rufinamide (20 µg/mL) in borate buffer (pH 9.0)

A graph was plotted by taking the concentration of the solutions on the x-axis and the corresponding absorbance values on the y-axis (Figure 5).

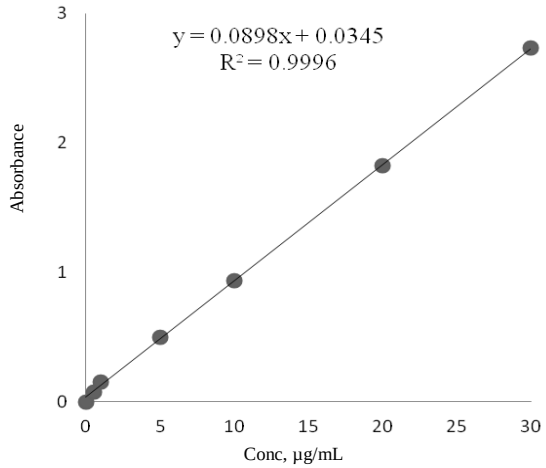

Figure 5. Calibration curve of rufinamide (Borate buffer pH 9.0)

Assay of commercial formulations (Tablets)

Rufinamide is available in the local market with brand names BANZEL (100, 200 and 400 mg.) and ^{Pr}BANZEL$^{TM®}$ (100, 200 and 400 mg.) were purchased. Twenty tablets were collected each brand, powdered and powder equivalent to 25 mg of the drug was weighed, extracted with acetonitrile separately, sonicated and make up to volume in two different 25 mL volumetric flasks (1 mg/mL) and filtered. Further dilutions were made from this stock solution with phosphate buffer and borate buffer for method A and B and analyzed according to the recommended procedure.

Precision and accuracy

The precision study was done by recording the absorbance of six replicates (20 µg/mL) for method A and B and the % RSD was calculated. Accuracy was evaluated by the recovery studies by the addition of 80%, 100% and 120% of pure drug solution to the pre-analysed formulation solution. For the present study RFM drug solution extracted from the formulation was taken and 80%, 100% and 120% of pure drug solution (*i.e*. 8, 10 and 12 µg/mL) were added to the 10 µg/mL and the % RSD was calculated.

Results and Discussion

The optical characteristics of the proposed methods were shown in Table 1. Beer's law was obeyed in the concentration range of 0.5-30 µg/mL and 0.5-30 µg/mL for the methods A and B respectively. The linear regression equations were found to be y = 0.0867x + 0.0241 and y = 0.0898x + 0.0345 for method A and B respectively with correlation coefficient 0.9998 and 0.9996 respectively for both methods.

The % RSD values for precision and accuracy studies of both the methods were found to be (RSD <2%) indicating that the methods are more precise and accurate. The percentage recovery was found to be 96.65-97.12 and 97.35-97.40 for method A and B respectively (Table 2). The proposed methods can be applied successfully for the determination of rufinamide in pharmaceutical formulations.

Table 1. Optical characteristics of rufinamide

Parameters	Method	
	A	B
Beer's Law limit, µg/mL	0.5-30	0.5-30
λ, nm	206	206
Molar extinction coefficient (Litre/mol^{-1}.cm^{-1})	2.172292×10^4	2.227076×10^4
Sandell's sensitivity (µg/cm^2/0.001absorbance unit)	0.01096	0.01069
Regression equation (Y*)		
Slope (a)	0.0867	0.0898
Intercept (b)	0.0241	0.0345
Correlation coefficient	0.9998	0.9996

Table 2 Analysis of rufinamide commercial formulation (Tablets)

Brand	Labeled Amount mg	*Amount obtained, mg		% Recovery*		% RSD*	
		Method		Method		Method	
		A	B	A	B	A	B
^{Pr}BANZEL™®	400	386.6	389.4	96.65	97.35	0.35	0.46
BANZEL®	400	388.5	389.6	97.12	97.4	0.28	0.65

**Mean of three determinations*

Conclusion

The present methods can be employed for the determination of rufinamide in pharmaceutical formulations successfully and there is no interference of excipients during the study.

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