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SHORT COMMUNICATION

# Development and validation of a stability indicating RP-HPLC method for the determination of Rufinamide

**B. Sai Pavan Kumar*, M. Mathrusri Annapurna, S. Pavani**

*Department of Pharmaceutical Analysis & Quality Assurance, GITAM Institute of Pharmacy, GITAM University, Visakhapatnam 530045, India*

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**Abstract** A stability-indicating RP-HPLC method was developed and validated for the determination of Rufinamide in tablet dosage forms using C 18 column (250 mm × 4.6 mm, 5 μm) with mobile phase consisting of water–acetonitrile (40:60, v/v) with a flow rate of 0.8 mL/min (UV detection 215 nm). Linearity was observed over the concentration range 1.0–200 μg/mL ($R^2$=0.9997) with regression equation $y$=113190 $x$+63053. Rufinamide was subjected to stress conditions including acidic, alkaline, oxidation, photolysis and thermal degradation. Rufinamide is more sensitive towards acidic degradation. The method was validated as per ICH guidelines.



## 1. Introduction

Rufinamide is an antiepileptic drug approved by the US Food and Drug Administration as an 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 pediatric patients [1]. Rufinamide is chemically known as 1-[(2, 6-difluorophenyl) methyl]-1 H-1,2,3-triazole-4 carboxamide (Fig. 1).

The mechanism of action of Rufinamide involves 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]. To date, all analytical methods described in literature for the determination of Rufinamide in biological fluids involve liquid chromatography [3–7], liquid chromatography–mass spectrometry [8] and HPLC [9] methods. In the present work, we developed a simple, precise, accurate, selective and robust liquid chromatographic method for the determination of Rufinamide in pharmaceutical dosage form as an alternative method.

## 2. Experimental

### 2.1. Chemicals and reagents

Rufinamide standard (purity≥98.0%) was obtained from Eisai Pharmaceuticals (Visakhapatnam, India). Acetonitrile (HPLC

*Corresponding author. Tel.: +91 8985143573; fax: +91 891 2795315.
E-mail address: saipavan23@gmail.com (B. Sai Pavan Kumar).

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grade), sodium hydroxide, hydrochloric acid and hydrogen peroxide were purchased from Merck (India). Rufinamide is available as tablets with brand names $^{Pr}$BANZEL$^{TM®}$ and BANZEL® with label claim of 100, 200 and 400 mg of drug. All chemicals were of analytical grade and used as received.

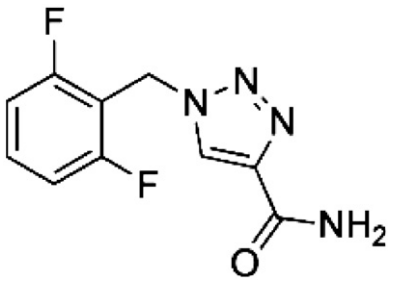


**Fig. 1** Chemical structure of Rufinamide.

### 2.2. HPLC instrumentation and conditions

Chromatographic separation was achieved by using a Shimadzu Model CBM-20 A/20 Alite HPLC system, equipped with an SPD M20A prominence photodiode array detector (250 mm × 4.6 mm, 5 µm particle size) maintained at 25 °C. Isocratic elution was performed using acetonitrile and water (60:40, v/v) with flow rate 0.8 mL/min. 20 µL of sample was injected into the HPLC system.

Rufinamide stock solution (1000 µg/mL) was prepared by accurately weighing 25 mg of Rufinamide in a 25 mL amber volumetric flask and making up to volume with mobile phase. Working solutions for HPLC injections were prepared on a daily basis from the stock solution in a solvent mixture of acetonitrile and water (60:40, v/v) (mobile phase). Solutions were filtered through a 0.45 µm membrane filter prior to injection.

20 tablets from each brand ($^{Pr}$BANZEL$^{TM®}$ and BANZEL®) were procured, weighed and crushed to a fine powder. Powder equivalent to 25 mg Rufinamide was accurately weighed into a

**Table 1** Comparison of the performance characteristics of the present method with the published methods.

| S. no. | Method/reagent | λ (nm) | Linearity (µg/mL) | Remarks | Ref. |
|---|---|---|---|---|---|
| 1. | HPLC (Robotic system) | 230 | 0.05–4.0 | Human plasma | [3] |
| 2. | HPLC/acetonitrile: methanol: potassium dihydrogen phosphate | – | 0.05–19.09 | Plasma (liquid-solid extraction) | [4] |
| 3 | HPLC/acetonitrile: methanol: potassium dihydrogen phosphate | – | 0.05–20 | Plasma and brain | [5] |
| 4 | HPLC/acetonitrile: methanol potassium dihydrogen phosphate buffer (pH 4.5) | 210 | 2–40 | Very narrow linearity range (UV/visible detector) | [6] |
| 5 | HPLC/methanol: dichloromethane:n-hexane | 230 | 0.25–20.0 | Plasma and saliva | [7] |
| 6 | LC–MS | – | 0.48–47.6 | Dried blood spots | [8] |
| 7 | HPLC/methanol: water (pH 3.0) | 220 | 10–60 | Very narrow linearity range | [9] |
| 8 | HPLC/acetonitrile: water (60:40, v/v) | 215 | 1.0–200 | Wide linearity range stability indicating method (PDA detector) | Present work |

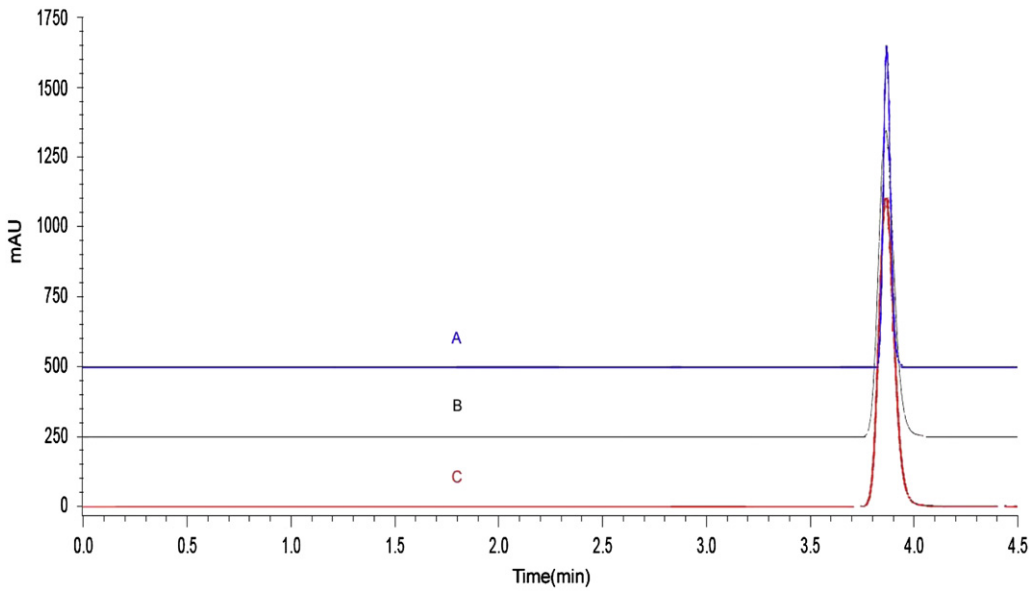


**Fig. 2** Representative chromatograms of Rufinamide (50 µg/mL) (A), $^{Pr}$BANZEL$^{TM®}$ (400 mg) (B), and BANZEL® (400 mg) (C).