Academic Sciences International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 6, Issue 3, 2014

Research Article

QUANTITATIVE ESTIMATION OF RILUZOLE USING SOLUBILIZING AGENT BY UV-SPECTROPHOTOMETRY

K. NAGA RAJU, T. SUNITHA, I. SUDHEER BABU

Dept of Pharmaceutical Analysis and Quality Assurance, Sir C R Reddy College of Pharmaceutical Sciences, Eluru, W. G Dt, A. P., India.
Email: nagaraju162@gmail.com

Received: 19 Feb 2014, Revised and Accepted: 29 April 2014

ABSTRACT

Objective: This study was designed to develop and validate a simple, rapid, and economical UV-spectrophotometric method using a solubilising agent for the estimation of Riluzole.

Methods: In this study, a solution of 2% SLS (Sodium Lauryl Sulphate) in PH 9.2 buffers was employed as the solubilising agent to solubilise a poorly water-soluble drug, Riluzole. In the UV-spectrophotometric method, Riluzole was estimated at 225 nm using solubilising agent.

Results: Solubilising agent used did not interfere in spectrophotometric analysis of Riluzole. Riluzole followed linearity in the concentration range of 1-5 µg/ml with a coefficient correlation of 0.998.

Conclusion: The developed method has shown to be linear (r2 = 0.9984), precise (%R. S. D of 0.87 and 0.84 at intra and inter day respectively), accurate (recovery of 100.37%) with limit of detection (0.54 µg/ ml) and limit of quantification of 1.64µg/ ml as per ICH guidelines.

Keywords: Riluzole, UVspectroscopyy, SLS (Sodium Lauryl Sulphate), PH 9.2 buffer.

INTRODUCTION

Riluzole is the only FDA-approved drug currently used for the treatment of amyotrophic lateral sclerosis (ALS), a progressive, fatal, neurodegenerative disorder caused by deterioration of voluntary muscle controlling motor neurons leading to paralysis state and long term disability [1]. Three mechanisms are proposed for action of RIL: inhibition of excitatory amino acid release, inhibition of events following stimulation of excitatory amino acid receptors and stabilization of the inactivated state of voltage-dependent sodium channels. RIL offers neuro-protective action and prolongs the life of ALS patient. *In vivo*, it has neuroprotective, anticonvulsant, and sedative properties [2].

RIL is chemically 6-(trifluoromethoxy) benzothiazol-2-amine. The structure of Riluzole is presented in Fig 1. It is very slightly soluble in water and is weakly basic (pKa3.5) in nature. Post oral administration, it is rapidly absorbed from gastro–intestinal tract and has an absolute bioavailability of about 60% in humans. It is extensively metabolized, primarily by cytochrome P450 1A2[3].

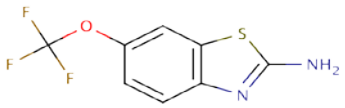

Fig. 1: Structure of Riluzole

Literature survey revealed that Riluzole was estimated analytically using different analytical techniques like UV spectroscopy [5], HPLC[5][7], HPTLC[7] and Stability indicating methods[5][6]. Most of the UV spectrophotometric methods developed employed organic solvents to solubilise the drug[8].Only one solubility enhancement method was reported for the estimation of Riluzole by using UV spectrophotometry, which used 5M sodium benzoate as a hydrotropic solubilising agent[4]. Drawbacks of organic solvents include their higher cost, toxicity, and pollution. In addition, Riluzole is poorly soluble in water. Therefore, the solubility enhancement technique may be a suitable alternative to exclude the use of organic solvents. Special systems are required to solubilise poorly water-soluble drugs. Out of many solubilising agents tried, there was a miraculous synergistic effect on enhancement in solubility of a poorly water-soluble drug by mixing 2% SLS in PH 9.2 buffers.

The objective of the present investigation is to develop simple, precise, accurate and economical UV-spectrophotometric method for the determination of Riluzole using suitable solubilising agent. The developed method was validated as per the ICH guidelines.

MATERIALS AND METHODS

Chemicals

Riluzole hydrochloride, PH 9.2 buffer capsules were purchased from Merck speciality pvt. Ltd. SLS was purchased from Merck speciality pvt. Ltd.

Instrumentation

A UV-visible spectrophotometer systronics pc based double beam spectrophotometer 2202 employed for all spectroscopic measurements, using a pair of 1 mm matched quartz cells.

Selection of solvent

2% SLS (Sodium Lauryl Sulphate) in PH 9.2 buffer solution was selected as a solvent for developing spectral characteristics of a drug. The selection was made after assessing the solubility in different hydrotropic solubilising agents.

Preparation of stock standard solutions

Stock standard solutions of Riluzole were prepared by dissolving 10 mg in a 100 mL volumetric flask containing 25 ml of 2% SLS (Sodium Lauryl Sulphate) in PH 9.2 buffer solution, the solution was heated slightly on a water bath to ensure complete dissolving and the volume was made up to the mark with the same to obtain the concentration 100 µg/ml. After appropriate dilutions, 10 µg/ml Riluzole was scanned in the UV-region, i. e. 200–400 nm. Riluzole showed λ_{max} of 225 nm in 2% SLS (Sodium Lauryl Sulphate) in PH 9.2 buffer solution.

Validation of the developed method [9]

Specificity and selectivity

The specificity of Riluzole was estimated by checking the interference and interaction of SLS with drug.

Accuracy

As a part of determining accuracy of the proposed method, different levels of drug concentrations (50%, 100%, and 150%) were prepared from independent stock solution and analysed. Accuracy was assessed as the percentage recovery and mean percentage recovery.

Precision

Repeatability was determined by using a drug concentration of 4 µg/ml prepared from independent stock solution and analysed. Inter-day and Intra-day variation was taken to determine the intermediate precision of the proposed method. The relative standard deviation (% RSD) of the predicted concentrations from the regression equation was taken as precision.

Linearity

To establish linearity of the proposed method, six separate series of solution of the drug (1-5 µg/ml using 2% SLS in P^H 9.2 buffer solution) were prepared and analysed. Least square regression analysis was done for the obtained data.

Detection limit (LOD) and Quantitation limit (LOQ)

The LOD and LOQ of Riluzole by the proposed method were determined using calibration standard. LOD and LOQ were calculated as 3.3σ/S and 10σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of y intercept of the regression equation.

Robustness

Robustness of the proposed method was determined by changing the wavelength of estimation by ±2 nm. Mean % recovery was determined.

RESULTS AND DISCUSSION

Absorption spectrum of Riluzole was estimated and λmax was found to be 225 nm. Calibration curve was plotted and the linear regression equation obtained was y = 0.1047x + 0.004 with regression co-efficient 0.9984. The method was validated in accordance with the current ICH guidelines. The study of Beer's-Lambert's law was checked by preparing standard solution at six different concentrations and the linearity of the calibration graphs and conformity of the UV-VIS measurement of the proposed methods to Beer's law were proven by the values of the correlation co- efficient of the absorptivity study.

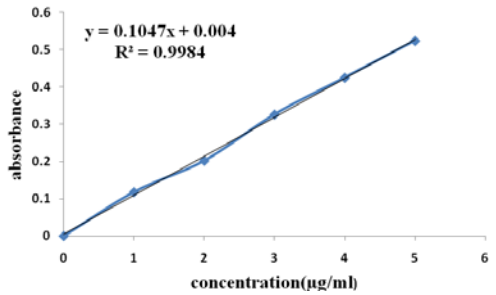

Fig. 2: Calibration/Standard curve for Riluzole

Table 1: Accuracy of Riluzole

Drug	Theoretical content		% recovery	Mean recovery
RIL	50%(1µg/ml)	1	102.5	100.66%
		2	101.0	
		3	98.5	
RIL	100%(3µg/ml)	1	99.25	100.45%
		2	100.7	
		3	101.4	
RIL	150%(5µg/ml)	1	100	100.02%
		2	100.9	
		3	99.16	Mean = 100.37%

The linear range of concentration for the analysis of riluzole was found to be 1-5 µg/ml for UV-spectrophotometric method and calibration curve was represented in figure-2. Mean % recoveries of riluzole by UV-VIS method were found to be 100.37% which was tabulated in table-1. The reproducibility and repeatability of the developed method were established by the study of precision. The % RSD was found to be 0.87 and 0.84 at intra and inter day respectively for UV-VIS spectroscopic method. Robustness of the proposed method was carried out and the results did not show any considerable statistical difference suggesting that the method developed was robust. Brief information regarding the results of the proposed method was presented in table– 2.

Table 2: Results of the developed method

Parameter	Result
λmax	225 nm
Beer's law limits (µg/ml)	1 – 5
Molar absorptivity (lit. Mole $^{-1}$. Cm^{-1})	$2.48 * 10^5$
Sandell's sensitivity (µg. cm^2/0.001 abs. unit)	$0.09411 * 10^{-2}$
Regression equation (y = mx + c)	y = 0.1047x + 0.004
m-slope	0.1047
c- intercept	0.004
Correlation co-efficient (r)	0.9984
Standard deviation	0.1465
RSD	0.4592
% range of error	
0.05 level	0.0122
0.01 level	0.1812
LOD (limit of detection)	4.61
LOQ (limit of quantification)	13.99

CONCLUSION

The developed UV-spectrophotometric method for determination of riluzole was found to be simple, accurate, precise, and economical. The method was proved to be robust and can be used for routine analysis of riluzole in bulk and in formulations.

ACKNOWLEDGEMENT

The authors are thankful to the management of Sir C. R. Reddy college of Pharmaceutical sciences for providing chemicals and excellent lab facilities.

REFERENCES

1. Habib AA, Mitsumoto H. Emerging drugs for amyotrophic lateral Sclerosis. Expert Opin Emerg Drugs 2011;16:537-58.
2. Hardiman O, Van den Berg LH, Kiernan MC. Clinical diagnosis and management of amyotrophic lateral sclerosis. Nat Rev Neurol 2011;7:639-49.
3. Bryson HM, Fulton B, Benfield P. Riluzole. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in amyotrophic lateral sclerosis. Drugs 1996;52:549-63.
4. MC Sharma, S Sharma. Validation of UV spectrophotometric method for determination of riluzole pharmaceutical formulation as hydrotropic solubilizing agents. World J Chem 2011;6(2):85-90.
5. Saleh OA, El-Azzouny AA, Aboul-Enein HY, Badawey AM. Riluzole: Validation of Stability-Indicating HPLC, D1 and DD1 Spectrophotometric Assays. J Chromatogr Sci 2014;52(6):539-46.
6. Neeha T, Bhargavi P, Jyothi AA, Devalarao G, Nalluri BN. Stability-indicating Method for the Estimation of Riluzole in Tablets. Indian J Pharm Sci 2013;75(3):372-6.
7. Phanjoubam Lothar. RP-HPLC and hptlc methods for the estimation of riluzole in tablet dosage form. IJBR 2010;1[3].
8. Phanjoubam Lothar, Rajashree Bhaskar Thube, Naveen Pattanashetty. Spectrophotomtric method for the estimation of riluzole in pharmaceutical dosage. Int J Pharm Sci Rev Res 2011;6(2)183-4.
9. ICH harmonised tripartite guideline validation of analytical procedures: text and methodology q2 (r1) current step 4 version parent guideline dated 27 october 1994 (complementary guideline on methodology dated 6 november 1996 incorporated in november 2005).