ejpmr, 2024, 11(7), 472-475

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

VALIDATED SPECTROPHOTOMETRIC METHOD FOR THE QUANTITATION OF REBAMIPIDE IN BULK AND PHARMACEUTICAL DOSAGE FORM

Bindhyashree K. M.*, Naveen Kumar G. S. and Sowmya H. G.

Department of Pharmaceutical Analysis Bharathi College of Pharmacy, Bharathinagara, (K M Doddi), Maddur Taluk, Mandya District, Karnataka, India-571422.

***Corresponding Author: Bindhyashree K. M.**

Department of Pharmaceutical Analysis Bharathi College of Pharmacy, Bharathinagara, (K M Doddi), Maddur Taluk, Mandya District, Karnataka, India-571422.

Article Received on 20/05/2024 **Article Revised on 10/06/2024** **Article Accepted on 30/06/2024**

ABSTRACT

Simple, precise and accurate zero order derivative spectroscopic method has been developed and validated for the estimation of Rebamipide in bulk and pharmaceutical dosage form. The drug shows maximum absorption (λ max) at 235nm in 0.1 N sodium hydroxide and obeys Beer's law in the concentration range of 1-6µg/ml. The linearity study was carried out and regression coefficient was found to be 0.999 and it has showed good linearity, precision during this concentration range. The percentage recovery was found to be 100.43 – 101.08. The LOD and LOQ were found to be 0.024 and 0.07µg/ml. The % relative standard deviation were found to be less than 2. According to ICH guidelines the technique has been validated for linearity, precision, accuracy, ruggedness, LOD and LOQ. The developed and validated method can be successfully applied for routine estimation of Rebamipide in bulk and pharmaceutical dosage form.

KEYWORDS: Rebamipide, Zero order derivative spectroscopy, Validation, Pharmaceutical formulation.

INTRODUCTION

Rebamipide is used for the treatment of stomach ulcers as an anti-ulcer drug. It is known that the anti-ulcer activity of Rebamipide is due to its enhancement of the protective gastric mucosal lining by increasing the concentration of prostaglandin E2 in the gastric mucosa and reducing free radical production. Both of which lead to improved gastric ulcer healing. Rebamipide as a mucosal protective drug, can not only increase the production of endogenous prostaglandins but also has the cytoprotective antiulcer effects.[1] Rebamipide is also used as an ophthalmic solution to treat patients suffering with dry eyes.[2] It is classified as a class IV drug according to the biopharmaceutical classification systems (BCS).[3]

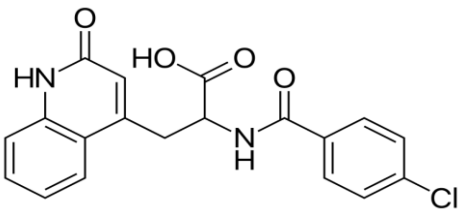

Figure 1: Structure of rebamipide.

Extensive literature survey reveals that few spectrophotometric methods.[4-7] RP-HPLC[8-10] and HPTLC[11-12] methods for the determination of the Rebamipide alone or in combination in various pharmaceutical formulations and biological fluids including stability studies, this gives information related to the analyte is surveyed for synthesis, physical and chemical properties, solubility and relevant analytical methods. Hence there is a need for the development of newer, simple, sensitive, rapid, accurate, and reproducible spectrophotometric, visible and chromatographic methods for the routine estimation of Rebamipide in bulk drug and pharmaceutical dosage form.

MATERIALS AND METHODS

Instrument: UV-visible double beam spectrophotometric, SHIMADZU (model UV-1800) with UV probe software. All weights were taken in analytical balance.

Chemicals: Rebamipide pure drug was obtained as a gift sample from Medreich pharmaceutical, Bengaluru and its pharmaceutical dosage Rebamipide 20 tablets (Rebagen-100) labelled claim 100mg from local pharmacy manufactured by Macleods pharmaceuticals Ltd.

Solvent: 0.1N NaOH is used as a solvent.

Selection of analytical wavelength: Appropriate dilution of Rebamipide were prepared from standard

stock solution and using spectrophotometer solution was scanned in the wavelength range 200-400nm. The absorption spectra obtained and show maximum absorbance at 235nm, as the wavelength for detection.

Preparation of standard solution: 100mg of Rebamipide was weighed accurately and transferred into 100ml volumetric flask and diluted in 0.1N NaOH up to mark. From this, the solution was further diluted into 100µg/ml and pipetted out 0.1, 0.2, 0.3, 0.4, 0.5 and 0.6ml into 10ml individual volumetric flask and diluted in 0.1N NaOH up to mark this gives 1, 2, 3, 4, 5 and 6µg/ml concentration.

Preparation of sample solution: 20 tablets of Rebamipide marketed formulations was weighed and powdered. A quantity of tablet powder equivalent to 100mg of Rebamipide was transferred into a 100ml of volumetric flask then it was diluted with 0.1N NaOH and made up to the mark.

METHOD AND VALIDATION

The method was validated according to the ICH guidelines.[13-15]

RESULTS AND DISCUSSION

Method: Zero order derivative spectroscopy.

Linearity: The linearity of an analytical method is its capacity to show the test results that are directly proportional to the concentration of the analyte in the sample within the range. The linearity was established in the range of 1-6µg/ml was measured at 235nm and absorbance values are shown in table-1. The calibration curve was prepared by plotting graph against the concentration and absorbance and therefore the graph shown in Fig-3. Statistical variables like slope, intercept, regression, correlation coefficient and sandell's sensitivity were determined and shown in table-2.

Precision: The precision of an analytical method expresses the closeness of a series of individual analyte measurements obtained from multiple sampling of the equivalent sample. Precision was established by intra-day and inter-day studies. Intra-day precision was determined by analysing the same concentration for six times in a same day. Inter-day precision was determined by analysing the same concentration daily for six days. Shown in table-3.

Accuracy: The accuracy of an analytical method says that closeness of test results obtained by that method to the true value. To assess the accuracy of the developed method, recovery studies were carried out at three different levels as 50%, 100%, and 150%. In which the formulation concentration holds it constant and varied pure drug concentration. Shown in table-4.

Ruggedness: The ruggedness is defined as the reliability of results when the method is performed under the variation in condition. This includes distinct analyst, laboratories, instruments, temperature etc. Ruggedness was determined between distinct analyst, the value of %RSD was found to be less than 2. (table-5)

LOD and LOQ: The limit of detection is an individual analytical method is the smallest amount of analyst in a sample which can be reliable detected by the analytical method. The limit of quantitation is a discrete analytical procedure is the smallest amount of analyte in a sample which can be quantitatively determined. LOD and LOQ were calculated by using following formula.

LOD = 3.3(SD)/S and LOQ = 10(SD)/S

LOD and LOQ value of Rebamipide were found be 0.024 and 0.416µg/ml.

Tables

Table 1: Results of calibration curve at 235nm by zero order spectroscopy.

Sl. No.	Concentration in µg/ml	Absorbance ±Standard deviation
1	0	0
2	1	0.147±0.0010
3	2	0.269±0.0022
4	3	0.405±0.0017
5	4	0.541±0.0027
6	5	0.699±0.0016
7	6	0.809±0.0020

**Average of six determinations.*

Table 2: Regression parameter of rebamipide by zero order spectroscopy.

Regression parameter	Results
Range (µg/ml)	1-6
Λmax (nm)	235
Regression equation	0.1358X+0.0025
Slope (b)	0.1358
Intercept (a)	0.0025

Correlation coefficient (r^2)	0.999
Sandell's equation	0.0074
Limit of detection (µg/ml)	0.02
Limit of quantification (µg/ml)	0.07

Table 3: Determination of precision results for Rebamipide at 235nm by zero order spectroscopy.

Concentration (µg/ml)	Intra-day Absorbance ±Standard deviation*	%RSD**	Inter-day Absorbance ±Standard deviation*	%RSD**
1	0.147±0.0010	0.680	0.143±0.0008	0.583
2	0.269±0.0022	0.743	0.273±0.0024	0.909
3	0.405±0.0017	0.419	0.406±0.0036	0.903
4	0.541±0.0027	0.496	0.542±0.0046	0.852
5	0.699±0.0016	0.228	0.699±0.0026	0.309
6	0.809±0.0020	0.247	0.811±0.0044	0.549

**Average of six determination, **percentage relative standard deviation.*

Table 4: Determination of Accuracy results for Rebamipide at 235nm by zero order spectroscopy.

Spiked level	Amount of sample (µg/ml)	Amount of standard (µg/ml)	Amount Recovered	%Recovery ±Standard deviation*	%RSD
50	3	1.5	4.54	100.43%±0.671	0.668
100	3	3	5.94	100.66±0.516	0.512
150	3	4.5	7.41	101.08±0.172	0.170

**Average of six determination, **percentage relative standard derivation.*

Table 5: Determination of Ruggedness results for Rebamipide at 235nm by zero order spectroscopy.

Analysts	Analyst 1	Analyst 2
Mean absorbance	0.405	0.406
±Standard deviation	0.0017	0.0016
%RSD	0.419	0.394

Average of six determinationpercentage relative standard deviation.*

Figures

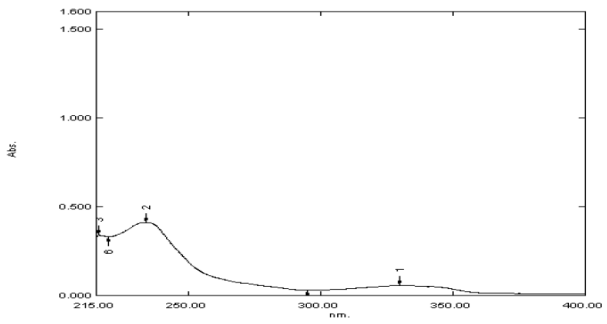

Fig. 2: Zero order spectrum of Rebamipide at 235nm.

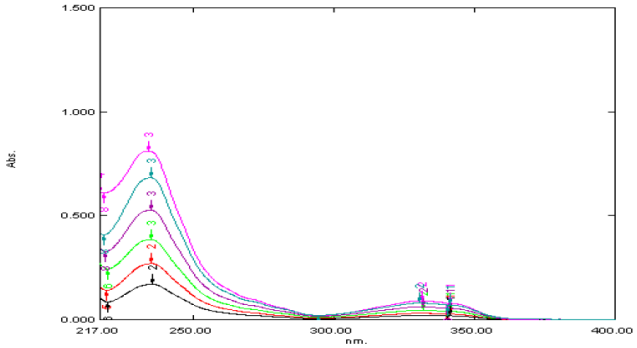

Fig. 3: Zero order overline spectra of Rebamipide showing absorbance at 235nm.

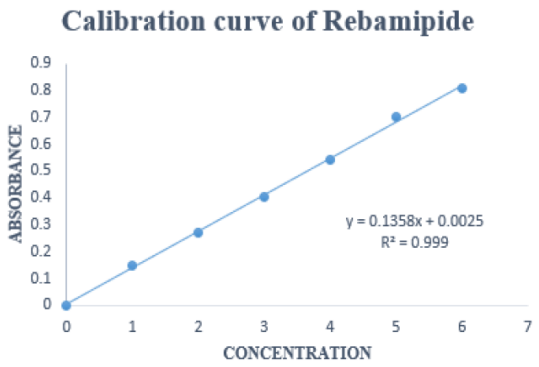

Fig. 4: Calibration curve of Rebamipide by zero order spectroscopy.

CONCLUSION

As per ICH guidelines, the present analytical work was carried out and met the acceptance criteria. It was concluded that the developed method was simple, specific, accurate, economical and sensitive and can be used for routine analysis of Rebamipide in bulk and pharmaceutical dosage forms.

ACKNOWLEDGEMENT

We authors wish to gratitude to our management, principal of Bharathi college of pharmacy for providing all facilities and also, we extend our thanks to all.

REFERENCE

1. Liu J, Xiong Z, Geng X, Cui M, Adinortey MB. Rebamipide with proton pump inhibitors (PPIs) versus PPIs alone for the treatment of endoscopic submucosal dissection-induced ulcers: a meta-analysis. BioMed Research International, 2020; 28, 2020: 1-0.
2. Shrivastava, S., Patkar, P., Ramakrishnan, R., Kanhere, M., & Riaz, Z. Efficacy of rebamipide 2% opthtalmic solution in the treatment of eyes. Oman J Ophthalmol, 2018; 11(3): 207-212.
3. Nagai N, Ishii M, Seiriki R, Ogata F, Otake H, Nakazawa Y, Okamoto N, Kanai K, Kawasaki N. Novel sustained-release drug delivery system for dry eye therapy by rebamipide nanoparticles. Pharmaceutics, 2020; 14, 12(2): 155.
4. Srivastava PK, Roy A. Development and validation of a new UV method for the analysis of rebamipide. Int J Pharmtech Res, 2011; 3(3): 1270-4.
5. Khaggeswar B, Reddy R, Bharadwaj R. New validation, UV Spectrophotometric method for the estimation of rebamipide and tramadol in bulk and dosage form. Der Pharmacia Letter, 2011; 3(1): 298-306.
6. Alqarni MA, Moatamed RS, Naguib IA, El Ghobashy MR, Farid NF. Development and validation of four spectrophotometric methods for assay of rebamipide and its impurity: application to tablet dosage form. J of AOAC Int, 2022; 1, 105(1): 299-308.
7. Manglani UR, Khan IJ, Soni K, Loya P, Saraf MN. Development and validation of HPLC-UV method for the estimation of rebamipide in human plasma. Ind J of pharm sci, 2006; 1, 68(4): 475-478.
8. Jeoung MK, Kim CS, Kim NH, Hong JT, Chung YB, Park Y, Kim KS, Moon DC. Determination of rebamipide in human plasma by HPLC. J of Liq Chromatogr and Rel Tech, 2004; 1, 27(12): 1925-35.
9. Son DC, Thuong N, Park ES, Chi SC. High performance liquid chromatographic analysis of rebamipide in human plasma. Anal Lett, 2005; 1, 38(6): 997-1005.
10. Sonawane S, Gide P. Optimization of forced degradation using experimental design and development of a stability-indicating liquid chromatographic assay method for rebamipide in bulk and tablet dosage form. Sci Pharm, 2011; 79(1): 85-96.
11. Patel p, poshiya p, chauhan g. Development and validation of high-performance thin layer chromatographic method for determination of rebamipide from its tablet dosage form. Int J Pharm Pharm Sci, 2014; 6(5): 606-610.
12. Shirkhedkar AA, Dhumal DM, Surana SJ. A sensitive and specific high-performance thin- layer chromatography—densitometry method for determination of rebamipide in the bulk material and in pharmaceutical formulation. J Planar Chromat Modern TLC, 2012; 25: 368-73.
13. ICH, Q2A text on validation of analytical procedures; 1994. https://database.ich.org/sites/default/files/Q2%28R1%29%20Guideline.pdf
14. ICH, Q2B validation of analytical methodology; 1996. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q2b-validation-analytical-procedures-methodology.
15. ICH, Q2 (R1) validation of analytical procedures: text and methodology; 2005. https://database.ich.org/sites/default/files/Q2%28R1%29%20Guideline.pdf