RESEARCH ARTICLE

Validated First-Order Derivative Ultraviolet Spectrophotometric Determination of Rebamipide in Pharmaceutical Products

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ABSTRACT

A very simple, accurate, precise, and reproducible process has been established for the estimation of rebamipide in pharmaceuticals. The literature review suggested that no UV method for quantitative estimation of first-order derivative for the rebamipide, accordingly a method has been developed and reported. As per the need for design a novel approach to analyze the drug utilizing dimethyl formamide as a solvent was identified. Rebamipide has absorbance maxima for first order derivative 314 nm. Rebamipide drug follows Beer's law in a range of concentration between 20 to 200 µg/mL. The recovery studies verified the proposed method's accuracy and findings were validated in accordance with ICH recommendations. The findings were deemed to be reliable and satisfactory. As a result, the suggested method can be used to quantitatively estimate Rebamipide in ordinary analysis work.

Keywords: Rebamipide, First order derivative, Estimation, Analysis, UV spectrophotometric.

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Conflict of interest: None

INTRODUCTION

Drug: Rebamipide

Structure of Rebamipide

As shown in Figure 1.

IUPAC Name: 2-[(4-chlorobenzoyl) amino]-3-(2-oxo-1H-quinolin-4yl) propanoic acid

Molecular Formula: $C_{19}H_{15}CIN_2O_4$

Molecular Weight: 370.8

Uses: Rebamipide is an amino acid analog used in the treatment of gastroduodenal ulcers.

Description: Rebamipide is white in color and amorphous powder.

Solubility Rebamipide is purely soluble in water and it's completely soluble in dimethyl formamide, dimethyl sulfoxide then slightly soluble in methanol and ethanol.

REVIEW OF LITERATURE

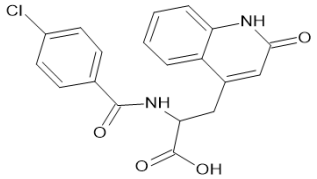
Literature review reveals that there are some analytical methods including high-performance thin-layer chromatography (HPTLC), High performance liquid chromatography (HPLC), and ultraviolet visible spectrophotometric methods using buffer systems are reported for the estimation of rebamipide[1-7] but still there is a lack of accurate, precise, economical zero order ultraviolet spectrophotometric process for rebamipide analysis in bulk and dosage forms. Many UV spectrophotometric methods are reported for other drugs in literature. [8-19]

MATERIALS AND METHOD

Materials

Standard drug with their suppliers

Rebamipide (Swapnroop Drugs and Pharmaceuticals Aurangabad, Maharashtra India.)



Rebamipide

Figure 1: Structure of rebamipide

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Tablet formulation

Brand name: Rebagen (Macleods), each film-coated tablet contains 100 mg of the drug

Reagent used

Dimethyl formamide, distilled water

Instrument used

A Shimadzu model UV-visible spectrophotometer UV-1900 with a 1-cm pair of quartz cells was used for the estimation.

Selection of media

Solubility and stability are the main criteria for media selection. In selected media drugs need be soluble as well and stable for enough time. For current work dimethyl formamide has been chosen as analytical solvent media.

Method

Selection of solvent

Dimethyl formamide was selected as a solvent because the drug was insoluble or sparingly soluble in other solvents.

Preparation of standard stock solution

A standard stock solution of rebamipide was prepared by dissolving accurately weighed quantities 10 mg Rebamipide in 10 mL of dimethyl formamide and relocated it to 10 mL volumetric flask. The content was adjusted with dimethyl formamide to get a stock solution of 1000 µg/mL.

Determination of measurement wavelength

After the preparation of a standard stock solution, the serial dilutions were prepared in the concentration range, i.e., 1, 3, 5, 7, and 9 µg/mL, and at an arbitrary concentration of 5 µg/mL solution was used to check the maximum wavelength of drug with dimethyl formamide solvent; more absorbance was obtained at 314 nm for first order with N = 3.

Linearity

Standard stock solution of rebamipide, relevant amount of solution was pipette out into 10 mL volumetric flask and dilution were made from dimethyl formamide that is 2000 µg/mL concentration solution to be working standard solutions of concentration 20, 50, 80, 110, 140, 170, and 200 µg/mL.

The range of concentration at which the drug's monitored linearity was preferred as a concentration range for analysis i.e., 20 to 200 µg/mL for rebamipide drug: (Table 1, Graph 1, Figures 1-3).

Table 1: Standard calibration table for Rebamipide

Sl. No	*Conc.(µg/mL)*	*Absorbance*
1.	20 µg/mL	0.008
2.	50 µg/mL	0.013
3.	80 µg/mL	0.020
4.	110 µg/mL	0.027
5.	140 µg/mL	0.034
6.	170 µg/mL	0.040
7.	200 µg/mL	0.047

Linearity Graph for Calibration of Rebamipide by First Order Derivative Method

Linearity graph for calibration of rebamipide is shown in Graph 1 and Figure 1.

Optical Parameters of the Calibration Curve

All the findings are consolidated and presented in the form of optical parameters are given in the Table 2.

Evaluation of Rebamipide from Dosage form (Tablet assay Study)

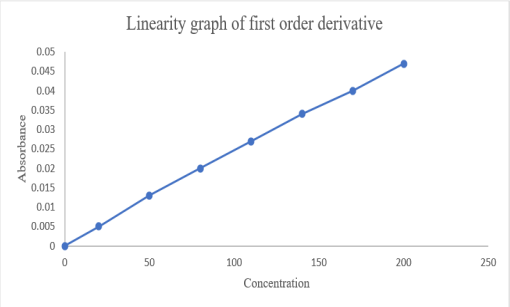
Standard stock solution is prepared by adding the 10 mg of Rebamipide drug into 10 mL of dimethyl formamide it means 1-mg/mL; then converted into a concentration of 1000 µg/mL. It is then converted into different concentrations like 20, 50, 80, 110, 140, 170, and 200 µg/mL, by using dimethyl formamide and it is scanned under 314 nm at N = 3. The results were found satisfactory.

Calibration of assay concludes that the absorbance is showing approximately the same and accurate as compared to the calibration of sample and all the concentrations of absorbance have linearity and the sample component contains many excipients but in the experiment of calibration of assay it does not harm in the result of absorbance

Recovery studies (Accuracy)

Recovery trials were used to gauge accuracy. Experiments with recovery were carried out by adding known amounts of powdered pure drug. The recovery was carried out at three levels of rebamipide standard concentration: 80, 100, and 120%.

For each accuracy level, three accuracy samples were created using the procedure outlined above. The percent recoveries were estimated using a formula after the solution was analyzed.



Graph 1: Linearity graph of first order derivative calibration curve for rebamipide

Table 2: Optical and regression parameters of the calibration curve

Parameters	*Results*
Measurement wavelength	314 nm
Slope	0.00213
Intercept	0.00222
Regression coefficient (r^2)	0.00227
Linearity range µg/mL	20–200 µg/mL

Figure 1: First-order spectrum of rebamipide for the concentration of 20 µg/mL

Figure 2: First-order spectrum of rebamipide for the concentration of 110 µg/mL

Figure 3: First-order spectrum of rebamipide for the concentration of 200 µg/mL

$$PERCENT\ RECOVERY = \frac{\text{OBSERVED QUANTITY OF DRUG ADDED IN SAMPLE}}{\text{QUANTITY OF ALL DRUG PRESENT IN SAMPLE}}$$

The recovery values are summarized in the discussion section.

Precision

Four independent samples of Rebamipide were carried out at four distinct times in the same laboratory to determine precision (inter-day). In the table, the precision values acquired four times were summarized in the discussion section.

RESULTS

The derivative spectra were acquired using a Shimadzu 1900 UV-visible spectrophotometer set to N = 4 and scanning standard solutions of rebamipide in dimethyl formamide (20 µg/mL each) from 300 to 375 nm at First order derivative. The greatest wavelength was determined to be 314 nm. At a wavelength of 314 nm, the plot of Rebamipide calibration curve was observed to be linear. At concentrations between 20 and 200 µg/mL, Beer's law was observed to be in operation. The most recent method was assessed and validated in accordance with international standards and requirements. The novel method for the quantitative investigation of rebamipide was subjected to a number of validation criteria, such as selectivity and specificity in the presence of excipients and formulation additives, linearity and range at various concentration levels, and calibration standards, where the determination range was optimized and accuracy was demonstrated through recovery studies at various concentration levels.

Table 3: Comparative statement of existing work and present work

S. No	*Research data*	*Present work*
1.	Work done on HPTLC Linearity range 100–600 Difference range in linearity is 100 Assay 100.58% is same as sample readings	I worked on UV Spectrophotometer Linearity range 20–200 µg/mL Difference graph in concentration is 30 µg/mL Assay 97.37% as same as sample readings
2	Work done on HPLC Concentration range between 10–500ng/ml Methanol as solvent Accuracy 95.93%	Worked on UV spectrophotometer Concentration range between 20–200 µg/mL dimethyl Formamide as solvent N = 3 Accuracy 100.003%
3	RP-HPLC used as an Instrument Potassium dihydrogen orthophosphate is used as a solvent Absorption maxima is 248nm by UV spectrum Accuracy is 100.23% Concentration range between 30–70 µg/mL	UV Spectrophotometer used as Instrument Dimethyl Formamide used as a solvent Absorption maxima is 314nm Accuracy is 100.003% N = 3 Concentration range between 20–200 µg/mL

DISCUSSION

Results from the approach were found to be suitable for Rebamipide in bulk and dosage forms, i.e., commercial tablet formulations for their first order derivative UV spectroscopy, with decreased standard deviation and coefficient of variation values within acceptable bounds. ICH criteria were used to validate the method for a number of metrics, including specificity, linearity, accuracy, precision, and repeatability. Because it only needs dimethyl formamide as a solvent and doesn't involve the use of expensive ingredients, this process is rather cheap. Pharmaceuticals containing rebamipide in bulk and tablet dose forms can be quantified without the interference of additives and with a significant and comparable level of accuracy and precision compared to other methods. The recently developed solution is less expensive than the ones that already exist (Table 3).

CONCLUSION

The experimental research suggests that a first order derivative has been developed for predicting rebamipide in pure dose form. The suggested approaches for a certain medicine were discovered to be exact and accurate. Conversely, this process is more reproducible. The outcomes and statistical traits demonstrate the simplicity, speed, accuracy, and precision of the proposed UV spectrophotometric technique. The spectrophotometric approach's most notable features are its speed and flexibility of use. These analytical methods are suitable for their intended purpose and meet ICH Q2/B requirements, according to the results of the validation parameters. The evaluation of the characteristics revealed the accuracy, precision, and sensitivity of UV spectrophotometric methods. The current UV spectrophotometric techniques can be used successfully for the quantitative analysis of rebamipide in pharmaceutical drug formulations for QC, where economy and time are crucial, as well as to ensure therapeutic efficacy, big props to their low cost and low maintenance. Such methods are preferred in small-scale industries.

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