RESEARCH ARTICLE

Validated Area Under Curve Quantitative UV Spectrophotometric Analysis of Rebamipide in Drug Formulations

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ABSTRACT

A very simple, accurately perfect, precisely repeatable procedure has been proposed for the estimate of rebamipide in medicines. Evaluation of previous works indicates the fact that, so far no UV spectrophotometric scheme for quantifiable estimate by area under curve technique for the drug rebamipide is not described. Therefore, there was a need to plan a different methodology to analyze the medicine employing dimethyl formamide in the form of solvent. This medication monitors Beer's law in the range of concentration 20 to 200 µg/mL in the ultraviolet range, particularly areas between 320 and 340 nm for are under curve because the absorption maximum was found to be 330 nm in the selected solvent. The recovery readings proved the offered technique's accuracy and outcomes were authenticated par accordance with the International Council for Harmonisation (ICH) references. The discoveries were reasoned to be consistent as well as agreeable. As a consequence, this optional technique was successfully used to estimate rebamipide quantitatively in conventional analytical applications.

Keywords: Rebamipide, Area under curve, Estimation, Analysis, UV spectrophotometric.

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INTRODUCTION

Drug: Rebamipide

Structure of Rebamipide 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 g/mole

Indications

Rebamipide is the analogue derivative of amino acids effective for the management of gastro-duodenal ulcerations.

Solubility

Rebamipide is partially aqueous solvable and absolutely soluble in dimethyl sulfoxide, dimethyl formamide, and marginally soluble in methyl alcohol and ethyl Alcohol.

Literature Survey

Analysis of past work discloses that nearly roundabout methods for analysis comprising high-performance thin layer chromatography (HPTLC), high-performance liquid chromatography (HPLC), UV spectrophotometric methods by means of buffer system are described for the estimate of rebamipide.[1-7] However, quietly, there is a deficiency of very accurate, highly precise, commercially economical spectrophotometric method by zero-order aimed at rebamipide determination of drugs in bulk and drug dosage formulations.[8-15] A lot of ultraviolet and visible spectrophotometric approaches are stated for former medications in past report writings.[16-19]

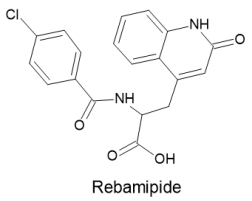

Figure 1: Structure of rebamipide

MATERIALS AND METHODS

Materials

API and its providers

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

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Tablet formulation

Trade name: Rebagen, manufactured by Macleods, film coated tablets containing 100 mg of rebamipide.

Reagents

Distilled water and dimethyl formamide.

Instrument

Shimadzu model UV-1900 UV-visible spectrophotometer with 1-cm matched quartz cells made use to carry determination.

Selection of solvent medium

Aqueous soluble ability and longer steadiness were core conditions required in the choice of medium. In the designated medium, drug must be solvable besides stable for a sufficient period. For the present work dimethyl formamide was selected as a methodical solvent medium.

Methods

Choice of solvent

Dimethyl formamide was carefully chosen medium as solvent since medicine was unsolvable, i.e., meanly solvable in tried solvent medium.

Preparing of normal stock solution

A typical store solution of rebamipide arranged by solubilizing correctly weighed measures of 10 mg API of rebamipide in 10 mL of dimethyl formamide and shifted into 10 mL volumetric flask. The volume was made up of dimethyl formamide for obtaining a store solution of 1000 µg/mL.

Determination of measurement wavelength

Subsequently, for preparing a typical stock store solution, sequential dilutes arranged within the ranges of concentrations: 1, 3, 5, 7 and 9 µg/mL and fixing a random strength of 5 µg/mL volume was employed to establish the maximum wavelength of absorption for rebamipide with dimethyl formamide as the solvent; peak absorbance was found at 330 nm with a smoothening factor of N = 3. The area between 320 and 340 nm was selected as a range for analytical area for measurement.

- *Linearity*

From the typical store solution of rebamipide, the appropriate volume of solution was pipetted into 10 mL volumetric flask and required dilutions completed from dimethyl formamide, specifically 2000 µg/mL strength solution selected as operational customary solutions of strengths 20, 50, 80, 110, 140, 170, and 200 µg/mL.

The concentration ranges where the drug's monitored linearity remained selected as an investigative concentration series, i.e., 20 to 200 µg/mL for rebamipide drug (Table 1, and Figures 2-5).

- *Photometric considerations for the calibration plot*

The optical parameters are given in the Table 2.

Assessment of drug content in dosage form (Tablet Assay)

Typical store solution equipped by the addition of 10 mg of rebamipide API into 10 mL volume dimethyl formamide, which means 1-mg/mL; then and there transformed into the strength 1000 µg/mL. This solution transformed as diverse concentrations of 20, 50, 80, 110, 140, 170 and 200 µg/mL, through dimethyl formamide and examined in the area between 320 to 340 nm at N = 3. The outcomes were established to be agreeable.

The conclusion of calibration and assays confirms that the absorbance display is almost identical plus perfectly matched to the standardization model and entire concentrations and absorbance readings following linearity as well as model constituent contains various additive excipients nonetheless then in the experimentation of tuning and assays it doesn't detriment outcome of absorbances.

- *Accuracy reviews (Recovery)*

Recovery observations were performed to decide the level of accuracy. Experimentations for recovery were performed by adding identified quantities of grounded API. This recovery

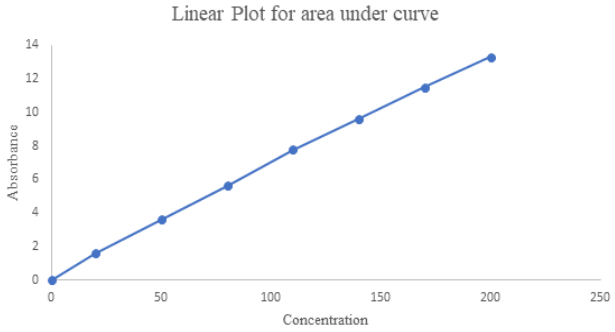

Figure 2: Linearity graph of area under curve calibration plot for rebamipide

Table 1: Typical calibration table for AUC

S. No	*Concentration (µg/mL)*	*AUC*
1.	20	2.171
2.	50	3.602
3.	80	5.619
4.	110	7.784
5.	140	9.604
6.	170	11.501
7.	200	13.291

Table 2: Optimum and regression limits of the calibration curve

Parameters	*Results*
Analytical wavelength (nm)	330
Measurement area (nm)	320–340
Slope	0.0645
Intercept	0.4473
Regression coefficient (r^2)	6.6634
Linearity range (µg/mL)	20–200

Figure 3: AUC curve of rebamipide for concentration of 20 µg/mL

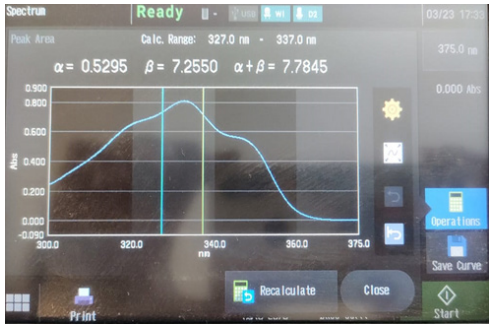

Figure 4: AUC curve of rebamipide for concentration of 110 µg/mL

Figure 5: AUC curve of rebamipide for concentration of 200 µg/mL

study was executed at three different levels of rebamipide customary concentrations: confidence levels of 80, 100, and 120%.

For every level of accuracy, three accuracy trials were carried out by the procedure delineated as before. The percentages of retrieval were assessed with a formula after the solution was analyzed.

$$PERCENTAGE\ RECOVERY = \frac{\text{OBSERVED QUANTITY OF DRUG IN TEST TRIAL}}{\text{QUANTITY OF EVERY COMPOUND INCLUDED IN TRIAL}}$$

Those recovery outcomes are given in the discussion segment.

- *Precision*

Four separate models of rebamipide were effected at four different periods at identical research labs for concluding precision studies for both intraday and inter-day. The precision standards attained in four spells were shortened in the discussion unit.

RESULTS

Firstly, zero-order spectra were assimilated by means of a Shimadzu 1900 UV-visible spectrophotometer where the smoothening factor was fixed as smoothening factor N = 4 and customary solutions containing rebamipide in the solvent dimethyl formamide (each of 20 µg/mL) scanned starting 300 nm till 375 nm at zero derivatives. The maximum absorption wavelength was resolute as 314 nm. In the area between the wavelengths of 320 to 340 nm, the calibration curve of rebamipide was established linear. At strengths of concentrations between 20 and 200 µg/mL, Beer's rule was perceived to be a straight line. This simple latest scheme was evaluated and authenticated in harmony with global criteria and needs. This unique technique for the quantifiable research on rebamipide was exposed to all different validation standards, for example, selectivity in addition to specificity in existence with a variety of formulation excipients, linearity as well as the range at several strength levels, and standardization criteria, wherever the resolving range was improved and correctness was confirmed and concluded recovery studies at a number of levels of application.

Table 3: Comparative report of prevailing work and proposed effort

S No	*Previous research statistics*	*Proposed work*
1.	Effort completed using HPTLC Linearity series 100–600 µg/mL Assay 100.58%	Present work by UV spectrophotometry Linearity series 20–200 µg/mL Assay 97.37%
2.	Reported using HPLC Quantification series amid 10–500 ng/mL Solvent system methyl alcohol Accuracy 95.93%	Work carried out by UV spectrophotometry Concentration range between 20–200 µg/mL Solvent system dimethyl formamide Area between 320 and 340 nm Accuracy 100.13%
3.	Instrument used RP-HPLC Buffer used potassium dihydrogen orthophosphate Detection wavelength is 248 nm by UV array Accuracy is 100.23% Quantification range amid 30–70 µg/mL	UV spectrophotometer used as instrument Solvent system dimethyl formamide Peak absorption is 330 nm Accuracy is 100.13% Area between 320 and 340 nm Concentration series amid 20–200 µg/mL

DISCUSSION

Outcomes of the methodology found appropriate to determine rebamipide quantitatively in API as well as dosage formulations, i.e., marketable tablet forms for the analysis by order derivative ultraviolet spectrophotometry, with lessened coefficient of variation values and standard deviation data with tolerable constraints. ICH benchmarks referred to authenticate the technique for quite a few metrics', comprising accuracy, precision, linearity, repeatability and specificity. Since the procedure needs only dimethyl formamide as the perfect solvent system, it does not implicate the usage of costly components. Also, this procedure is relatively economical. Medications comprising rebamipide in API and tablet dosage formulations may be computed deprived of the intervention of additional excipients and through a noteworthy and equivalent level of accurate and precise data associated to former approaches. In comparison with techniques developed in recent times, solvent systems is less costly than those that were previously used (Table 3).

CONCLUSION

This present investigational study proposes an area under the curve method, which is established for calculating the amount of rebamipide in API and dosage formulations. The recommended methodologies for a definite medication are revealed to be accurate and meticulous. On the other hand, this procedure is further reproducible. These decisions and statistical outcomes prove the easiness, rapidity, accuracy, and precision of the offered UV spectroscopic area under curve procedure. The spectroscopic methodology's utmost prominent features are its speediness and suppleness of usage. This analytical scheme is appropriate for its proposed persistence and passes ICH Q2/B necessities, agreeing with outcomes of the authentication considerations. Assessment of the parameters showed the sensitivity, accuracy with precision of present area under curve (AUC)-UV spectroscopic approaches. Present AUC-UV spectroscopic procedure may be carried out effectively for the quantifiable investigation of Rebamipide in medication preparations for Quality Control, wherever economy and time are vital, in addition to guaranteeing the therapeutic efficiency vast advantage of their economic besides lower conservation. These techniques remain ideal now in small-scale industrial establishments.

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