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: $C_{19}H_{15}ClN_2O_4$

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 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.

MATERIALS AND METHOD

Materials

Standard drug with their suppliers
Rebamipide (Swapnoop Drugs and Pharmaceuticals Aurangabad, Maharashtra India.)

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.

RESEARCH ARTICLE

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

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Figure 1: Structure of rebamipide
**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**

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Conc. (µg/mL)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>20 µg/mL</td>
<td>0.008</td>
</tr>
<tr>
<td>2.</td>
<td>50 µg/mL</td>
<td>0.013</td>
</tr>
<tr>
<td>3.</td>
<td>80 µg/mL</td>
<td>0.020</td>
</tr>
<tr>
<td>4.</td>
<td>110 µg/mL</td>
<td>0.027</td>
</tr>
<tr>
<td>5.</td>
<td>140 µg/mL</td>
<td>0.034</td>
</tr>
<tr>
<td>6.</td>
<td>170 µg/mL</td>
<td>0.040</td>
</tr>
<tr>
<td>7.</td>
<td>200 µg/mL</td>
<td>0.047</td>
</tr>
</tbody>
</table>

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

**Table 2: Optical and regression parameters of the calibration curve**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement wavelength</td>
<td>314 nm</td>
</tr>
<tr>
<td>Slope</td>
<td>0.00213</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.00222</td>
</tr>
<tr>
<td>Regression coefficient (r²)</td>
<td>0.00227</td>
</tr>
<tr>
<td>Linearity range µg/mL</td>
<td>20–200 µg/mL</td>
</tr>
</tbody>
</table>
Spectrophotometric Determination of Rebamipide

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.

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.

**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).

**Table 3: Comparative statement of existing work and present work**

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

**PERCENT RECOVERY** = \( \frac{\text{OBSERVED QUANTITY OF DRUG ADDED IN SAMPLE}}{\text{QUANTITY OF ALL DRUG PRESENT IN SAMPLE}} \)
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.

REFERENCES