Riluzole: Validation of Stability-Indicating HPLC, D1 and DD1 Spectrophotometric Assays

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A stability-indicating reversed-phase high-performance liquid chromatographic assay procedure has been developed and validated for riluzole in the presence of its oxidative degradation products. The liquid chromatographic separation was achieved and compared isocratically on C18 Zorbax ODS and Poroshell 120 EC-C18 columns by using a mobile phase containing methanol–water, pH = 3.10 (70:30, v/v), at a flow rate of 1 mL/min and ultraviolet detection at 264 nm. The method was linear over the concentration ranges of 20–200 μg/mL (r = 0.9997) and 10–200 μg/mL (r = 0.9995). The limit of detection and quantitation for the two columns were 2 and 6 μg/mL and 1 and 3 μg/mL, respectively.

Moreover, spectrophotometric methods were applied for the determination of riluzole in the presence of its oxidative degradation products by using first derivative spectrophotometry at 252.5 and 275.0 nm. The method was linear over the concentration range of 1–20 μg/mL (r = 0.9995 and 0.9996) at the studied wavelengths, with limits of detection and quantitation of 0.1 and 0.3 μg/mL. In addition, the first derivative ratio spectrophotometry (DD1) method was applied for the determination of riluzole in the presence of its alkaline degradation product at 252.0, 278.5 and 306.3 nm by using 100 μg/mL of alkaline degraded riluzole as a divisor; riluzole was additionally determined in the presence of its hydrogen peroxide oxidative degradation products at 252.5, 275.0 and 305.0 nm by using 200 μg/mL of oxidative degraded riluzole as a divisor. The DD1 method was linear over the concentration range of 1–20 μg/mL (r = 0.9996, 0.9995 and 0.9996 for the alkaline degradation product at the three studied wavelengths, respectively; and r = 0.9995, 0.9996 and 0.9995 for the oxidative degradation product at the three studied wavelengths, respectively), with limits of detection and quantitation of 0.1 and 0.3 μg/mL for both alkaline and oxidative degradation products. The two studied chromatographic and spectrophotometric methods were comparable and display the required accuracy, selectivity, sensitivity and precision to assay riluzole in bulk and pharmaceutical dosage forms. Degradation products resulting from the stress studies did not interfere with the detection of riluzole, which indicates that these are stability-indicating assays.

Introduction

Riluzole is an interesting drug that is used for treating several pathological conditions. It is chemically known as 2-amino-6-trifluoromethoxy benzothiazole (Figure 1). It acts as an antiglutamatergic agent. It is used in the treatment of several diseases such as Parkinson’s disease (PD) (1), amyotrophic lateral sclerosis (ALS) (2), ischemia (3) and multiple sclerosis (MS) (4). It is well absorbed (60% oral bioavailability) with peak plasma concentrations after 1–1.5 h and 96% plasma protein binding. High-fat meals decrease absorption and reduce the area under the concentration–time curve (AUC) by approximately 20% and peak blood levels by approximately 45%. In addition, riluzole enhances the anti-seizure action of conventional antiepileptic drugs like valproate, phenobarbital and ethosuximide against pentylenetetrazole-induced convulsions in mice (5).

Several methods have been reported for the determination of riluzole in a variety of matrices, such as rat brain (6) mouse plasma (7) and human plasma or serum (8). These methods were performed by using liquid chromatography–electrospray ionization tandem mass spectrometry (LC–ESI-MS-MS) (9) and spectrophotometry (10). Moreover, several methods of analysis have been reported for the determination of riluzole in bulk, dosage tablet formulations and human serum by spectrophotometric techniques (11), electrochemical and voltammetric analyses (12), densitometric analyses (13) and stability-indicating high-performance liquid chromatography (HPLC) methods (14, 15).

The aim of this work is to perform a comparative study between two chromatographic stability-indicating HPLC methods by using two stationary phases and two spectrophotometric first derivative (D1) and first derivative ratio (DD1) assays for the analysis of riluzole in the presence of its degradation products in bulk and tablet formulations.

Experimental

Chemicals and reagents

Riluzole standard bulk powder was obtained from Sanofi-Aventis (Paris, France). Rilutek, film-coated tablets containing 50 mg of riluzole, were also obtained from Sanofi-Aventis (Batch 8GN3E).

Methanol was obtained from Merck (Darmstadt, Germany). All chemicals were of analytical grade. Purified HPLC grade water was obtained by reverse osmosis, filtration through a Milli-Q system (Millipore Milford, MA) and used as a mobile phase.

Instrumentation and conditions

The HPLC unit was an Agilent 1100 series apparatus equipped with a quaternary pump, a vacuum degasser, a column oven, a diode array ultraviolet (UV) detector and HP Chemstation software. The columns were C18 Zorbax ODS (4.6 × 150 mm i.d., 5 μm) and Poroshell 120 EC-C18 (4.6 × 100 mm i.d., 2.7 μm) from Agilent Technologies (Palo Alto, CA). Separation was achieved by using a mobile phase consisting of methanol–water, pH = 3.10 (70:30, v/v), at a flow rate of 1 mL/min. The temperature of the columns was maintained at 20°C and an injection volume of 20 μL was used. The mobile phase was filtered through a 0.45 μm ChromTech Nylon-66 filter and degassed in.
an ultrasonic bath. For the analysis of forced degradation samples, the photodiode array detector was used in scan mode with a scan range of 200–500 nm. Peak homogeneity was expressed in terms of peak purity values, which were obtained directly from the spectral analysis report obtained with the instrument software. All absorption spectra and derivatives were recorded with a UV 1601 double beam spectrophotometer with 1 cm quartz cuvettes (Shimadzu Corporation, Kyoto, Japan).

**Preparation of stock and standard solutions**

A stock solution of riluzole (1 mg/mL) was prepared in HPLC-grade methanol. The stock solution was protected from light by using aluminum foil and stored for one week at 4°C; the solution was found to be stable during this period. In the HPLC assay, aliquots of the standard stock solution of riluzole were transferred into 25 mL volumetric flasks by using A-grade bulb pipettes, and the solutions were completed to volume with methanol to produce final concentrations of 20, 30, 50, 80, 100, 120, 150, 180 and 200 μg/mL.

In spectrophotometric assay, aliquots of the standard stock solution of riluzole were transferred into 10 mL volumetric flasks by using A-grade bulb pipettes and the solutions were completed to volume with methanol to produce final concentrations of 1, 2, 5, 8, 10, 12, 15, 18 and 20 μg/mL.

**Preparation of tablets for assay**

Five tablets were weighed and ground to a fine powder. A portion of the powdered tablets equivalent to 50 mg was accurately weighed into a 50 mL A-grade volumetric flask and 25 mL of methanol was added. The volumetric flask was sonicated for 20 min to ensure complete dissolution of riluzole. The solution was completed to the volume with methanol. Suitable aliquots of the solution were filtered through a 0.45 μm nylon filter and completed as previously described mentioned for both HPLC and spectrophotometric assays.

**Forced degradation studies of authentic riluzole and its tablet formulation**

To determine whether the proposed analytical methods are stability-indicating, riluzole tablets and powder were stressed under various conditions to conduct forced degradation studies, according to the regulatory guidance in International Conference on Harmonization (ICH) Q2B and Q3B and Food and Drug Administration (FDA) 21 CFR Section 211 (2003), which requires the development and validation of stability-indicating potency assays. Unfortunately, the current guidance documents did not indicate detailed degradation conditions that are based on trial and error. Because riluzole is practically soluble in methanol, it was used as a co-solvent in riluzole degradation studies.

**Oxidation**

Solutions for oxidation studies were prepared by dissolving 20 mg of authentic riluzole and powdered tablets containing the equivalent of 20 mg of riluzole in methanol–3% H2O2 (20:80%, v/v); these were protected from light and stored at room temperature for three days.

**Acid degradation studies**

Solutions for acid degradation studies were achieved by refluxing 50 mg of authentic riluzole and powdered tablets containing an equivalent to 50 mg of riluzole in 2M hydrochloric acid at 100°C in an oil bath for 24 h. The reaction mixture was neutralized with NaOH (10%) and extracted with ethyl acetate, dried (Na2SO4 anhydrous) and evaporated. The residue was dissolved in methanol (50 mL) and 2 mL was removed and diluted to 10 mL with methanol.

**Alkali degradation studies**

Solutions for alkali degradation studies were performed by refluxing 50 mg of authentic riluzole and powdered tablets containing an equivalent to 50 mg of riluzole in 1M sodium hydroxide at 100°C in an oil bath for 24 h. The alkaline degradation product was diluted with water and extracted with ethyl acetate (3 x 5 mL). The combined extracts were dried (anhydrous Na2SO4) and evaporated. The residue was dissolved in methanol (50 mL) and 2 mL was removed and diluted to 10 mL with methanol.

**Neutral degradation studies**

Solutions for neutral degradation studies were prepared in methanol and water (20:80%, v/v), protected from light and stored at room temperature for three days.

**Temperature stress studies**

Standard riluzole and its powdered tablets were exposed to dry heat (90°C) in an oven for three days.

**Photostability degradation assay**

Bulk riluzole powder, powdered tablets and methanolic solution were exposed to light to determine the effect of irradiation on the stability of riluzole in the solid state and solution form. Approximately 50 mg of standard riluzole powders were spread on a glass dish in a layer that was less than 2 mm in thickness. Solutions of standard riluzole powders (0.2 mg/mL) were prepared in methanol.

All samples for photostability testing were placed in a light cabinet (Thermolab, India) and exposed to light for 40 h, resulting in an overall illumination ≥ 200 Wh/m², at 25°C with UV radiation at 320.0–400.0 nm. Control samples, which were protected from light with aluminum foil, were also placed in the
light cabinet and concurrently exposed following removal from the light cabinet.

Results

HPLC method development and optimization were used for the separation and the method was validated for the determination of riluzole in bulk and in pharmaceutical dosage forms. The stressed samples were initially analyzed by using a mobile phase consisting of methanol–water, pH = 3.10 (70:30, v/v), at a flow rate of 1 mL/min with UV detection at 264 nm.

Validation

The methods were validated with respect to parameters such as linearity, limit of quantitation (LOQ), limit of detection (LOD), precision, accuracy, selectivity and recovery.

Linearity

The calibration curves constructed for riluzole were linear over the concentration ranges of 20–200 and 10–200 µg/mL using C18 Zorbax ODS and Poroshell 120 EC-C18 columns, respectively (Figure 2); peak areas of riluzole were plotted versus riluzole concentration and linear regression analysis was performed on the resultant curve.

Typically, the regression equations for the calibration curves were found to be:

\[ y = 0.0049x + 0.0125; r = 0.9997 \text{ using the C18 Zorbax ODS column;} \]
\[ y = 0.005x + 0.015; r = 0.9995 \text{ using the Poroshell 120 EC-C18 column} \]

where \( y \) is the area under the peak, \( x \) is the concentration in µg/mL and \( r \) is the correlation coefficient.

LOQ and LOD

The LOQ and LOD were determined based on signal-to-noise ratios. The LOQs were found to be 6 and 3 µg/mL with resultant relative standard deviations (RSDs) of 0.579 and 0.870% (\( n = 5 \)); the LODs were found to be 2 and 1 µg/mL using the C18 Zorbax ODS and Poroshell 120 EC-C18 columns, respectively.

Precision

The precision of the assay was investigated with respect to both repeatability and reproducibility. Repeatability was investigated by injecting nine replicate samples of the suggested concentrations, 40, 80 and 120 µg/mL of the standard; the mean concentrations were found to be 40.12, 80.42 and 120.62 with associated RSD values of 0.721, 0.654 and 0.492%, respectively, using the C18 Zorbax ODS column. For the Poroshell 120 EC-C18 column, the mean concentrations were found to be 40.24, 80.21 and 120.88 with associated RSD values of 0.532, 0.731 and 0.832%, respectively. The inter-day precision was assessed by injecting the samples with the previously mentioned concentrations on three consecutive days, resulting in mean concentrations of riluzole of 40.43, 80.63 and 120.74 µg/mL and associated RSDs of 0.832, 0.741 and 0.622%, respectively, when using C18 Zorbax ODS column. For the Poroshell 120 EC-C18 column, the mean concentrations were found to be 40.52, 80.32 and 120.91 with associated RSD values of 0.621, 0.922 and 0.881%, respectively. The ruggedness of the method and the RSD values were assessed by a comparison of the intra-day and inter-day assay results for riluzole that were performed by two analysts in the same laboratory. It was found that these did not exceed 3%, which indicated the ruggedness of the method. The retention time (\( R_t \)) of riluzole was 4.22 min with RSD of 0.732%.

Robustness

The robustness of the method and the RSD values were assessed by small changes in wavelength, 264.0 ± 2 nm, and temperature, 20 ± 1°C; RSDs were 1.264 and 0.941% for the C18 Zorbax ODS column and 0.296 and 0.412% for the Poroshell 120 EC-C18 column. Small changes in the wavelength and temperature showed no significant effect using the two columns, but RSD values indicate that the Poroshell 120 EC-C18 column possesses higher robustness than the C18 Zorbax ODS column.

Accuracy

The accuracy of the assay was determined by the interpolation of replicate (\( n = 6 \)) peak areas of three accuracy standards (40, 80 and 120 µg/mL) from a calibration curve, which was prepared as previously described. In each case, the percent relevant errors were calculated. The resultant concentrations when using the C18 Zorbax ODS column were 40.11 ± 0.010 µg/mL (mean ± SD), 80.32 ± 0.032 and 120.61 ± 0.051 µg/mL, with percent relevant errors of 0.352, 0.533 and 0.781%, respectively. The resultant concentrations when using the Poroshell 120 EC-C18 column were 40.08 ± 0.013 µg/mL (mean ± SD), 80.23 ± 0.022 and 120.33 ± 0.016 µg/mL, with percent relevant errors of 0.521, 0.732 and 0.432%, respectively. Small values of SD for both columns showed the high accuracy of the methods and no significant difference between the two columns.

Selectivity

The results of stress testing studies indicated that this method is highly selective for riluzole. The degradation of riluzole was found to be similar for both the tablets and bulk powder. Photodiode array detection was also used to determine the selectivity of the method and to evaluate the homogeneity of the drug peak. Chromatographic peak purity data were obtained from the spectral analysis report and a peak purity value greater than 0.999 indicated a homogenous peak. The peak purity values of riluzole in chromatograms of stressed samples were in the range of 0.999–1 for both the tablets and bulk powder, indicating homogenous peaks and establishing the selectivity of the assay method.

Recovery

A known amount of riluzole standard bulk powder was added to aliquots (\( n = 18 \)) of tablet contents and mixed, and the powder was extracted and diluted to yield a starting concentration of...
120 μg/mL. This solution was analyzed and the assay was repeated \((n = 9)\) over three consecutive days to obtain intermediate precision data. The observed concentration of riluzole for the C18 Zorbax ODS column was found to be 120.34 ± 0.342 μg/mL (mean ± SD). The RSD was 0.562% with a corresponding percentage recovery value of 100.33%. Also, the observed concentration of riluzole for the Poroshell 120 EC-C18 column was 119.80 ± 0.235 μg/mL with RSD of 0.722% and a corresponding percentage value of 99.92%.

**Stability studies**

All stressed samples in both solid states and solution forms remained colorless. No decomposition was observed upon exposure of riluzole to light, in solid and solution states, in a photo-stability chamber at room temperature. In acidic and neutral media, riluzole was stable and no degradation was observed under the studied conditions. On the other hand, it was found that approximately 90% degradation of the drug occurred in alkaline medium and approximately 33% was degraded after treating with 3% \(\text{H}_2\text{O}_2\) for three days by using C18 Zorbax ODS column. Additionally, 91% degradation of the drug occurred in alkaline medium and approximately 29% was degraded on treating with 3% \(\text{H}_2\text{O}_2\) for three days by using the Poroshell 120 EC-C18 column.

**Assay**

The proposed method was applied for the determination of riluzole tablet formulations. The results of these assays yielded 99.65% (RSD = 0.654%) and 99.80% (RSD = 0.724%) of the expected amount of the tablets when using the C18 Zorbax ODS and Poroshell 120 EC-C18 columns, respectively. These results indicated that the method is selective for the assay of riluzole without interference from the excipients used in the dosage forms.

**Discussion**

**Stability-indicating method for the analysis of riluzole in presence of its alkaline and oxidative hydrogen peroxide degraded products by HPLC**

Simple HPLC methods were adopted for the simultaneous determination of riluzole and its alkaline and oxidative hydrogen peroxide degraded products in bulk powder. To optimize the proposed HPLC methods, all of the experimental conditions were investigated by using C18 Zorbax ODS and Poroshell 120 EC-C18 columns.

To optimize the mobile phase, different systems were tried for chromatographic separation of the two components by combining homogenous design and solvent polarity optimization. The best resolution was achieved using a mobile phase consisting of methanol–water, \(\text{pH} = 3.1\) (70:30, v/v), which provided good resolution and sensitivity for all components.

A linear relationship was obtained between the peak area and the concentration of riluzole in the presence of its alkaline and oxidative hydrogen peroxide degraded products; these were found to be in the ranges of 20–200 μg/mL when using the C18 Zorbax ODS column and 10–200 μg/mL when using the
Poroshell 120 EC-C18 column. The linear regression equations were computed as:

$$y = 0.0049x + 0.0125; r = 0.9997$$ for the C18 Zorbax ODS column;
$$y = 0.005x + 0.015; r = 0.9995$$ for the C18 Zorbax ODS column

where $y$ is the area under the peak, $x$ is the concentration in $\mu g/mL$ and $r$ is the correlation coefficient.

Results obtained by applying the HPLC procedure showed that riluzole can be simultaneously analyzed in the presence of its alkaline and oxidative hydrogen peroxide degraded products, with mean recovery values of $100.45 \pm 0.767\%$ for the C18 Zorbax ODS column and $99.99 \pm 0.665\%$ for the Poroshell 120 EC-C18 column (Table I).

The proposed methods have been applied to the assay of riluzole in its tablet form without any interference from the excipients; results showed mean $\pm$ SD values of $99.65 \pm 0.652$ and $99.80 \pm 0.723$ when using the C18 Zorbax ODS and Poroshell 120 EC-C18 columns, respectively. The validity of the procedure was further assessed by applying the standard addition technique; results showed mean $\pm$ SD of $100.17 \pm 0.477$ and $100.45 \pm 0.455$ when using C18 Zorbax ODS and Poroshell 120 EC-C18 columns, respectively.

**Stability-indicating method for the analysis of riluzole in presence of its oxidative degradation products using H$_2$O$_2$ by D1 spectrophotometric method**

Overlapping of absorption spectra was observed for riluzole in the presence of its H$_2$O$_2$ degraded products. This overlapping was solved by the use of D1 spectrophotometry, as shown in Figure 3.

The obtained first derivative spectra were differentiated with respect to wavelength D1 values (Figures 4 and 5), which showed acceptable linearity and accuracy at 252.5 and 275.0 nm.

The linear regression equations were found to be:

$$y = 0.025x + 0.0213; r = 0.9995$$ at 252.5 nm;
$$y = -0.0309x - 0.0346; r = 0.9996$$ at 275 nm

where $y$ is the peak amplitude of the D1 value at 252.5 and 275.0 nm, $x$ is the concentration in $\mu g/mL$ and $r$ is the correlation coefficient. Results obtained by applying the D1 procedure showed that riluzole can be simultaneously analyzed in the presence of its H$_2$O$_2$ degraded products with mean recovery values of $99.72 \pm 0.448\%$ and $99.97 \pm 1.056\%$ at 252.5 and 275.0 nm, respectively (Table II).

Also, the proposed method was applied to the assay of riluzole in its tablet form without interference from the excipients; results showed mean $\pm$ SD of $100.21 \pm 1.229$ and $99.90 \pm 1.396$ at 252.5 and 275.0 nm, respectively.

### Table I

<table>
<thead>
<tr>
<th>HPLC with C18 Zorbax ODS column</th>
<th>HPLC with Poroshell 120 EC-C18 column</th>
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<tr>
<td><strong>Mean ± SD</strong></td>
<td><strong>100.45 ± 0.767</strong></td>
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</table>

Figure 3. Zero-order absorption spectra of riluzole (12 \mu g/mL) and its alkaline degraded (50 \mu g/mL) and hydrogen peroxide degraded (200 \mu g/mL) products in methanol.

Figure 4. First derivative spectra of riluzole (12 \mu g/mL) and its hydrogen peroxide degradation product (200 \mu g/mL).

Figure 5. First derivative spectra of riluzole (1–20 \mu g/mL) in methanol.
with respect to wavelength (Figure 6). DD1 values showed good linearity and accuracy at 252.0, 278.5 and 306.3 nm. The obtained first derivative ratio spectra were differentiated with respect to wavelength (Figure 6). DD1 values showed good linearity and accuracy at 252.0, 278.5 and 306.3 nm.

The linear regression equations were found to be:

\[ y = 0.0198x + 0.0113; \quad r = 0.9996 \text{ at } 252.0 \text{ nm}; \]
\[ y = -0.0223x - 0.0074; \quad r = 0.9995 \text{ at } 278.5 \text{ nm}; \]
\[ y = -0.0194x - 0.0116; \quad r = 0.9996 \text{ at } 306.3 \text{ nm} \]

where \( y \) is the peak amplitude of the DD1 value at 252.0, 278.5 and 306.3 nm, \( x \) is the concentration in \( \mu g/mL \) and \( r \) is the correlation coefficient. Results obtained by applying the DD1 procedure showed that riluzole can be simultaneously analyzed in the presence of its alkaline degraded products with mean recovery values of 100.19 ± 0.717, 100.10 ± 1.458 and 100.04 ± 0.748% at 252.0, 278.5 and 306.3 nm, respectively (Table II).

The proposed method was applied to the assay of riluzole in its tablet form without any interference from the excipients; results showed mean ± SD of 99.12 ± 0.448 and 99.97 ± 1.056 at 252.0, 278.5 and 306.3 nm, respectively.

**Stability-indicating method for the analysis of riluzole in presence of its alkaline degraded products by DD1 method**

The proposed method was applied to the assay of riluzole in its tablet form without any interference from the excipients; results showed mean ± SD of 99.12 ± 0.448 and 99.97 ± 1.056 at 252.0, 278.5 and 306.3 nm, respectively (Table II). The obtained first derivative ratio spectra were differentiated with respect to wavelength (Figure 6). DD1 values showed acceptable linearity and accuracy at 252.0, 275.0 and 305.0 nm.

The linear regression equations were found to be:

\[ y = 0.878x + 0.0676; \quad r = 0.9995 \text{ at } 252.5 \text{ nm}; \]
\[ y = -0.1125x - 0.1441; \quad r = 0.9996 \text{ at } 275.0 \text{ nm}; \]
\[ y = -0.335x - 0.0411; \quad r = 0.9995 \text{ at } 305.0 \text{ nm} \]

where \( y \) is the peak amplitude of the DD1 value at 252.5, 275.0 and 305.0 nm, \( x \) is the concentration in \( \mu g/mL \) and \( r \) is the correlation coefficient. Results obtained by applying the DD1 procedure showed that riluzole can be simultaneously analyzed in the presence of its oxidative degraded products with mean recovery values of 99.96 ± 0.532, 99.95 ± 0.705 and 99.96 ± 0.737% at 252.5, 275.0 and 305.0 nm, respectively (Table III). The proposed method was applied to the assay of riluzole in its tablet form without any interference from the excipients; results showed mean ± SD of 99.12 ± 0.448 and 99.97 ± 1.056 at 252.0, 278.5 and 306.3 nm, respectively.

**Stability-indicating method for the analysis of riluzole in presence of its oxidative degradation products by \( \text{H}_2\text{O}_2 \) by DD1 method**

The theory of derivative ratio spectrophotometry (16) was considered to solve the problem of overlapping absorption spectra of riluzole in the presence of its oxidative degraded products by \( \text{H}_2\text{O}_2 \) (Figure 3). Riluzole can be assayed in the presence of its oxidative degraded products by dividing the absorption spectra of different concentrations of riluzole in the range of 1–20 µg/mL by the absorption spectrum of 200 µg/mL of oxidative degraded riluzole.

The obtained first derivative ratio spectra were differentiated with respect to wavelength (Figure 6). DD1 values showed acceptable linearity and accuracy at 252.0, 275.0 and 305.0 nm.

The linear regression equations were found to be:

\[ y = 0.0194x - 0.0116; \quad r = 0.9996 \text{ at } 306.3 \text{ nm} \]
A statistical comparison of the results obtained by the proposed methods (HPLC, D1 and DD1 spectrophotometry) and the method described by Clarke (17), which depends on UV spectrophotometric determinations of riluzole in pure drug form, is shown in Tables V and VI. The calculated \( t \) and \( F \)-values were lower than the tabulated values (18), which revealed that there is no significant difference with respect to accuracy and precision determined through the assay of variables. Blind samples of pure riluzole of different concentrations were calculated from their regression equations. The repeatability was measured by analyzing each concentration of riluzole three times by the proposed methods and calculating the RSD. The results of the proposed methods showed that they are accurate, precise, specific and rugged, according to the RSD values of intra-day and inter-day determinations.

**Conclusion**
The two chromatographic and two spectrophotometric methods were comparable and showed the required accuracy, selectivity,
sensitivity and precision to assay riluzole in bulk and pharmaceutical dosage forms. The results of forced stress tests were undertaken according to ICH guidelines. Degradation products resulting from the stress studies did not interfere with the detection of riluzole, which indicates that these are stability-indicating assays.

The proposed methods are simple, accurate, precise, specific, and have the ability to separate the drug from its degradation products and tablet excipients. The proposed methods are suitable for the routine analysis of riluzole in either bulk powder or pharmaceutical dosage forms.

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