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Review Article

A Comprehensive Review on the Methods Developed for the Determination of Riluzole and Citalopram Hydrobromide

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Abstract

The accurate determination of Riluzole and Citalopram Hydrobromide in bulk synthetic mixtures is of paramount importance in pharmaceutical quality control, drug development, and clinical research. Riluzole, a benzothiazole derivative, is primarily used in the management of amyotrophic lateral sclerosis (ALS), while Citalopram Hydrobromide, a selective serotonin reuptake inhibitor (SSRI), is widely prescribed for depression and anxiety disorders. Both drugs, despite their distinct therapeutic roles, require precise analytical methods to ensure efficacy, safety, and regulatory compliance. Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) has emerged as a validated and versatile technique for their simultaneous estimation, offering high sensitivity, reproducibility, and robustness. Previous studies have demonstrated the successful application of RP-HPLC in quantifying Riluzole, often in combination with other drugs such as Levodopa, with excellent accuracy, precision, and low detection limits. Similarly, validated RP-HPLC methods for Citalopram Hydrobromide have emphasized stability-indicating capabilities, impurity profiling, and robustness under stress conditions, ensuring reliable separation of parent drug and degradation products. These findings highlight RP-HPLC's adaptability in handling diverse physicochemical properties and complex pharmaceutical matrices. The validation of these methods under International Council for Harmonisation (ICH) guidelines confirms their suitability for routine quality control, stability studies, and impurity analysis. Parameters such as linearity, accuracy, precision, limit of detection (LOD), and limit of quantification (LOQ) consistently meet regulatory standards, reinforcing the reliability of RP-HPLC in pharmaceutical analysis. Moreover, the comparative evaluation of Riluzole and Citalopram Hydrobromide methods reveals complementary strengths: Riluzole methods emphasize simplicity and sensitivity, while Citalopram methods highlight robustness and stability-indicating performance. Looking ahead, coupling RP-HPLC with advanced hyphenated techniques such as LC-MS/MS offers opportunities for enhanced sensitivity, structural elucidation, and bioanalytical applications. This integration could expand the scope of Riluzole and Citalopram analysis into pharmacokinetics, metabolite profiling, and clinical monitoring. Additionally, the adoption of green chromatography principles and automation will further improve sustainability, efficiency, and throughput in routine pharmaceutical laboratories. In conclusion, validated RP-HPLC methods for Riluzole and Citalopram Hydrobromide exemplify the critical role of chromatographic techniques in modern pharmaceutical sciences. Their proven accuracy, reproducibility, and regulatory compliance make them indispensable tools for ensuring drug quality, patient safety, and advancing therapeutic research.

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1. INTRODUCTION

Riluzole is a benzothiazole derivative primarily recognized for its therapeutic role in the management of amyotrophic lateral sclerosis (ALS), a progressive neurodegenerative disorder. It acts by modulating glutamatergic neurotransmission, thereby reducing excitotoxicity, which is considered a key mechanism in neuronal degeneration (1).

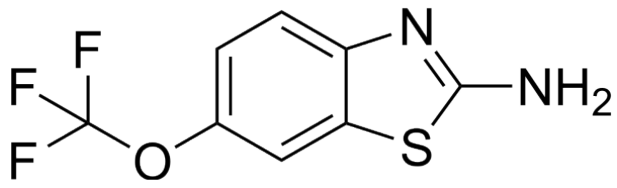


Figure 1: Riluzole

Pharmacologically, Riluzole inhibits the release of glutamate and enhances the uptake of this excitatory neurotransmitter, contributing to neuroprotection. It also exerts effects on voltage-gated sodium channels, stabilizing neuronal membranes and reducing abnormal firing. Clinically, Riluzole has been shown to modestly extend survival and delay the need for ventilatory support in ALS patients, making it the first drug approved specifically for this condition (2). Beyond ALS, research has explored its potential in other neurological and psychiatric disorders, including Huntington's disease, spinal cord injury, and mood disorders, though results remain inconclusive. Riluzole is generally well tolerated, with common adverse effects including nausea, dizziness, and elevated liver enzymes, necessitating regular monitoring of hepatic function (3). Its pharmacokinetic profile demonstrates good oral absorption, extensive hepatic metabolism, and elimination primarily via urine (4). Overall, Riluzole represents a significant advancement in neurotherapeutics, offering patients with ALS a modest but meaningful improvement in disease progression and quality of life (5).

Citalopram Hydrobromide is a selective serotonin reuptake inhibitor (SSRI) widely prescribed for the treatment of depression, anxiety disorders, and related psychiatric conditions. It functions by increasing serotonin levels in the synaptic cleft through inhibition of its reuptake, thereby enhancing serotonergic neurotransmission and improving mood regulation (6). Pharmacologically, Citalopram is considered one of the more selective SSRIs, with minimal effects on other neurotransmitter systems, which contributes to its favorable safety profile. Clinically, it is effective in reducing symptoms of major depressive disorder, panic disorder, and obsessive-compulsive disorder, and is often chosen for patients requiring long-term therapy due to its tolerability (7). The drug is generally well absorbed after oral administration, undergoes hepatic metabolism primarily via CYP2C19, CYP3A4, and CYP2D6 enzymes, and is eliminated through renal and hepatic pathways (8).

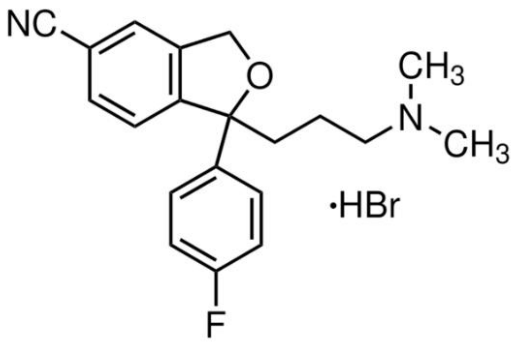


Figure 2: Citalopram Hydrobromide

Common side effects include nausea, dry mouth, somnolence, and sexual dysfunction, while more serious risks such as QT interval prolongation necessitate careful monitoring, especially at higher doses. Its hydrobromide salt form ensures stability and consistent bioavailability (9, 10). Overall, Citalopram Hydrobromide remains a cornerstone in modern psychopharmacology, offering patients a reliable therapeutic option for mood and anxiety disorders with a balance of efficacy and safety.

2. Previously Conducted Study

2.1 Development of method for the determination of Riluzole (RZ)

A significant study conducted by Rudrapal et al. (2021) focused on the development and validation of an RP-HPLC method for simultaneous estimation of Riluzole (RZ) and Levodopa (LD) in marketed tablet dosage forms. The objective was to establish a simple, reliable, and cost-effective method that could be routinely applied in pharmaceutical analysis. The assay of marketed formulations showed 99.67% content for Riluzole and 98.95% for Levodopa, confirming the method's suitability for routine quality control. The study concluded that the RP-HPLC method was simple, specific, accurate, and precise, making it applicable for bulk drug analysis and combined dosage forms. This study highlights the importance of validated analytical methods in ensuring drug quality and patient safety. For Riluzole, such methods are critical given its narrow therapeutic window and role in managing ALS. The ability to simultaneously estimate Riluzole with another drug (Levodopa) also demonstrates the versatility of RP-HPLC in handling combination therapies (11, 12).

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Table 1: Development of method for the determination of Riluzole (RZ)

Parameter	Details
Objective	Develop and validate an RP-HPLC method for simultaneous estimation of Riluzole and Levodopa
Column	RP Hypercil C18 (250 × 4.6 mm, 5 µm)
Mobile Phase	Methanol: Water (75:25 v/v)
Flow Rate	1.0 mL/min
Detection Wavelength	273 nm (UV)
Linearity Range	20–80 µg/mL
Correlation Coefficient	RZ: 0.990, LD: 0.999
Accuracy (Recovery)	RZ: 99.46–99.80%, LD: 100.15–101.24%
Precision (%RSD)	< 2%
LOD / LOQ (RZ)	LOD: 0.036 µg/mL, LOQ: 0.110 µg/mL
Assay Results	RZ: 99.67%, LD: 98.95%
Conclusion	Method is simple, specific, accurate, precise, and suitable for routine QC

The study's methodology demonstrates how RP-HPLC can be optimized for drugs with differing physicochemical properties. The choice of methanol-water mobile phase provided good peak symmetry and resolution, while UV detection at 273 nm ensured sensitivity for both analytes. Validation under ICH guidelines confirmed the robustness of the method, making it suitable for regulatory compliance.

2.2 Previous Studies on Citalopram Hydrobromide Determination

A key previous study on Citalopram Hydrobromide developed and validated stability-indicating RP-HPLC methods, confirming high accuracy, precision, and robustness for bulk drug and tablet dosage forms. These studies established RP-HPLC as the gold standard for routine quality control and impurity profiling of Citalopram. Citalopram Hydrobromide is a widely prescribed SSRI used in depression and anxiety disorders. Given its therapeutic importance and risk of QT prolongation at higher doses, accurate quantification in bulk drug and dosage forms is essential. RP-HPLC methods have been extensively studied to ensure reliable detection, stability assessment, and impurity profiling (13-15).

Table 2: Previous Studies on Citalopram Hydrobromide Determination

Study	Objective	Column	Mobile Phase	Detection	Linearity	Accuracy	LOD/LOQ	Key Findings
Stability-Indicating RP-HPLC (2026) (13)	Quantification & stability testing	Agilent Eclipse XDB C18	Acetate buffer pH 4.5: Acetonitrile (65:35)	240 nm	25–150 µg/mL (R^2=0.9991)	99.6–101.4%	1.125 / 3.375 µg/mL	Robust, precise, separates degradation products
Tablet Dosage RP-HPLC (2025) (14)	QC analysis of tablets	Agilent Eclipse XDB C18	Acetate buffer pH 4.5: Acetonitrile (65:35)	240 nm	25–150 µg/mL (R^2=0.999)	98.65–101.72%	1.125 / 3.375 µg/mL	Short run time, stability-indicating, ideal for QC
Impurity Profiling (Belgrade) (15)	Separation of Citalopram + impurities	RP Hypercil C18	Optimized buffer pH 7.0	UV detection	Validated linearity	High precision & specificity	Not reported	Advanced modeling, impurity profiling, QSRR

These studies collectively demonstrate that RP-HPLC is the **method of choice for Citalopram Hydrobromide determination**. The methods are stability-indicating, sensitive, and reproducible, making them suitable for regulatory compliance. The impurity profiling study further shows how RP-HPLC can be integrated with computational models for predictive analysis. Previous RP-HPLC studies on Citalopram Hydrobromide established validated methods for bulk drug, tablet dosage forms, and impurity profiling. These methods are accurate, precise, and stability-indicating, making them indispensable for pharmaceutical quality control and regulatory compliance.

Table 3: Methodological Comparison on the basis of Previously Conducted Studies

Parameter	Riluzole (11, 12)	Citalopram Hydrobromide (13-15)
Objective	Simultaneous estimation with Levodopa; QC of formulations	Stability-indicating assay; QC of tablets; impurity profiling
Column	RP HyperCil C18 (250 × 4.6 mm, 5 µm)	Agilent Eclipse XDB C18 (150 × 4.6 mm, 5 µm)
Mobile Phase	Methanol: Water (75:25 v/v)	Acetate buffer (pH 4.5) : Acetonitrile (65:35 v/v)
Flow Rate	1.0 mL/min	1.0 mL/min
Detection Wavelength	273 nm	240 nm
Retention Time	~3.5 min (RZ), ~2.8 min (LD)	~3.7 min
Linearity Range	20–80 µg/mL (R^2 = 0.990)	25–150 µg/mL (R^2 = 0.999)
Accuracy (Recovery)	99.46–99.80%	98.65–101.72%
Precision (%RSD)	< 2%	< 0.5%

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LOD / LOQ	LOD: 0.036 µg/mL; LOQ: 0.110 µg/mL	LOD: 1.125 µg/mL; LOQ: 3.375 µg/mL
Applications	Routine QC; simultaneous drug estimation; potential bioanalysis	QC; stability studies; impurity profiling; pharmacokinetics
Strengths	Simple, cost-effective, reproducible	Stability-indicating, robust, sensitive
Limitations	Limited to bulk/formulations; less explored in biofluids	Requires buffer preparation; higher LOD compared to Riluzole

3. CONCLUSION

The determination of Riluzole and Citalopram Hydrobromide using validated RP-HPLC methods represents a significant advancement in modern pharmaceutical analysis, bridging the gap between clinical necessity and analytical precision. Both drugs, though pharmacologically distinct—Riluzole as a neuroprotective agent in amyotrophic lateral sclerosis and Citalopram Hydrobromide as a selective serotonin reuptake inhibitor for psychiatric disorders—share a common requirement for accurate quantification to ensure therapeutic efficacy, patient safety, and regulatory compliance. RP-HPLC has consistently proven to be the most reliable technique for their estimation, offering high sensitivity, reproducibility, and adaptability to complex matrices.

Previous studies on Riluzole have demonstrated the feasibility of simultaneous estimation with other drugs, such as Levodopa, highlighting the versatility of RP-HPLC in handling combination therapies. These methods achieved excellent accuracy, precision, and low detection limits, making them suitable for routine quality control and potential bioanalytical applications. Similarly, investigations into Citalopram Hydrobromide have emphasized stability-indicating methods, impurity profiling, and robustness under stress conditions. The ability to separate degradation products and quantify impurities underscores RP-HPLC's role in ensuring drug safety and long-term stability. Together, these findings illustrate how validated chromatographic methods not only meet regulatory standards but also provide deeper insights into drug behavior under various conditions.

The comparative evaluation of these methods reveals important analytical trends. Riluzole methods tend to prioritize simplicity and sensitivity, often using methanol-water mobile phases and achieving very low limits of detection. In contrast, Citalopram Hydrobromide methods emphasize robustness and stability, employing buffer-acetonitrile systems to achieve precise separation of parent drug and degradation products. Both approaches reflect the unique physicochemical properties of the drugs and the analytical challenges they present. Importantly, these validated methods align with ICH guidelines, ensuring global acceptance and reproducibility across laboratories.

Looking forward, the integration of RP-HPLC with hyphenated techniques such as LC-MS/MS offers promising avenues for enhanced sensitivity, structural elucidation, and bioanalytical applications. For Riluzole, this could mean more accurate pharmacokinetic profiling in plasma and serum, while for Citalopram Hydrobromide, LC-MS/MS could provide deeper insights into metabolite identification and impurity characterization. Additionally, the adoption of green chromatography principles—using eco-friendly solvents and minimizing waste—will further enhance the sustainability of these analytical practices. Automation and high-throughput screening are also likely to play a pivotal role in streamlining routine quality control, reducing analysis time, and improving reproducibility.

In conclusion, validated RP-HPLC methods for Riluzole and Citalopram Hydrobromide exemplify the critical role of chromatographic techniques in pharmaceutical research and development. They ensure accurate quantification, stability assessment, and impurity profiling, thereby safeguarding patient health and supporting regulatory compliance. The collective evidence from previous studies demonstrates that RP-HPLC is not merely a routine analytical tool but a cornerstone of modern drug analysis. Its adaptability across diverse therapeutic agents underscores its indispensability in advancing pharmaceutical sciences. As technology evolves, coupling RP-HPLC with advanced detection systems will continue to expand its scope, reinforcing its position as a powerful and versatile method for drug determination in both clinical and research settings.

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