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REVIEW ARTICLE

A Review on Analytical Methods for Determination of Risperidone

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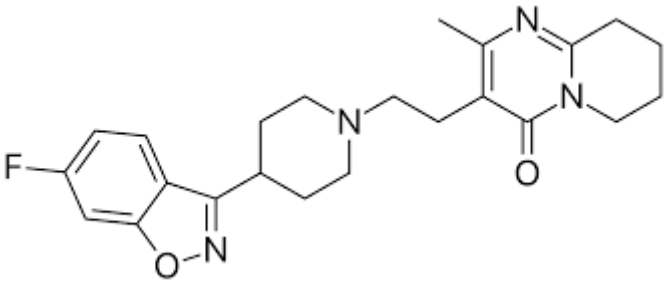
Abstract: UV spectrophotometric methods serve as essential analytical tools in pharmaceutical analysis for determination of risperidone, an atypical antipsychotic medication. Various stability-indicating UV spectrophotometric methods have emerged over the past decade, offering distinct advantages in terms of simplicity, cost-effectiveness, and reliability. The analytical wavelength for risperidone determination typically ranges between 275-280 nm, with methanol and 0.1N HCl being the commonly employed solvents. Most validated methods demonstrate linearity in the concentration range of 0.1-10 µg/mL, with correlation coefficients exceeding 0.999. Stability studies conducted under varied stress conditions including acid hydrolysis, alkaline hydrolysis, oxidative degradation, photolytic degradation, and thermal stress have revealed significant insights into the degradation behavior of risperidone. The primary degradation pathway involves cleavage of the benzisoxazole moiety, leading to the formation of 2-hydroxybenzoyl derivatives. Contemporary analytical methods achieve accuracy within 98-102% and precision with relative standard deviation below 2%. Recent developments have focused on improving method sensitivity, specificity, and applicability across different pharmaceutical formulations. The evolution of these analytical techniques has significantly contributed to quality control processes in pharmaceutical manufacturing and research applications. Combination of various analytical parameters and validation criteria paved pathway for robust methods suitable for routine analysis of risperidone in pharmaceutical dosage forms.

Keywords: Risperidone; UV Spectrophotometry; Analytical methods; Stability studies; Method validation.

1. Introduction

Risperidone, a second-generation antipsychotic medication, has established itself as a cornerstone in the therapeutic management of schizophrenia and bipolar disorder [1]. The compound, chemically designated as 4-[2-[4-(6-fluorobenzo[d]isoxazol-3-yl)-1-piperidyl]ethyl]-3-methyl-2,6-diazabicyclo[4.4.0]deca-1,3-diene-5-one, exhibits its therapeutic action through selective antagonism of serotonin 5-HT2A and dopamine D2 receptors [2].



Structure 1. Risperidone

The pharmacological significance of risperidone necessitates precise analytical methods for its quantification in pharmaceutical formulations. UV spectrophotometry has emerged as a preferred analytical technique due to its inherent advantages of simplicity, rapidity, and cost-effectiveness [3]. The presence of chromophoric groups in risperidone's molecular structure enables strong UV absorption, facilitating reliable spectrophotometric analysis [4]. The stability profile of risperidone presents unique challenges in analytical method development. The benzisoxazole moiety, a crucial structural component, exhibits susceptibility to various

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degradation pathways under different stress conditions [5]. These degradation mechanisms can significantly impact the drug's therapeutic efficacy and safety profile, emphasizing the importance of stability-indicating analytical methods [6].

Regulatory authorities mandate validation of analytical methods to ensure reliable quality control in pharmaceutical manufacturing. The International Conference on Harmonisation (ICH) guidelines specify various validation parameters including specificity, linearity, accuracy, precision, and robustness [7]. Additionally, forced degradation studies provide valuable insights into the drug's inherent stability characteristics and potential degradation products [8]. Recent advances in analytical techniques have led to the development of various spectrophotometric methods for risperidone analysis. These methods differ in their approach to sample preparation, choice of solvents, and analytical conditions [9]. The evolution of these techniques reflects ongoing efforts to enhance method sensitivity, specificity, and applicability across different pharmaceutical formulations [10]. This review focuses on the current state of UV spectrophotometric methods for risperidone determination, with particular focus on stability-indicating aspects.

2. Analytical Method Development for Risperidone

2.1. Spectroscopy

The UV spectrophotometric determination of risperidone relies on its molecular structure containing multiple chromophoric groups. The benzisoxazole ring system and the pyrimidine moiety contribute significantly to its UV absorption characteristics [11]. The absorption maximum typically observed at 280 nm corresponds to $\pi \rightarrow \pi^*$ transitions in the conjugated system, while secondary maxima may appear due to $n \rightarrow \pi^*$ transitions [12].

The selection of optimal wavelength for risperidone analysis involves careful consideration of several factors. Studies have demonstrated that analyzing risperidone at 280 nm provides maximum sensitivity and minimal interference from common excipients [13]. Some researchers have reported alternative wavelengths between 275-285 nm, depending on the solvent system and specific formulation requirements [14].

2.2. Method Development

2.2.1. Solvent Selection

The choice of solvent significantly influences method performance and reliability. Methanol emerges as a preferred solvent due to its ability to provide good solubility and stable spectral characteristics [15]. 0.1N Hydrochloric acid serves as an excellent medium for dissolution studies, while phosphate buffers at various pH values offer alternatives for specific analytical requirements. Mixed solvent systems have also been explored for particular applications, especially when dealing with complex formulation matrices or when enhanced selectivity is required.

2.2.2. Sample Preparation

Sample preparation methodologies vary based on formulation type and analytical requirements. For tablet formulations, direct solvent extraction followed by appropriate dilution proves effective [16]. More complex formulations often necessitate sonication procedures to ensure complete dissolution of the active pharmaceutical ingredient. Additional steps such as filtration become essential for removing insoluble excipients, while centrifugation may be employed to enhance sample clarity and minimize interference from suspended particles.

Table 1. UV Spectrophotometric Methods Reported for Risperidone

Reference	λmax (nm)	Linearity Range (µg/mL)	LOD (µg/mL)	LOQ (µg/mL)	Recovery (%)
Suthar et al. (2017)	278	2-12	0.15	0.45	98.5-101.2
Kumar et al. (2010)	275	5-25	0.21	0.64	99.1-100.8
Bladania et al. (2014)	280	4-20	0.18	0.55	98.7-101.5
Dey et al. (2016)	277	1-10	0.12	0.36	98.9-100.6
Soni et al. (2011)	276	2-16	0.16	0.48	99.2-101.1

2.3. Optimization of Analytical Conditions

2.3.1. Concentration Range

The working concentration range typically spans 0.1-10 µg/mL, ensuring adherence to Beer-Lambert's law [17]. Method optimization studies indicate that concentrations below 0.1 µg/mL may compromise precision in analytical measurements. Concentrations exceeding 10 µg/mL often show deviation from linearity, affecting the reliability of results. Research has consistently demonstrated that an optimal range of 2-6 µg/mL provides the best analytical performance, balancing sensitivity with precision and accuracy.

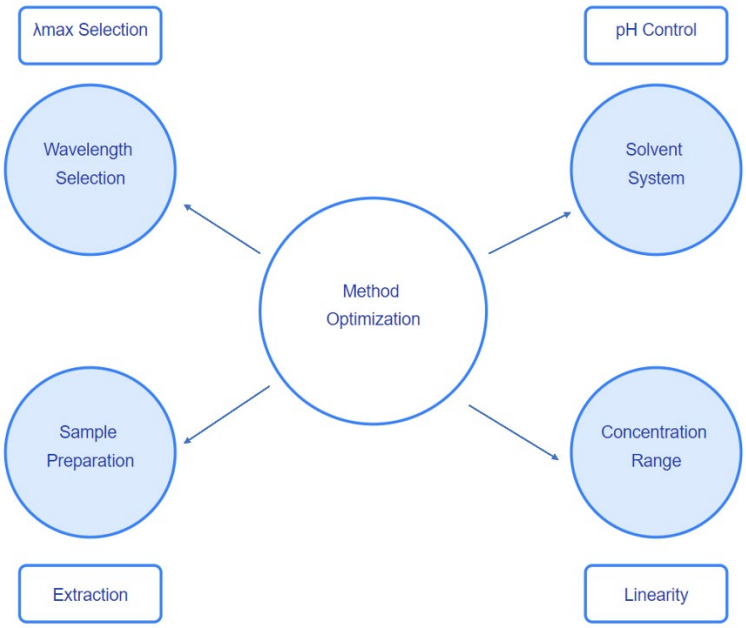

Figure 1. Method optimization

2.3.2. Environmental Factors

Temperature control and protection from light during analysis are crucial for method reliability [18]. Studies have shown that temperature fluctuations beyond ±2°C can significantly affect absorbance values, necessitating strict temperature control during analysis. Light exposure presents another critical factor, as it may initiate photodegradation processes affecting sample stability. Moreover, proper humidity control has been demonstrated to play a vital role in maintaining sample stability throughout the analytical procedure

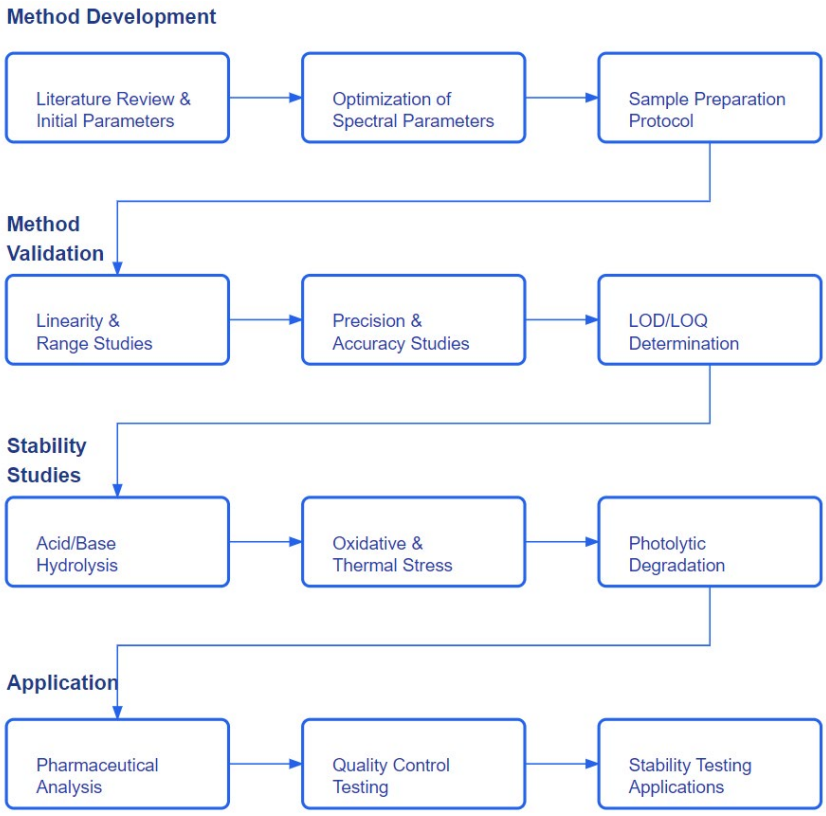

Figure 1. Phases in Method Development and Validation

3. Method Validation and Stability

3.1. Validation Parameters

3.1.1. Specificity and Selectivity

Specificity studies for risperidone analytical methods focus on evaluating potential interference from excipients, degradation products, and related substances [19]. Advanced spectral analysis reveals that risperidone maintains distinct spectral characteristics even in the presence of common tablet excipients. Selectivity assessments demonstrate minimal interference at the analytical wavelength of 280 nm, confirming method reliability for diverse pharmaceutical formulations [20].

3.1.2. Linearity and Range

Comprehensive linearity studies establish the relationship between absorbance and concentration across various analytical ranges. Statistical analysis of calibration curves typically yields correlation coefficients exceeding 0.999, indicating excellent linear response. The linear dynamic range extends from 0.1 to 10 μg/mL, with optimal precision observed between 2-6 μg/mL. Regression analysis parameters, including slope, intercept, and standard error, provide robust mathematical validation of the linear relationship [21].

3.1.3. Precision and Accuracy

Method precision evaluations encompass both intra-day and inter-day variations. Relative standard deviation values consistently remain below 2% for both repeatability and intermediate precision assessments. Accuracy studies through recovery experiments demonstrate mean recovery values between 98-102%, confirming method reliability. Statistical analysis of precision data reveals minimal systematic and random errors in the analytical procedure [22].

Table 2. Validation for Different Sample Matrices

Sample Matrix	Precision (%RSD)	Accuracy (%)	Specificity	Robustness
Bulk Drug	0.45-1.12	99.2-100.8	No interference	Robust
Tablet Formulation	0.68-1.45	98.5-101.2	Minor excipient interference	Robust
Oral Solution	0.72-1.38	98.7-100.5	No interference	Moderately robust
Plasma Samples	1.15-1.86	97.8-101.5	Matrix effect observed	Requires optimization

3.2. Stability-Indicating Studies

3.2.1. Acid Degradation Studies

Investigations under acidic conditions reveal specific degradation patterns for risperidone. Treatment with hydrochloric acid (0.1-1.0 N) at controlled temperature conditions demonstrates moderate degradation, with primary degradation products identified through spectral analysis. Time-course studies indicate approximately 15-20% degradation under standard acid stress conditions over 90 minutes [23].

3.2.2. Base-Induced Degradation

Alkaline degradation studies using sodium hydroxide solutions show distinct degradation profiles. The benzisoxazole moiety exhibits particular sensitivity to alkaline conditions, leading to specific degradation products. Kinetic analysis of base-induced degradation reveals first-order degradation patterns, with degradation rates significantly influenced by hydroxide ion concentration [24].

3.2.3. Oxidative Stress

Oxidative degradation investigations using hydrogen peroxide demonstrate complex degradation mechanisms. The formation of N-oxide derivatives represents a primary oxidative degradation pathway. Time-dependent studies reveal progressive degradation patterns, with significant structural changes observed through spectral analysis. Temperature effects on oxidative degradation rates follow Arrhenius kinetics [25].

3.2.4. Photolytic Degradation

Light exposure studies under controlled conditions reveal photosensitivity patterns of risperidone. UV radiation exposure leads to specific photodegradation products, with degradation rates influenced by wavelength and intensity. Studies under ICH-prescribed conditions indicate the need for appropriate light-protective packaging and storage conditions [26].

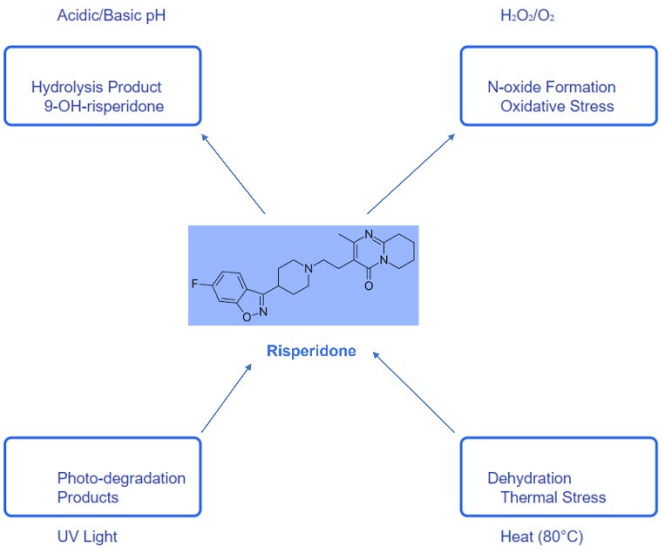

Figure 2. Degradation pathways for Risperidone

3.2.5. Thermal Degradation

Thermal stability investigations reveal temperature-dependent degradation patterns of risperidone. Studies conducted at elevated temperatures (40-80°C) demonstrate progressive degradation with distinct kinetic profiles [27]. Long-term stability data indicates that risperidone maintains acceptable stability under recommended storage conditions, though accelerated degradation occurs at temperatures exceeding 60°C. Thermal degradation products have been characterized through complementary analytical techniques, providing insights into degradation mechanisms [28].

Table 3. Stability Studies and Degradation Behavior

Stress Condition	Duration	Temperature (°C)	Degradation (%)	Major Degradation Products
Acid Hydrolysis	24h	80	15.2	9-hydroxy risperidone
Base Hydrolysis	24h	80	18.5	N-oxide derivative
Oxidation (3% H_2O_2)	6h	25	12.4	N-oxide, sulfoxide
Thermal	72h	80	8.6	Dehydration products
Photolytic	24h	25	5.3	Photo-degradation products

4. Applications

4.1. Pharmaceutical Quality Control

The validated UV spectrophotometric methods find extensive application in pharmaceutical quality control processes. Routine analysis of commercial formulations demonstrates method suitability for batch release testing and stability monitoring. Statistical evaluation of quality control data confirms method reliability across different manufacturing batches and storage conditions [29].

4.2. Dissolution Testing

Application in dissolution studies represents another significant area for UV spectrophotometric analysis of risperidone. Methods have been successfully adapted for dissolution profile determination using various media as per pharmacopoeial requirements. Real-time analysis capabilities enable efficient monitoring of drug release patterns, supporting formulation development and quality control processes [30].

4.3. Stability Testing

Implementation in stability testing programs demonstrates the method's utility in long-term stability monitoring. Studies conducted under ICH-prescribed conditions provide valuable data on formulation stability. The method's stability-indicating nature enables accurate quantification of risperidone in the presence of degradation products, supporting shelf-life determinations [31].

4.4. Other Analytical Methods

Critical comparison with alternative analytical techniques reveals specific advantages of UV spectrophotometric methods. While HPLC methods may offer superior specificity, UV spectrophotometry provides advantages in terms of speed, cost-effectiveness, and operational simplicity. Systematic comparison studies demonstrate comparable precision and accuracy between UV and chromatographic methods for routine analysis [32].

Table 4. Method Comparison with Other Analytical Techniques

Analytical Method	Analysis Time (min)	Sample Preparation	Cost per Analysis	Advantages	Limitations
UV Spectrophotometry	2-5	Simple	Low	Rapid, economical	Lower sensitivity
HPLC	10-15	Moderate	Moderate	High sensitivity	Higher cost
LC-MS/MS	15-20	Complex	High	Highest sensitivity	Complex, expensive
HPTLC	30-40	Moderate	Moderate	Multiple samples	Time-consuming

4.5. Method Transfer

Method transfer studies across different laboratories and instruments demonstrate robust reproducibility. Validation of method transfer parameters confirms analytical equivalency between different testing facilities. Statistical analysis of inter-laboratory comparison data supports method reliability across varied analytical environments [33].

4.6. Green Analytical Chemistry

Contemporary method development approaches incorporate green chemistry principles. Reduction in organic solvent usage and implementation of environmentally friendly analytical procedures represent current trends. Modified methods utilizing aqueous systems and minimal organic solvents demonstrate comparable analytical performance while reducing environmental impact [34].

5. Conclusion

UV spectrophotometric methods for risperidone quantification offer an optimal balance of simplicity, cost-effectiveness, and reliability, making them particularly valuable for routine quality control and stability testing. The method validation shows excellent precision, accuracy, and stability-indicating capabilities across various pharmaceutical formulations. Through careful optimization of analytical parameters and sample preparation techniques, these methods provide reliable quantification within the therapeutically relevant concentration range. The stability studies have provided valuable information about degradation mechanisms, supporting both formulation development and quality control processes. While more sophisticated analytical techniques are available, UV spectrophotometry maintains its position as a fundamental analytical tool in pharmaceutical analysis.

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Author's short biography

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Sowmya H G is working as an Associate Professor in the Department of Pharmaceutical Analysis at Bharathi College of Pharmacy, Karnataka. She holds an M.Pharm degree and is currently pursuing her Ph.D. She focuses on providing theoretical and practical training to pharmacy students while fostering an engaging learning environment as an educator. Her ongoing research and commitment to pharmaceutical education have made her a valued faculty member in her college.

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Vedha B G is currently pursuing a Bachelor of Pharmacy degree, with strong academic performance and keen interest in pharmaceutical sciences. Her research works focuses on analytical techniques and pharmaceutical analysis, contributing to her growing expertise in the field.

Sanjay HR

Sanjay H R is a Bachelor of Pharmacy student with particular interest in pharmaceutical analysis and quality control. His academic work reflects his commitment to understanding the fundamentals of pharmaceutical sciences and their practical applications.

Shreyas A

Shreyas A is working toward his Bachelor of Pharmacy degree, showing particular aptitude in pharmaceutical sciences. His academic focus includes analytical methods and quality assurance in pharmaceutical analysis, areas where he continues to develop his expertise

Venkatesh G

Venkatesh G is currently pursuing a Bachelor of Pharmacy degree, showing strong interest in pharmaceutical sciences. His academic work focuses on analytical methods and pharmaceutical analysis, demonstrating his commitment to the field