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Quantitative UV-spectrophotometry estimation of risperidone using hydrotropic solubilization phenomenon

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Abstract

The aim of present study was to develop simple and economical UV- Spectrophotometric method for estimation of Risperidone using Area Under Curve (AUC) technique with the application of hydrotropic solubilisation phenomenon. Aqueous urea solution (30% *v/v*) was used as a hydrotropic agent for solubilising risperidone. The method is based upon integration of area under curve for analysis of risperidone in the wavelength range of 265.0 - 287.40 nm. The drug followed linearity in the concentration range of 4 - 24 µg/mL with correlation coefficient value $r^2 > 0.99$. The proposed method was validated for accuracy, precision, repeatability and ruggedness as per ICH guidelines. The proposed method was applied for qualitative and quantitative estimation of risperidone in pharmaceutical formulation and results were found in good agreement with the label claimed. This developed method can be used for routine analysis of Risperidone in bulk and tablets.

Keywords: Risperidone; UV- Spectrophotometry - Area under Curve; UV-Spectrophotometry, Hydrotrophy

1. Introduction

Risperidone (RIS) is chemically 4-[2-[4-(6-fluorobenzo[d]isoxazol-3-yl)-1-piperidyl] ethyl]-3-methyl- 2,6-diazabicyclo[4.4.0]deca-1,3-dien-5-one [1]. It is an atypical antipsychotic drug which is mainly used to treat schizophrenia. It is a dopamine antagonist possessing anti-serotonergic, anti-adrenergic and anti- histaminergic properties. It is practically insoluble in water [2]. Several methods such as HPLC-MS/MS [3], RP-HPLC [4-6], HPTLC [7] and UV-spectrophotometric [8] have been reported for the estimation of risperidone in bulk, pharmaceutical formulation and biological fluids. These all methods involve the use of organic solvents for solubilising the drug.

Hydrotropic agents are anionic organic salts which, at high concentrations, considerably enhance the aqueous solubility of poorly soluble solutes. Hydrotropy is a solubilization phenomenon whereby addition of large amount of second solute results in an increase in the aqueous solubility of another solute. However, the term has been used in the literature to designate non-micelle-forming substances, either liquids or solids, organic or inorganic, capable of solubilizing insoluble compounds [9, 10]. Hydrotropy is suggested to be superior to other solubilization method, such as miscibility, micellar solubilization, co-solvency and salting in, because the solvent character is independent of pH, has high selectivity and does not require emulsification.[11]

To our notice, so far no UV- spectrophotometric method using Area Under Curve (AUC) has been reported for the determination of risperidone in bulk and tablets.

Therefore, an attempt has been made to develop UV- spectrophotometric method using Area Under Curve (AUC) technique with the application of hydrotropic solubilisation phenomenon for the determination of risperidone in bulk and tablets. Further, to validate developed method for accuracy, precision, repeatability, and ruggedness as per ICH guidelines [12].

2. Materials and Methods

2.1 Chemicals and Reagents

Risperidone working standards were obtained as generous gifts from Wockhardt ltd. Aurangabad, India. Urea (A.R. Grade) was purchased from Merck Ltd., Worli, Mumbai, India. Tablets **(RESPIDON)** was purchased from local market, containing RIS 4 mg per tablet.

2.2 Instrumentation

For proposed UV- Spectrophotometry method, UV-Visible spectrophotometer (Shimadzu 2450 with UV Probe 2.21 software) and a pair of 1 cm matched quartz cells were used.

2.3 Preparation of stock Standard Solutions

As risperidone is practically insoluble in water; urea is used as hydrotropic agent for enhancing the solubility of drug in water.

Stock standard solution of 100 µg/ml of risperidone was prepared in aqueous urea solution (30 % *v/v*). The working standards were prepared by dilution of the stock standard solution.

2.4 UV - Spectrophotometry Method using AUC Technique:

It involves the calculation of integrated value of absorbance with respect to the wavelength between the two selected wavelengths λ1 and λ2. From the spectrum of risperidone, the AUC in the wavelengths between 265 - 287.40 nm was selected for the analysis.

2.5 Linearity studies

An appropriate volumes of risperidone in the range of 0.4 – 2.4 mL were transferred into series of six separate 10 mL volumetric flasks and volume was made up to mark with 30 % aqueous urea solution to get concentrations in the range of 04 – 24 µg/mL. The AUC between the wavelength ranges of 265 - 287.40 nm was measured and calibration curves were plotted as concentrations *versus* AUC.

2.6 Analysis of Marketed Formulation

To determine the content of risperidone in marketed formulation (label claim: 4 mg risperidone per tablet); twenty tablets were accurately weighed, their mean weight determined and crushed into fine powder. A quantity of tablet powder equivalent to 10 mg of risperidone was transfer into 100 ml volumetric flask containing 50 mL of 30 % urea solution, sonicated for 15 min, volume was made up to the mark using same solvent and filtered through Whatmann filter paper No. 41. An appropriate volume was further diluted to 10 mL mark. The analysis was repeated for six times and determination were done using calibration curve. The results are shown in **Table 1**.

2.7 Validation of Method

The method was validated for accuracy, precision, sensitivity and ruggedness as per International conference on Harmonization (ICH) guidelines.

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2.7.1 Accuracy:

The accuracy of the proposed method was evaluated using recovery studies at three different levels i.e. 80%, 100% and 120%. To the pre-analyzed sample solutions (8 μg/mL), known amounts of stock standard solutions were added at different levels, the solutions were reanalyzed by the proposed method and area under curve was recorded at selected wavelengths. The experiments were repeated for three times.

2.7.2 Precision:

The precision of the method is studied as repeatability, intra-day and inter-day precision. Repeatability was determined by analyzing RIP (12 µg/mL) for six times.

Intra-day precision was determined by analyzing the 8, 12, and 16 µg/mL of risperidone for three times in the same day. Inter-day precision was determined by analyzing the same concentration of the solutions daily for three days.

2.7.3 Sensitivity:

The sensitivity of proposed method was estimated in terms of limit of detection (LOD) and limit of quantification (LOQ) which were calculated using formulae "LOQ = 10 ×N/B" and "LOD = 3.3 ×N/B," where "N" is standard deviation of the amplitudes or peak areas of the RIS (n = 3), taken as a measure of noise, and "B" is the slope of the corresponding calibration curve. For determining sensitivity different volume of stock solution in the range 4 - 8 µg/mL was prepared. The procedure was repeated in triplicate.

2.7.4 Ruggedness:

The ruggedness of the proposed method is determined by analysis of aliquots (12 µg/mL) from homogenous sample lots by two analyst using same operational and environmental conditions.

3. Results and Discussion

Risperidone is practically insoluble in water; therefore, 30% urea solution as hydrotropic agent was used for solubilisation of risperidone. There was no interference of urea solution in the estimation of risperidone in bulk as well as tablets. Risperidone obeyed linearity in the concentration range of 04 - 24 µg/mL, with correlation coefficient (r2 > 0.99). Marketed formulation was analyzed. The results showed good agreement between the amounts estimated, and those claimed on label. Percent label claims are very close to 100, with low values of standard deviation, % coefficient of variation, and standard error. The results are shown in **Table 1**. Precision was studied as repeatability (% RSD < 2) and inter and intra-day variations (%RSD < 2). The accuracy of method was determined by calculating mean percentage recovery. It was determined at 80,100 and 120 % level. The ruggedness of the methods was studied by two different analysts using the same operational and environmental conditions. The results for % recovery, precision, repeatability and ruggedness are shown in **Table 2**.

Table 1: Analysis of tablets

Drug	Amount taken (µg/mL)	Amount found ± S.D. (µg/mL)	%Amount found ± S.D.
RIS	12	11.92 ± 0.18	99.34 ± 1.56

Table 2: Summary of Validation parameters

Parameters	*Results*
Linearity (range)	04 - 24µg/mL
y = mx + C	Y = 0.1731x - 0.0166
Correlation coefficient	0.999
% Recovery (*n*=9)	99.37 – 99.75%
Precision (% R.S.D.)	
Intra-Day (*n*=9)	0.84 - 1.65
Inter-Day (*n* =9)	0.94 - 1.87
Repeatability (*n*=6)	0.87
Ruggedness (*n*=6)	
Analyst I	99.49 ± 1.31
Analyst II	99.47 ± 1.64

n= number of estimations

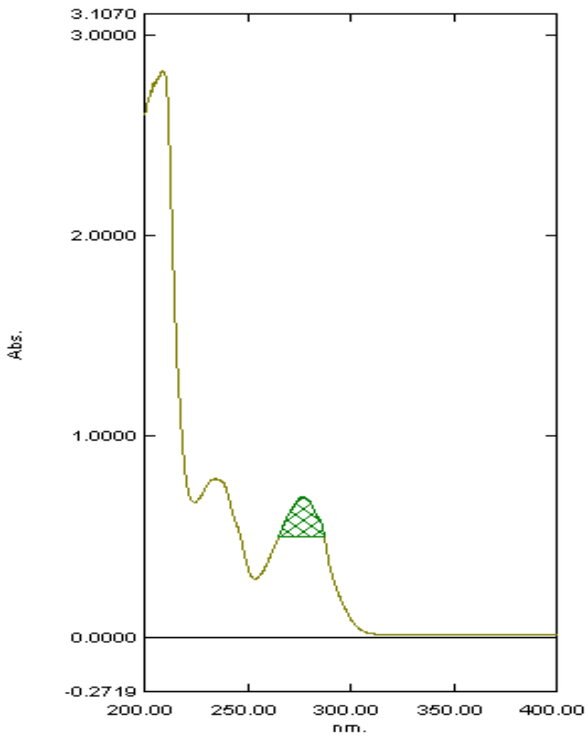

Fig. 1: UV- Spectrum of risperidone in 30 % *w/v* urea solution showing the selection of area under curve between 265 - 287.40 nm

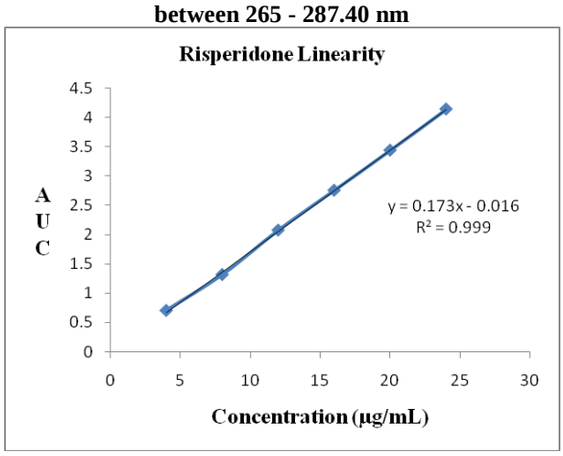

Figure 2: Linearity curve for Risperidone

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