

Spectrophotometric Estimation of Risperidone in Tablets

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Jayanna *et al.*: Spectrophotometric Estimation of Risperidone

A simple, rapid and highly sensitive spectrophotometric method is developed for the determination of risperidone in tablet formulation. The method is based on the oxidation of drug using potassium permanganate in alkaline medium and excess potassium permanganate oxidizes 1,10-phenanthroline Fe(II). The measurement of decrease in absorbance of 1,10-phenanthroline Fe (II) was done at 415 nm. The beer's law is obeyed in the concentration range of 5.0 to 40.0 µg/ml and molar absorptivity is found to be 7.3932×10^4 l/mol/cm. The proposed method is well suited for the pharmaceutical formulations.

Key words: Risperidone, potassium permanganate, 1,10-phenanthroline Fe (II), oxidation, tablets, spectrophotometry

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The commonly used analytical techniques for the determination of risperidone are differential pulse polarography^[1] chemiluminescence assay^[2], HPLC-MS/MS^[3], chiral chromatography^[4], LC-MS^[5], LC-tandem mass spectrometry^[6], LC with electrochemical detection^[7,8] LC with UV detection^[9], LC with coulometric detection^[10] and visible spectrophotometric method^[11]. Colorimetric determination of drugs using the ferric chloride assay is simple and rapid. However it offers relatively low resolution and cannot be used to determine total drug concentrations. The reddish orange color of 1,10-phenanthroline Fe (II) complex^[12] is extremely stable in acidic as well as in alkaline medium. Hence it is used in the present method. The aim of the present work is to develop simple method for the determination of risperidone in different dosage form. The proposed method stands atop over the reported method with respect to sensitivity and the method neither requires extraction nor prior separation of the drug.

Risperidone was received from Max India's Pharmaceutical Division, Nanjanagud, Mysore. Tablets Risperdal (risperidone; 2 mg/tablet) of Johnson and Johnson Limited, Mumbai, India and Rispond (risperidone; 3, 2, and 1 mg/tablet) of Micro Labs Limited, Bangalore, India were purchased from local market. Potassium permanganate and anhydrous potassium carbonate of Glaxo Ltd., Mumbai, India, 1,10-phenanthroline monohydrate of E. Merck, India and ferrous sulphate heptahydrate of S. D. Fine Chem., Mumbai, India were procured and were of analytical

grade. UV/Vis spectrophotometer with 10 mm matched quartz cells were used for absorbance measurement

Standard stock solution of risperidone (100 µg/ml) was prepared by dissolving 10 mg of risperidone in distilled water and diluted to 100 ml. Potassium permanganate (0.0012 mol/l) and potassium carbonate (0.1 mol/l) were prepared by dissolving 20 mg of potassium permanganate and 1383 mg of potassium carbonate, respectively in distilled water and diluted to 100 ml. 1,10-Phenanthroline Fe (II) sulphate prepared by dissolving 1500 mg of 1,10-phenanthroline monohydrate and 700 mg of ferrous sulphate in 100 ml water. 10 ml of this solution was diluted to 100 ml.

Different aliquots of the standard risperidone (05 to 40 µg/ml) were transferred into a series of 10 ml volumetric flasks. Warmed on a water bath for about 5 min and to each one of these flasks 1.0 ml potassium permanganate (0.0012 M) followed by 1.0 ml of potassium carbonate were added. Again warmed on a water bath for about 1 min and 0.5 ml of 1,10-phenanthroline Fe (II) was added. The volume was made up to 10 ml with water and mixed thoroughly. Absorbance of these solutions were measured at 415 nm making zero absorbance with distilled water.

The calibration curve was prepared by recommended procedure as shown in fig. 1. Linear relationships between absorbance and concentration held over range of 05 to 40 µg/ml and other parameters are given in Table 1. The high value of the correlation coefficient close to unity corroborates the linearity of the calibration plot. The high sensitivity of the method was indicated by the relatively high value of molar absorptivity and low values of Sandell's sensitivity.

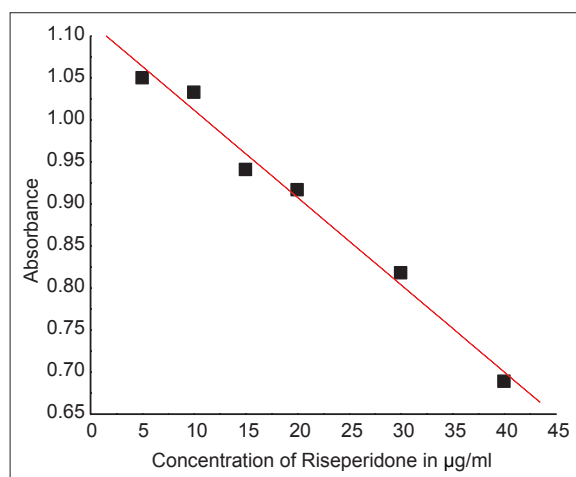


Fig. 1: Calibration graph of risperidone.

The calibration curve for risperidone was prepared and linear relationships between absorbance and concentration held over range of 5 to 40 µg/ml. Risperidone + warm on water bath (for 5 min) 1.0 ml KMnO_4 + 1.0 ml K_2CO_3 + warm on water bath (for 1 min) + 0.5 ml 1,10-phenanthroline Fe (II) + diluted to 10 ml.

TABLE 1: OPTICAL CHARACTERISTICS OF THE PROPOSED PROCEDURE

Parameters	Risperidone
λ_{max} , nm	415
Beer's limit (µg/ml)	10-55
Molar absorptivity ($\text{l mol}^{-1}\text{cm}^{-1}$)	7.3932×10^4
Sandel sensitivity ($\mu\text{g cm}^{-2}/0.001\text{A}$)	0.005521
Correlation coefficient	-0.99247
Regression equation	
Slope (b)	-0.01038
Intercept (a)	1.11565
Standard deviation	0.0186

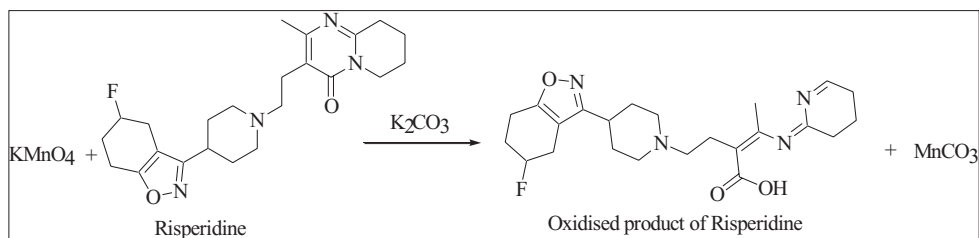


Fig. 2: Possible reaction scheme of the method.

Precision of the proposed method was described by performing repeatability within the day (intraday precision) and intermediate precision on different days (interday precision) in three replicates. Repeatability and intermediate precision was performed for three different concentrations 10, 20 and 30 μg . The amount, relative error percentage (% RE) and relative standard deviation (% RSD) were found to be 9.98, 0.2, 0.86, 20.05, 0.25, 1.45 and 30.15, 0.5, 1.23 and 10.05, 0.5, 1.57, 19.98, 0.1, 0.65 and 30.12, 0.4, 1.98, respectively. The low values of the relative standard deviation percentage and relative error percentage specify the high precision and the good accuracy of the proposed method.

The robustness of the method was estimated by making small incremental changes in volume of potassium carbonate and effect of change was studied on the absorbance of the colored system. Alter has no influence on results. Further robustness of the method is that it does not involve extraction. The Ruggedness of the method was illustrated for the same concentration 10 μg under instrument I (UV Spectrophotometer Model-117, Systronics) and instrument II (UV Spectrophotometer Model-1800, Hitachi) and by two analysts in the same laboratory. Amount and relative standard deviation in both instances were found to be 9.99, 0.55, 10.02, 1.76 and 9.96, 1.65, 9.98, 0.86. The low intermediate precision values (% RSD) in both instances indicating ruggedness of the method.

The effect of excipients was examined by determining 10 $\mu\text{g}/\text{ml}$ of risperidone in presence of different excipients such as starch, glucose, cellulose, lactose and talc at different concentrations present in tablet formulation. The results specify that there is no interference from any excipients because redox reaction takes place in weak alkaline medium. For the analysis of the formulation ten tablets of risperidone were weighed and finally powdered. The powder equivalent to 10 mg was weighed accurately

and dissolved in water. The residue was filtered into 100 ml volumetric flask. The residue was washed repeatedly with distilled water and washings were added to the filtrate. Final volume of filtrate was made up to the mark with distilled water and was analyzed according to the recommended procedure. The amount and relative standard deviation (%RSD) for the formulations Risperdal of 2 mg and Rispond of 1 mg, 2 mg and 3 mg were found to be 2.01, 0.18 and 1.04, 0.52, 2.05, 0.68 and 2.98, 0.3, respectively.

The method is based on the oxidation of risperidone with potassium permanganate in alkaline medium. The color of 1,10-phenanthroline Fe (II) decreases quantitatively in the presence of excess potassium permanganate and oxidized drug due to oxidation of Fe (II) to Fe (III). The possible reaction scheme of the method is shown in fig. 2. The color is stable for 5 h for the concentration of drug in the range of 5-20 $\mu\text{g}/\text{ml}$ and 1 h in the range of 25-40 $\mu\text{g}/\text{ml}$. It was reported in the previous work^[13] that absorbance was measured after 30 min of preparation of standard drug solution using potassium permanganate. In the present method absorbance was measured after the preparation of standard drug solution. The developed method is found to be simple, sensitive and accurate. The excipients present in the tablet dosage form did not hinder with the determination of risperidone. Hence, method can be used successfully for the determination of risperidone in tablet formulation.

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