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Research Article

Simple Cost Effective and Ecofriendly Spectrophotometric Method Development and Validation for Quantitative Estimation of Risperidone Using Hydrotropic Agent

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Abstract: The present work describes a novel, accurate, sensitive and economic safe spectrophotometric method was developed by application of hydrotropy, using 2M sodium benzoate solution as hydrotropic solubilizing agent, for the quantitative determination of poorly water soluble Risperidone in tablet dosage form. There were more than 48 times enhancements in the solubility of risperidone increases in hydrotropic solution as compared to solubilities in distilled water. Risperidone shows maximum absorbance at 234nm. 2M sodium benzoate and other tablets excipients did not show any absorbance above 220 nm and thus no interference in the estimation was seen. Risperidone was obeyed Beer,s law in the concentration range of 2 to 10µg/ml (r^2= 0.999) in hydrotropic solvent with mean recovery ranging from 99.04±0.258 to 99.82±0.105 %. Proposed method is new, simple, economic, safe, rapid, accurate and reproducible. The developed methods were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values. The method can be used for routine analysis in both research laboratories and pharmaceutical and chemical industries to analyze the drugs without the use of organic solvents thus make the environment eco-friendly.

Keywords: Risperidone, 2M sodium benzoate, Spectrophotometry, Eco-friendly, Hydrotropic.

INTRODUCTION

Risperidone (RIS) is belonging to the chemical class of benzisoxazole derivatives and chemically, it is 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 with molecular formula $C_{23}H_{27}FN_4O_2$ (Fig.1) (The Merck Index. 2001). Risperidone is official in BP 2007 (British Pharmacopoeia. 2007). Risperidone is atypical psychotropic agent and used as an antipsychotic for bipolar disorder, borderline personality disorder, drug intoxication, brief drug-induced psychosis and other schizophreniform and psychiatric disorder. Risperidone is mostly metabolized by alicyclic hydroxylation and oxidative *N*-dealkylation (Tripathi, K. D. 2013). Literature review for risperidone analysis revealed several methods based on different technique, such as; Visible spectrophotometric methods (Goyal, A., & Singhvi, I. 2008); HPLC with UV detection (Baldaniya, S. L. *et al.*, 2008); LC-MS and HPLC-ESI/MS assay for its quantification in plasma and serum (Huang, M.Z. *et al.*, 2008; Zhou, Z. *et al.*, 2004; Bartlett, M. G. *et al.*, 2007; Subbaiah, G. *et al.*, 2006); Chiral Chromatography (Danel, C. *et al.*, 2007); Pulse polarography (Joshi, A. *et al.*, 2006); Chemiluminescence assay (Song, Z., & Wang, C. 2004); LC with Coulometric Detection (Schatz, D.S., & Saria, A. 2000). However, there is no method reported for quantification of RIS in tablet dosage forms by hydrotropy. Hydrotropic solubilization is the phenomenon by which aqueous solubility of poorly water soluble drugs and insoluble drugs increases. Various techniques have been employed to enhance the aqueous solubility and hydrotropy is one of them. Sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate and sodium acetate are the most common examples of hydrotropic agents utilized to increase the water solubility of the drug. Maheshwari, R.K. (2005 and 2006) and Jain, N. *et al.*,

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(2010; 2011; 2011b; 2013; Jain, R. *et al.*, 2012; 2013a; 2013b; 2017; Jain, D.K. *et al.*, 2015; 2015b;) have analyzed various poorly water-soluble drugs using hydrotropic solubilization phenomenon for single drug or in combination viz. Frusemide, ketoprofen, amlodipine besylate, pramipexole dihyrochloride, olmesartan maedoxamil, lomefloxacin, furazolidone, entacapone, metronidazole & ofloxacin, ornidazole, tinidazole, metronidazole & furazolidone. Various organic solvents such as methanol, chloroform, dimethyl formamide and acetonitrile have been employed for solubilization of poorly water-soluble drugs to carry out spectrophotometric analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solution may be a proper choice to preclude the use of organic solvents. UV/VIS spectroscopy is an instrumental technique of choice for the mentioned purpose in industrial laboratories due to its simplicity and ease of operation. Therefore, it was thought worthwhile to employ this hydrotropic solution to extract out the drug from fine powder of tablets to carry out spectrophotometric estimation.

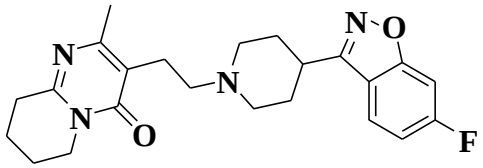

Figure 1 Chemical Structure of Risperidone

EXPERIMENTAL PROCEDURE

MATERIALS AND METHODS

Reference standard of RIS was a generous gift from Bioplus life science Pvt. Ltd. Bangalore., (India) sodium benzoate from Merck Chemical Division, Mumbai. Commercial tablets of RIS, was procured from the local drug market. Label claim of RIS in tablet is 2mg. Reverse Osmosis Water was used throughout the study. A Labindia 3000+ UV/VIS spectrophotometer with 1 cm matched quartz cells was used for the estimation.

Preliminary Solubility Studies

Solubility of RIS was determined in distilled water and hydrotropic solution of 2 M sodium benzoate solution at 25±1°C. There was more than 48 folds solubility enhancement in hydrotropic solution, as compare to distilled water. The enhancement of solubility is due to the hydrotropic solubilization phenomenon.

Preparation of Calibration Curve

Standard stock solutions were prepared by dissolving separately 100 mg of drug in 80 ml hydrotropic solution containing 2M sodium benzoate and the flask was sonicated for about 10 min to solubilize the drug and the volume was made up to the mark with hydrotropic agent to get a concentration of 1000µg/ml (Stock-A) for drug. Aliquots of 2.5 ml withdrawn with help of pipette from standard stock solution A of RIS and transferred into 25 ml volumetric flask separately and diluted up to 25 ml with RO Water that gave concentration of 100 µg/ml (Stock-B). Aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml and 1.0 ml withdrawn with help of pipette from standard stock solution (Stock-B) in 10 ml volumetric flask and volume was made up to 10 ml with RO Water. This gave the solutions of 2µg/ml, 4µg/ml, 6 µg/ml, 8µg/ml and 10µg/ml respectively for RIS. Spectral data shown in Table-1 and calibration curve in Fig 2 & 3.

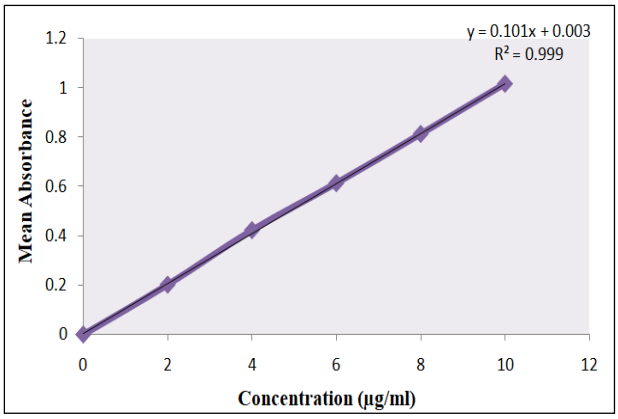

Figure 2Calibration Curve of RIS

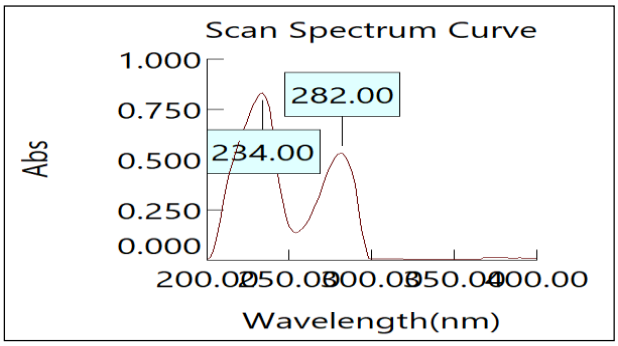

Figure 3 UV Spectra of Risperidone

Table 1: Optical Characteristic and Linearity Data of Risperidone

S. no.	Parameter	Risperidone
1	Working λ	234
2	Beer's Law Limit	2-10
3	Correlation Coefficient (r^2)*	0.999
4	Slope (m) *	0.101
5	Intercept (c)*	0.003
6	No of Sample (n)	15

*Average of five determination

Analysis of Tablet Formulation

Twenty marketed tablets of RIS was weighed and ground to a fine powder; amount equal to 2mg of RIS was taken in 10 ml volumetric flask. The RIS present in this amount of tablet powder was 2 mg. Then 4 ml of sodium benzoate solution was added and the flask was sonicated for about 10 min to solubilize the drug present in tablet powder and the volume was

made up to the mark with hydrotropic solution. After sonication filtration was done through Whatman filter paper No. 41. Filtrate was collected and further diluted with RO Water to get the final concentrations of both drugs in the working range. The absorbance's of final dilutions were observed at selected wavelengths and the concentrations were obtained from calibration curve method. The procedure was repeated for five times.

Linearity

Linearity of drug was established by response ratios of drugs. Response ratio of drug calculated by dividing the absorbance with respective concentration. Then a graph was plotted between concentration and response ratio.

Recovery Studies

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The recovery studies were carried out by adding known amount of standard solution of RIS to preanalysed tablet solutions. The resulting solutions were then re-analysed by proposed methods. Whole analysis procedure was repeated to find out the recovery of the added drug sample. This recovery analysis was repeated at 3 replicate of 5 concentrations levels.

Precision Studies

Precision of the methods was studied at three level as at repeatability, intermediate precision (Day to Day and analyst to analyst) and reproducibility. Repeatability was performed by analyzing same concentration of drugs for five times. Day to day was performed by analyzing 5 different concentration of the drug for three days in a week.

RESULT AND DISCUSSION

Based on the solubility and stability and spectral characteristics of the drug, 2M sodium benzoate was selected as hydrotropic agent. RIS after solubilized in the selected hydrotropic agent was scanned in spectrum mode and 234 nm was selected as wavelength for estimation considering the reproducibility and variability of the obtained result. The developed method was found to be linear in the range of 2 to 10µg/ml with correlation coefficient (r2) of 0.999 in sodium benzoate. The mean percent label claims of tablets of RIS in formulation estimated by the proposed method were found to be 97.50 to 98.90 in sodium benzoate. These values are close to 100, indicating the accuracy of the proposed analytical method. Low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method table 2. The values of mean percent recoveries were also found to be ranging from 99.04 to 99.82% in 2M sodium benzoate table 3. Result of precision at different level was found be within acceptable limits (RSD ‹ 2) table 4.

Table 2: Analysis of Tablet Formulation of RIS

Conc. Present (µg/ml)	Replicate-1		Replicate-2		Replicate-3	
	Conc. Found (µg/ml)	% Conc. Found	Conc. Found (µg/ml)	% Conc. Found	Conc. Found (µg/ml)	% Conc. Found
2	1.98	99.00	1.95	97.50	1.95	97.50
4	3.95	98.75	3.96	99.00	3.94	98.50
6	5.96	99.33	5.93	98.83	5.89	98.17
8	7.99	99.88	7.96	99.50	7.91	98.88
10	9.94	99.40	9.91	99.10	9.89	98.90

Table 3: Results of Recovery Studies on Marketed Formulations

Recovery Level %	% Recovery (Mean±SD)*
80	99.04±0.258
100	99.05±0.400
120	99.82±0.105

Table 4: Results of Precision (%R.S.D.)

PARAMETER		
Precision (%R.S.D.)*	Repeatability	0.033
	Day to Day	0.050
	Analyst to Analyst	0.033
	Reproducibility	0.071

*Average of five determination

CONCLUSION

It was, thus, concluded that the proposed method is new, simple, cost effective, accurately, precise, safe and free from pollution and can be successfully employed in the routine analysis of risperidone in bulk drug and tablet dosage forms. Presence of hydrotropic agent do not shows any significant interference in the spectrophotometric assay thus further confirming the applicability and reproducibility of the developed method.

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