The Pharma Innovation

ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

Received: 21-02-2013
Accepted: 29-03-2013

Vol. 2 No. 2 2013
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Difference Spectrophotometric Method for the Determination of Risperidone in Bulk and Tablet Dosage Form

Mrs. Sheeja Velayudhan Kutty[1], Dr. Yellinah Hari Babu[2], Greeshma S[3*], Vidhya P M[4]

1. Assistant professor, Department of Pharmaceutical Analysis, Grace College of Pharmacy, Kodunthirapully post, Palakkad, Kerala, India.
2. Principal and HOD Department of Pharmaceutical Analysis, Grace College of Pharmacy, Kodunthirapully post, Palakkad, Kerala, India.
3. Department of Pharmaceutical Analysis, Grace College of Pharmacy, Kodunthirapully post, Palakkad, Kerala, India.
   [Email: greeshmasivarajan@gmail.com]
4. Department of Pharmaceutical Analysis, Grace College of Pharmacy, Kodunthirapully post, Palakkad, Kerala, India.

The study aims to develop a simple, sensitive, rapid, accurate and precise difference spectrophotometric method for the determination of risperidone in bulk drug and tablet dosage form. In to two sets of 10 ml volumetric flasks, aliquots of standard drug solution (100µg/ml) in methanol were transferred and diluted the first set with 0.1N HCl and the other with 0.1N NaOH to get a concentration of 2-12 µg/ml for both the sets. Risperidone has exhibited maximum absorbance at about 239 nm and 277 nm in acidic and basic solution respectively. Beer's law was obeyed in the concentration range of 2-12µg/ml with a linear regression value 0.997. Interday and Intraday studies showed high degree of repeatability. Recoveries obtained do not differ significantly from 100% showed that there was no interference from the common excipients used in the tablet formulation indicating accuracy and reliability of the method

Keyword: Risperidone, Difference spectroscopy, Tablets, Validation

1. Introduction

Risperidone is psychotropic agent used to treat schizophrenia, action of which is mediated through a combination of dopamine Type 2 (D_2) and serotonin Type 2 ($5HT_2$) receptor antagonism. It is a selective monoaminergic antagonist with high affinity for $5HT_2$, D_2 and H_1 histaminergic receptors[1,2]. It belongs to chemical class of benzisoxazole derivatives and is 3-[2-[4-(6-fluoro-1, 2-benzisoxazol-3-yl)-1-piperidinyl] ethyl]-6, 7, 8, 9-tetrahydro-2-methyl-4H-pyrido- [1, 2-a]-pyrimidin-4-one(Fig.1)with molecular formula of $C_{23}H_{27}FN_4O_2$ and molecular weight of 410.49. [3]

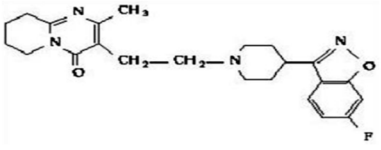

Fig1: chemical structure of Risperidone

Literature survey revealed that various methods have been reported for estimation of Risperidone in biological matrices such as plasma with help of LC / tandem mass spectrometry and by using MEPS-LC-UV method. [4, 5] Few stability-indicating methods have been reported for determination of Risperidone in bulk powder and tablets in presence of its degradation products. [6, 7] However very few methods were reported for quantitation of Risperidone in tablet dosage forms in the literature. [8, 9] The objective of the present investigations was to develop a simple, accurate and economical spectrophotometric method for estimation of Risperidone in tablet formulations. The method is free from interference when excipients are present. The essential features of a difference spectrophotometric assay are that the measured value is the difference in absorbance between two equimolar solutions of the analyte in different chemical forms, which exhibit different spectral characteristics. The simplest and most commonly employed technique for altering the spectral properties of analyte is the adjustment of the pH by means of aqueous solution of acids, alkali. [10]

2. Materials and Methods

A SHIMADZU model PHARMASPEC-1800 UV-Vis spectrophotometer with 1.0 cm matched cells was used for the electronic spectral measurements. Risperidone and all other chemicals used were analytical reagent grade. Risperidone pure drug was generously provided by Torrent Pharmaceuticals Pvt ltd (Ahmadabad, India), as a gift sample. The commercially available tablet "Risdone 2" (Intas Pharmaceuticals Dehradun) containing 2mg of Risperidone was procured from the local market. Freshly prepared 0.1 N sodium hydroxide, 0.1 N hydrochloric acid, methanol and distilled water were used in the present analysis.

2.1 Preparation of standard stock solution

The standard Risperidone 10mg was weighed accurately and transferred to volumetric flask (100 ml). It was dissolved properly in methanol and made up to the mark to get a concentration of 100µg/ml.

2.2 Preparation of working standard solution

Working standard solution was prepared by series of dilutions of 0.2 – 1.2 ml of standard stock solution to 10 ml with 0.1N HCl and 0.1N NaOH separately to get concentrations of 2-12µg/ml for Risperidone. These solutions were used to determine absorption maxima, Beer's law and linearity.

2.3 Determination of λ max

By appropriate dilution of two standard drug solutions with 0.1N HCl and 0.1N NaOH solutions containing 10 µg/ml of Risperidone was prepared and was scanned separately over the range of 400 to 200 nm against the reagent blank. From the spectrum obtained, the λ max was found to be 239 nm and 277 nm in acidic and basic solutions respectively. (fig 2, 3)

2.4 Procedure for calibration curve

Working standard solution was prepared to get concentrations of 2-12µg/ml separately using 0.1N HCl and 0.1N NaOH and the absorbance were measured at 239 nm and 277 nm in acidic and basic solutions respectively against reagent blank. Calibration curve was prepared by plotting concentration versus difference in absorbance and found to be linear in the concentration range of 2-12µg/ml. (fig 5, table 2)

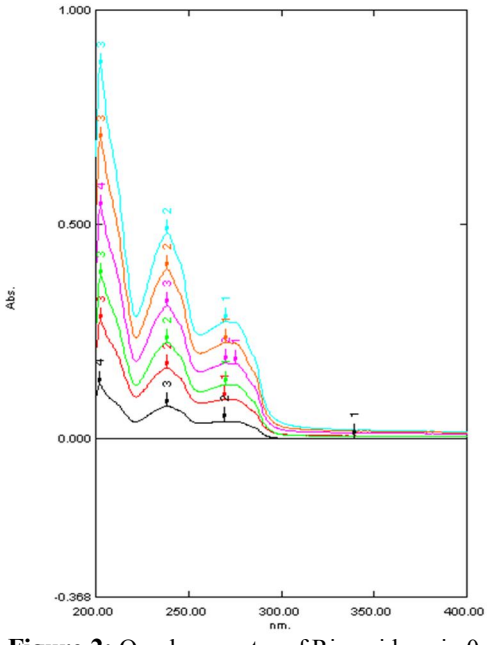

Figure 2: Overlay spectra of Risperidone in 0.1N HCl at 239 nm

3 Results and Discussion

The method was found to be simple, economical, selective and sensitive. The statistical parameters clearly indicate the reproducibility and accuracy of the method. Analysis of Risperidone in its dosage forms showed no interference from the common excipients and additives. Difference spectrophotometry by indicating pH of the medium may be recommended for routine and quality control analysis of the investigated drug in tablets.

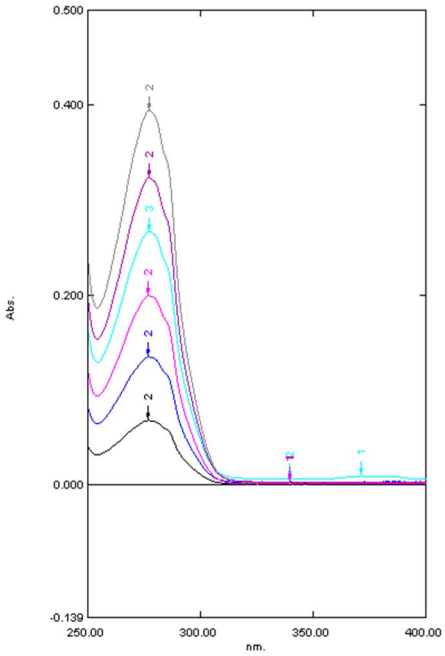

Figure 3: Overlay spectra of Risperidone in 0.1N NaOH at 277nm

3.1 Analysis of tablet formulation

Ten tablets were accurately weighed and triturate thoroughly to get fine powder. The powder equivalent to 10mg of Risperidone was weighed and transferred in to 100 ml volumetric flask. The contents of the flask were dissolved in the 50 ml of the methanol with the aid of ultrasonication for 10 minutes. The solution was filtered through Whatmann filter paper no.41 and volume was made up to 100ml with methanol. From the resultant solution, further dilutions were prepared with 0.1N HCl and 0.1N NaOH separately to get final concentration of Risperidone. The absorbance was measured at selected wavelengths and concentration of each analyte was determined with the equation obtained from calibration curve. (Table 1)

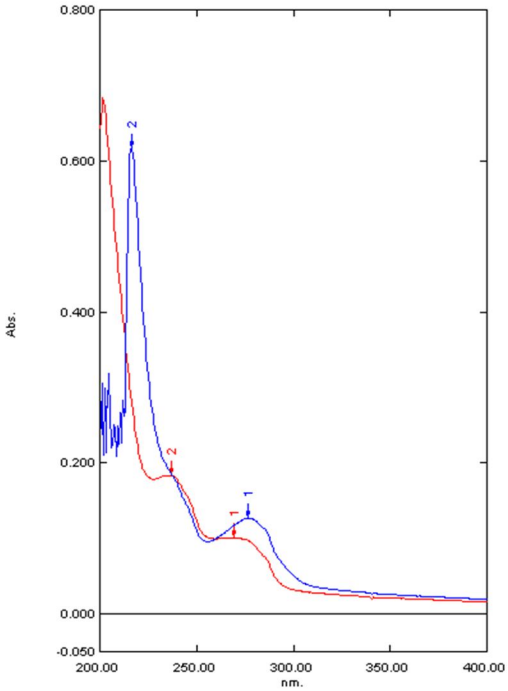

Figure 4: spectra of tablet formulation

Table 1: Analysis of marketed formulation

formulation	Label claim	Amount estimated	% Amount estimated	%RSD
Tab Risdon	2mg	1.9893mg	99.465	0.487

3.2 Method validation

Linearity

Working standard solution was prepared by series of dilutions of 0.2 – 1.2 ml of standard stock solution to 10 ml of 0.1N HCl and 0.1N NaOH separately to get concentrations of 2-12µg/ml for Risperidone. These solutions were scanned in the wavelength range of 400 – 200nm, and the absorbance was measured at 239 nm and 277 nm in acidic and basic solutions respectively against reagent blank. Calibration curve was prepared by plotting concentration versus difference in absorbance and found to be linear in the concentration range of 2-12µg/ml. (fig 5, table 2)

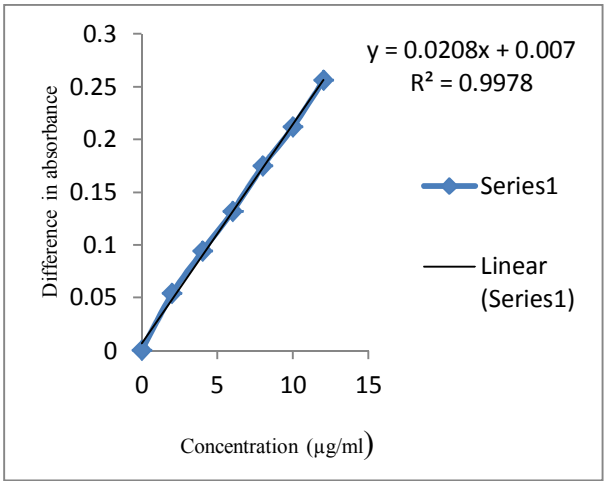

Fig 5: Linearity of Risperidone

Table: 2 Linearity of Risperidone by Difference spectrophotometry

Sl.no	Concentration of Risperidone (µg/ml)	Absorbance at 239nm (0.1N HCl)	Absorbance at 277nm (0.1N NaOH)	Difference in Absorbance
1	2	0.122	0.068	0.054
2	4	0.229	0.135	0.094
3	6	0.331	0.199	0.132
4	8	0.442	0.267	0.175
5	10	0.536	0.324	0.212
6	12	0.651	0.395	0.256

Precision

Precision of the method was determined by performing Interday variation, intraday variation and repeatability studies and expressed in the forms of %RSD. In Interday variation, the absorbances of working standard solutions of Risperidone (2-12 µg/ml) were measured on three consecutive days. In intraday variation the absorbance were measured three times a day. In repeatability study, six determinations of the fixed concentration of both acidic and basic solutions of the drug were analyzed separately. (Table 3)

Table 3: Precision data

	Fortified amount (µg/ml)	Amount found (µg/ml)	%RSD
Intraday (n=3)	4	3.89	1.07
	6	5.91	0.52
	8	7.96	0.61
Inter day (n=3)	4	3.98	0.48
	6	5.94	0.63
	8	7.82	0.61
Repeatability (n=6)	6	6.11	0.87

Accuracy (Recovery studies)

The accuracy of the proposed method was determined by calculating the recoveries of Risperidone by the standard addition method. It was determined by preparing solutions of different concentrations at 80%, 100% and 120% in which the amount of marketed formulation was kept constant and the amount of pure drug was varied. The amount of Risperidone was estimated by applying obtained values to the regression line equation. (Table 4)

LOD and LOQ

In this study, LOD and LOQ were based on the standard deviation of the response (σ) and the slope of the corresponding curve (S) using the following equation.

$$LOD = 3.3\sigma/S$$
$$LOQ = 10\sigma/S$$

Where σ is the standard deviation of the response of blank, S is the slope of calibration curve. (Table 5)

Table 4: Recovery Study

Level of addition (%)	Formulation (µg/ml)	Addition of pure drug (µg/ml)	% Recovery of pure drug	%RSD
80	10	8	99.53	0.064
100	10	10	99.0	0.066
120	10	12	100.60	0.331

Table 5: Validation parameters of Risperidone

Parameters	Values
λ max	239 nm (0.1N HCl) 277 nm (0.1N NaOH)
Linearity range	2-12µg/ml
Regression equation	Y= 0.020x+0.007
slope	0.020
intercept	0.007
Correlation coefficient	0.997
LOD	0.287µg/ml
LOQ	0.870µg/ml
Molar Absorptivity (mean)	228.18

4. Conclusions

Risperidone exhibits a substantial difference in absorbance in the two solvents that is in 0.1N HCl and 0.1N NaOH. So determination of Risperidone by difference spectrophotometry was attempted. Beer's law was obeyed in the concentration range of 2-12µg/ml with a linear regression value 0.997. Interday and Intraday studies showed high degree of repeatability of an analytical method under normal operating conditions. The %RSD for precision, which was less than 2% Indicates that the method is precise. Recoveries obtained do not differ significantly from 100% showed that there was no interference from the common excipients used in the tablet formulation indicating accuracy and reliability of the method.

5. Acknowledgment

We express our sincere thanks to Torrent pharmaceuticals private limited, Ahmadabad, India for providing the gift sample of Risperidone, and also we are grateful to the Principal and staffs of Grace College of Pharmacy, Kodunthirapully, Kerala, India for providing the facilities to carry out the present work.

2. References

1. Martindale the complete drug reference, thirty fifth edition volume 1 page no.921 – 922
2. K D Tripathi Essentials of medical pharmacology sixth edition page no. 167 – 429
3. The Merck Index, thirteenth edition compound no.8316, page no 1478
4. anickam Aravagiri and Stephen R. Marder Simultaneous determination of Risperidone and 9- hydroxyrisperidone in plasma by liquid chromatography/electro spray tandem mass spectrometry J. Mass Spectrum. 35, 718–724 (2000)
5. Roberto Mandrioli, Laura Mercolini, Domenica Lateana, Giancarlo Boncompagni, Maria Augusta raggi. Analysis of Risperidone and 9-hydroxy Risperidone in human plasma, urine and saliva by MEPS-LC-uv.jchromb.2010.11.033
6. P. Suthar, S. A. Dubey, S. R. Patel, A. M. Shah1. Determination of Risperidone and forced degradation behaviour by HPLC in tablet dosage form IJPRIF Vol.1, No.3, pp 568-574
7. Zarna R Dedania, Ronak R Dedania, Navin R sheth, jigar B Patel and bhavana Patel Stability Indicating HPLC Determination of Risperidone in Bulk Drug and Pharmaceutical Formulations international journal of analytical chemistry volume 2011
8. Kulkarni, S, Chhabra, G, Shivani, Method Development and validation of UV spectrophotometric method for the determination of Risperidone in bulk and tablets formulation.IJPCR Volume 1 Issue 1 2012
9. Moynul Hasan, Abdullh Al Masud and Jamiuddin Ahmed Development and validation of spectrophotometric method for the determination of Risperidone in bulk drug and pharmaceutical formulation IJPSR, 2011; Vol. 2(2): 378-382
10. AH Beckett, JB Stenlake practical pharmaceutical chemistry, fourth edition, part two, Page no 293-296

11. V. Amudhavalli, K. S. Lakshmi, Dheeraj Varma Kalidindi, Ramya Sree Surapaneni, Rudraraju S. R. K. Raju and Vamsi Kumar Pichikala Difference Spectrophotometric Estimation of Abacavir sulphate in Bulk and Tablet dosage form J. Chem. Pharm. Res., 2011, 3(3):119-122
12. Hapse S.A, Kadaskar P.T, Shirsath A.S Difference spectrophotometric estimation and validation of Ibuprofen from bulk and tablet dosage form Der Pharmacia Lettre, 2011, 3 (6):18-23.