IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
May 2018 Vol.:12, Issue:2

Spectrophotometric Method for the Determination of Risperidone in the Presence of Trihexyphenidyl HCl by Ion-Pair Complex Method Using Bromo Cresol Green

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

I. Lakshmi Prasanna*[1], G. T. Naidu[1], Nuzhath Fathima[2], I. E. Chakravarthy[2], G. Abdul Huq[3]

1. Department of Physics, Rayalaseema University, Kurnool.518007, AP.

2. Department of Chemistry, Rayalaseema University, Kurnool.518007, AP

3. Department of Chemistry,School of Sciences, Maulana Azad National Urdu University,Hyderabad, 500032,TS.

Submission: 22 April 2018
Accepted: 28 April 2018
Published: 31 May 2018

Keywords: Spectrophotometry, Risperidone, Trihexyphenidyl HCl, Ion-pair complex, Bromo Cresol Green, Pharmaceutical Formulations.

ABSTRACT

A simple, rapid, sensitive, accurate, precise and economical spectrophotometric method has been developed for the estimation of Risperidone in pharmaceutical formulations. During the course of study, it was observed that acidic solution of the drug formed colored ion-association complexes with Bromo Cresol Green (BCG) which is soluble in methanol. This property of the drug was followed for the development of a spectrophotometric method for analysis of drug. The complex of Risperidone with Bromo Cresol Green showed λ_{max} at 440 nm. The linearity range for Risperidone was 10 µg/ml -250 µg/ml. Recovery studies gave satisfactory results indicating that none of common additives and excipients interfere with the assay method.

HUMAN JOURNALS
www.ijppr.humanjournals.com

INTRODUCTION

Risperidone,3-[2-[4-(6-fluoro-1,2-benzisoxazole-3-yl)piperidin-1-yl]ethyl]-2-methyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one, is a benzisoxazole antipsychotic, reported to be an antagonist to dopamine D2 and serotonin (5HT2), adrenergic, and histamine (H1) receptors[1,2] . A few chromatographic methods have been reported in the literature for the analysis of risperidone in pharmaceutical preparations either alone, with its degradation products or with other compounds. Other techniques for the determination of Risperidone from pharmaceutical dosage form also have been reported.

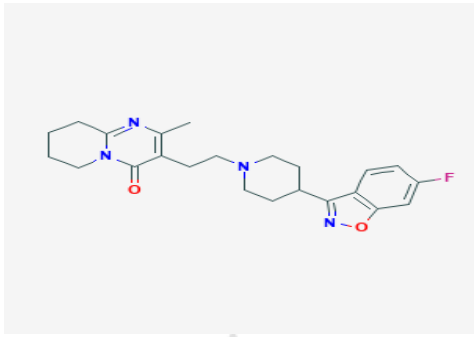

Fig: 1 Structure of Risperidone

These techniques include extractive colorimetry, chemiluminescence[3,4], capillary zone electrophoresis and non-aqueous titration. There are numerous methods to quantify Risperidone and 9-OH-Risperidone enantiomers[5-10] in biological fluids, including HPLC-DAD, HPLC with electrochemical detection, MEPS–LC–UV, LC-MS/MS and affinity capillary electrophoresis and H1 NMR spectroscopy. These methods are complicated, costly and time-consuming in comparison to a simple UV method.

Trihexyphenidyl HCl is used to treat symptoms of Parkinson's disease or involuntary movements due to the side effects of certain psychiatric drugs (antipsychotics such as chlorpromazine/haloperidol). Trihexyphenidyl HCl belongs to a class of medication called anticholinergics that work by blocking a certain natural substance (acetylcholine). This helps decrease muscle stiffness, sweating, and the production of saliva, and helps improve walking ability in people with Parkinson's disease. Anticholinergics can stop severe muscle spasms of the back, neck, and eyes that are sometimes caused by psychiatric drugs.

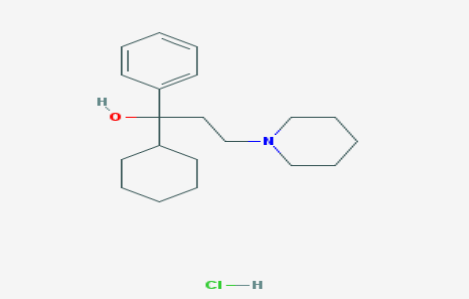

Fig:2 Structure of Trihexyphenidyl HCl

It can also decrease other side effects such as muscle stiffness/rigidity (extrapyramidal signs-EPS). Further, it is noticed that there are a very few methods reported on the development and validation of the estimation of Risperidone are which include High-Performance Liquid Chromatography (HPLC) methods[11-12]. Since not much attention has been given to developing newer analytical UV Spectrophotometric methods[13-14] for the quantitative determination of such an effective and potential drug in the dosage form and in the pharmaceutical formulations form, the authors are prompted to take up this study and develop suitable new, rapid, sensitive, precise and accurate method for the determination of Risperidone. The results obtained in the present investigations are communicated in this work.

MATERIALS AND METHODS

(A) Instruments used

(i) Spectrophotometer: A Single beam UV-Spectrophotometer Model SP-UV200 with 1 cm matched quartz cuvettes is employed throughout the study for all absorbance measurements.

(ii) pH Meter: A digital ELICO-pH Meter Model LI-120 is used for pH measurements.

(B) Preparation of Reagents and Solutions

(i) Risperidone solution: 50 mg of pure Risperidone is dissolved in methanol and the volume of the resulting solution is adjusted to the mark in the 50 ml standard flask with methanol. This is used as the stock solution of the drug. The working solution with concentration 100 µg/ml of the drug is prepared by suitably diluting the stock solution as and when required.

(ii) Trihexyphenidyl HCl solution: 50 mg of pure Trihexyphenidyl HCl is dissolved in methanol and the volume of the resulting solution is adjusted to the mark in the 50 ml

standard flask with methanol. This is used as the stock solution of the drug. The working solution with concentration 100 µg /ml of the drug is prepared by suitably diluting the stock solution as and when required.

(iii). Bromo Cresol Green solution (0.5% w/v): Bromo Cresol Green is prepared by dissolving 500 mg of Bromo Cresol Green in 100 ml of distilled water.

(iv) Buffer solution pH 3.5 (Potassium acid phthalate - HCl): The potassium acid phthalate – HCl Buffer solution is prepared by diluting a mixture of 50 ml of 0.2M potassium acid phthalate and 8.4 ml of 0.2M HCl to 200 ml with distilled water and the pH is adjusted to 3.5.

All other chemical substances and reagents employed in the present investigations are of AR Grade only.

RESULTS AND DISCUSSION

Risperidone in the presence of Trihexyphenidyl HCl, when treated with Bromo Cresol Green (BCG), forms a yellow colored Ion pair complex. This Ion-Pair complex formation reaction is spectrophotometrically monitored to develop a method for the determination of the purity of the drug. In this process, a detailed investigation is done to arrive at the optimization of various parameters such as wavelength of maximum absorbance (λ_{max}), the effect of concentration of buffer solution (pH 3.5) and Bromo Cresol Green on the absorbance of Ion Pair complex and the procedures adopted in each case are described as follows:

Absorption Spectrum of Ion Pair Complex: - The absorption spectrum of the Ion – Pair complex formed between Risperidone in the presence of Trihexyphenidyl HCl and Bromo Cresol Green is obtained in order to fix the wavelength of maximum absorbance and its experimental procedure is as follows.

2 ml of Risperidone solution (100 µg/ml),1 ml of Trihexyphenidyl HCl (100 µg/ml), 2 ml of BCG solution (0.5% w/v), 3 ml of buffer solution of pH 3.5 and 1 ml of methanol are taken in a 10 ml standard flask the resulting solution is made up to the mark with distilled water. Then the absorbance values of the Ion- pair complex formed is measured in the wavelength range 380 nm to 500 nm against the reagent blank. The results obtained are used to draw a graph

between the wavelength and the absorbance values. This graphical representation is called the absorption spectrum which is as shown in figure 3 below.

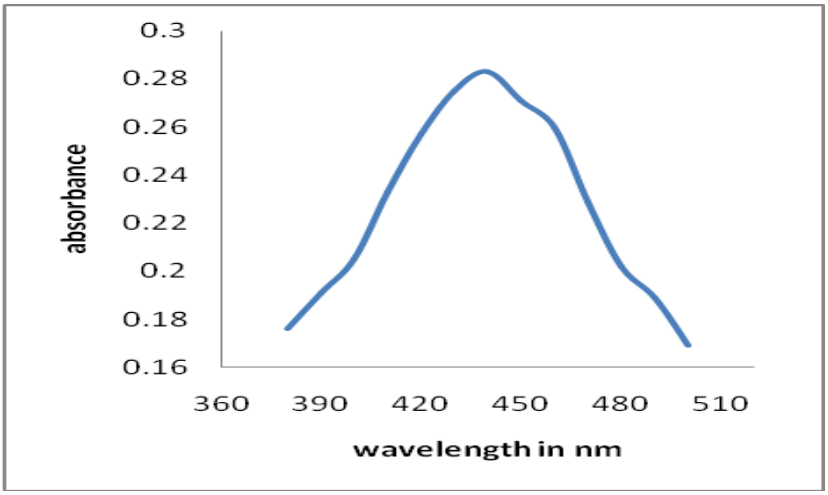

Fig.3: Absorption Spectrum of Ion-Pair complex of Risperidone with BCG

It is seen from the above graph of the absorption spectrum, the maximum absorbance is obtained at 440 nm. Hence for all further studies, a wavelength of 440 nm is fixed.

Effect of Buffer solution of pH 3.5:- The effect of buffer solution of pH 3.5 on the absorbance of ion pair complex is studied by taking varying volumes of (x ml) buffer solution of pH 3.5 in a series of 10 ml standard flasks, keeping the volume of Risperidone solution fixed at 2 ml. To each flask, 2.5 ml of BCG solution (0.5% w/v) and 2 ml of methanol are added followed by the addition of distilled water to make up each 10 ml flask to mark. The absorbance of each solution is recorded at 440 nm against the suitable blank. The results are as tabulated below in table 1.

Table.1: Effect of Buffer Solution pH 3.5

2 ml Risperidone (100 µg/ml) + 1 ml of Trihexyphenydyl HCl + x ml of buffer solution (pH 3.5) + 2.5 ml of BCG solution (0.5% w/v) + 1.5 ml of methanol + (3-x) ml distilled water = Total volume kept at 10 ml each. **λ_{max} = 440nm.**

S. No	Vol.of Risperi -one in ml	Vol.of Trihexyp- henydyl HCl in ml	Vol. of Buffer Solution in ml x ml	Vol.of BCG in ml	Vol.of Metha -nol in ml	Vol. of distilled water in ml (3-x)	Total volume in each flask in ml	Absorb -ance
1	2.0	1.0	0.5	2.5	1.5	2.5	10	0.431
2	2.0	1.0	1.0	2.5	1.5	2.0	10	0.428
3	2.0	1.0	1.5	2.5	1.5	1.5	10	0.375
4	2.0	1.0	2.0	2.5	1.5	1.0	10	0.360
5	2.0	1.0	2.5	2.5	1.5	0.5	10	0.361

From the above Table 1, it is observed that 0.5 ml of buffer solution of pH 3.5 are necessary to achieve maximum absorbance. Hence for all further studies, a volume of 0.5 ml of buffer solution of pH 3.5 is fixed.

Effect of Bromo Cresol Green (BCG) Concentration: - The effect of Bromo Cresol Green on the absorbance of Ion – Pair complex is studied by taking varying volumes of (x ml) of BCG in a series of 10 ml standard flasks. After taking x ml (0.5 ml to 2.5 ml) of BCG in each flask, 0.5 ml of buffer solution of pH 3.5, 2 ml of drug solution of Risperidone, 2 ml of methanol are added and the resulting solution is made up to 10 ml using distilled water. The absorbance of each solution is recorded at 440 nm against a suitable blank. The results obtained are mentioned in table 2 as shown below.

Table.2 - Effect of BCG on Ion- Pair complex

2 ml Risperidone (100 µg/ml) + 1 ml of Trihexyphenydyl Hcl(100 µg/ml) + 0.5 ml Buffer solution (pH 3.5) + x ml (0.5 ml to 2.5 ml) of BCG solution (0.5% w/v) + 2 ml of methanol + (4.5--x) ml distilled water = Total volume kept at 10 ml each**.** **λ_{max} = 440nm.**

S. No	Vol.of Risperi -done in ml	Vol.of Trihexyp- henydyl HCl in ml	Vol.of Buffer Solution in ml	Vol. of BCG solution x ml	Vol.of Methan ol in ml	Vol.of distilled water in ml (4.5-x)	Total volume in each flask in ml	Absorb -ance
1	2.0	1.0	0.5	0.5	2.0	4.0	10	0.207
2	2.0	1.0	0.5	1.0	2.0	3.5	10	0.269
3	2.0	1.0	0.5	1.5	2.0	3.0	10	0.312
4	2.0	1.0	0.5	2.0	2.0	2.5	10	0.393
5	2.0	1.0	0.5	2.5	2.0	2.0	10	0.401
6	2.0	1.0	0.5	3.0	2.0	1.5	10	0.401

From the data presented in the above Table 2, it is clear that 2.5 ml of BCG solution are necessary to get maximum absorbance. Hence 2.5 ml of BCG solution is fixed for further studies.

Effect of concentration of drug Risperidone: - This study leads to the effect of the drug Risperidone concentration on the absorbance of Ion – Pair complex under established optimal experimental conditions. The recommended procedures for the calibration curve and for the obedience of Beer-Lambert's law for the quantitative spectrophotometric determination of the drug Risperidone is as follows:-

Calibration Curve: Obedience of Beer-Lambert's Law: -Various aliquots (x ml i.e., 0.5 ml to 2.5 ml) of Risperidone solution (100 µg/ml) are taken in a series of 10 ml standard flask. To each flask, 1 ml of Trihexyphenidyl HCl solution (100 µg/ml), 0.5 ml of buffer solution of pH 3.5,2 .5ml of BCG solution (0.5% w/v), 2 ml of methanol followed by distilled water are added so as to make the total volume in each case at 10 ml. The contents of each flask are shaken well and allowed to stand for a minute for equilibration. The absorbance of each solution is measured at 440 nm against a suitable reagent blank which is prepared in a similar manner but devoid of drug solution. The results obtained are mentioned in below Table 3 and figure 4.

Table.3: Calibration Curve – Obedience of Beer- Lambert's Law

x ml (0.5 ml to 2.5 ml) of Risperidone solution (100 µg/ml) + 1 ml of Trihexyphenydyl HCl solution (100 µg/ml) + 2.5 ml of buffer solution of pH 3.5 + 2 ml BCG solution (0.5% w/v) + 1.5 ml methanol + (3-x) ml distilled water = Total volume kept at 10 ml in each case. λ_{max} = 440 nm

S. No	Vol.of Risperidone (100 µg/ml) x ml	Amount of Risperidone in µg/ml	Vol.of Trihexyphenidyl HCl (100 µg/ml) in ml	Vol.of Buffer Solution in ml (pH 3.5)	Vol.of BCG solution in ml	Vol.of Methanol in ml	Vol.of distilled water in ml (3-x)	Total Vol. in each flask in ml	Absorbance
1	0.5	50	1.0	2.5	2.0	1.5	2.5	10	0.063
2	1.0	100	1.0	2.5	2.0	1.5	2.0	10	0.124
3	1.5	150	1.0	2.5	2.0	1.5	1.5	10	0.174
4	2.0	200	1.0	2.5	2.0	1.5	1.0	10	0.234
5	2.5	250	1.0	2.5	2.0	1.5	0.5	10	0.283

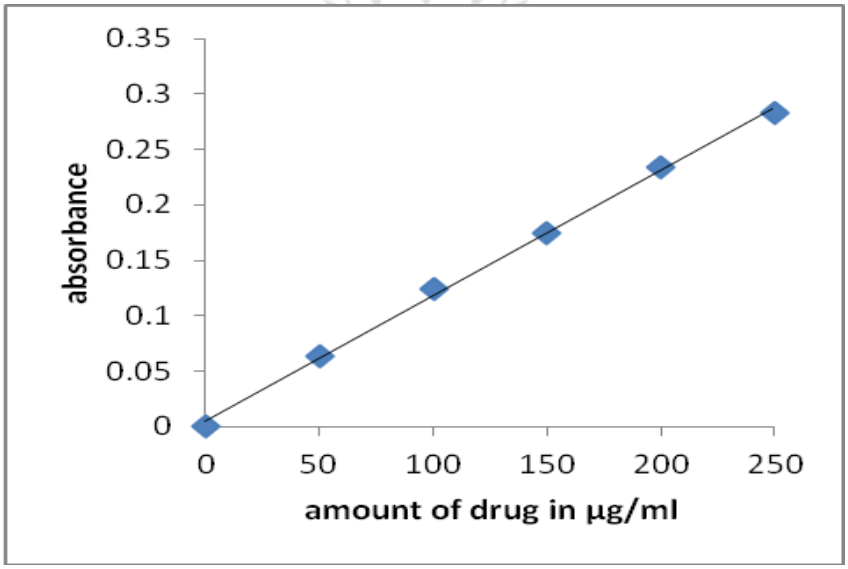

Fig.4: Calibration curve –Verification of Beer-Lambert's Law

It is clear from the data presented in the above table and from the calibration straight line the absorbance values increased linearly with the increase in the amount of the drug. This verifies the Beer-Lambert's law and suggests that the method can be successfully employed for the spectrophotometric quantitative determination of the drug Risperidone in the range 10 µg/ml

to 250 µg/ml. The molar absorptivity and the Sandell sensitivity of the method are found to be 1.1616×10^{4} lit/mole/cm and 0.0353µg/ml/cm^2 respectively.

Stoichiometric composition of Ion-Pair Complex: Job's continuous variation method: - The composition of the Ion – Pair complex between the drug Risperidone and the reagent BCG is established by the Job's continuous variation method. In this method, the equimolar concentrations (5 x 10^{-4} M) of both the drug and BCG are varied continuously keeping the total volume of mixed solution as constant at 10 ml. In each case, the absorbance is measured at 440 nm against a suitable blank. The data obtained are presented in Table 4 and the figure 5 as shown below.

Table 4: Job's Continuous Variation Method

0.5 ml to 4.5 ml of Risperidone solution(5 x 10^{-4} M) +1 ml of Trihexyphenydyl HCl solution(5 x 10^{-4} M) + 2.5 ml of buffer solution of pH 3.5 + 4.5 ml to 0.5 ml of BCG solution (5 x 10^{-4} M) + 1.5 ml of methanol = Total volume kept at 10 ml in each case.

λ_{max}=440 nm

S. No	Vol. of Risperidone (5 x 10^{-4}M) V_1 in ml	Vol.of Trihexyphenidyl HCl (5 x 10^{-4}M) in ml	Vol. of Buffer Solution of pH 3.5 in ml	Vol. of BCG (5 x 10^{-4} M) V_2 in ml	Vol. of Methanol in ml	Total vol. in ml	Vol. fraction (x) of the drug (V_1/V_1+V_2)	Absorbance
1	0.5	.0	2.5	4.5	1.5	10	0.1	0.121
2	1.0	1.0	2.5	4.0	1.5	10	0.2	0.222
3	1.5	1.0	2.5	3.5	1.5	10	0.3	0.301
4	2.0	1.0	2.5	3.0	1.5	10	0.4	0.451
5	2.5	1.0	2.5	2.5	1.5	10	0.5	0.567
6	3.0	1.0	2.5	2.0	1.5	10	0.6	0.215
7	3.5	1.0	2.5	1.5	1.5	10	0.7	0.150
8	4.0	1.0	2.5	1.0	1.5	10	0.8	0.090
9	4.5	1.0	2.5	0.5	1.5	10	0.9	0.060

The data in the above table are plotted in the form of a graph between volume fraction of the drug i.e., (V_1/V_1+V_2) on X-axis and the absorbance values on Y-axis. The graph obtained is as shown below in figure 5.

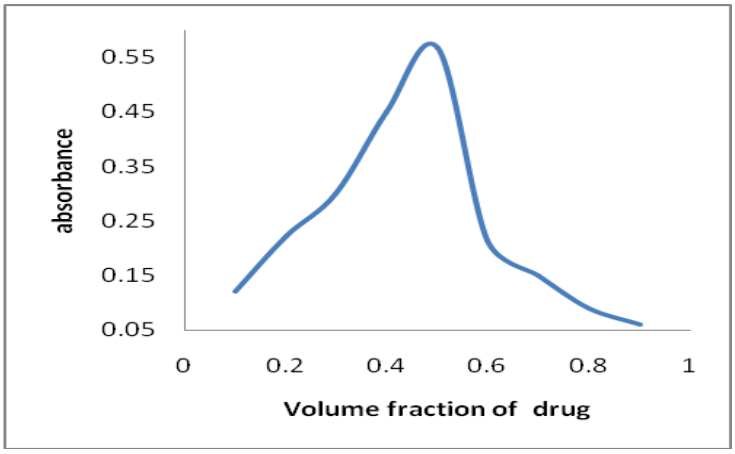

Fig 5: Job's Continuous Variation Method

From the graph shown above, it is found that one mole of the drug is reacting with 1 mole of BCG, thereby establishing the stoichiometry of the Ion-Pair complex as 1:1 (Drug: BCG)

Assay of Risperidone drug in pharmaceutical formulations: - The recommended procedure for the quantitative micro determination of Risperidone drug is applied for the assay of the drug in the dosage form of the commercial tablets and also in pharmaceutical formulations. The assay is carried out as follows: 20 tablets of Risperidone are weighed and finely powdered. An accurately weighed portion of the powdered sample equivalent to 50 mg of Risperidone is taken in a 50 ml volumetric flask containing 25 ml of methanol and is sonicated for about 20 minutes. The resultant solution is filtered through Whatman filter paper No.41 into another 50 ml volumetric flask. The filter paper is washed several times with methanol and the washings are added to the filtrate. The final volume is made up to the mark with methanol. Now, 5 ml of the filtrate of the sample solution is diluted to 10 ml with methanol and treated as per the recommended procedure of calibration. From this, the amount of the drug present in the sample is computed from the calibration curve. The results obtained are as shown in Table 5 below.

Table 5: Assay of Risperidone in Tablets

Sample	The labeled amount in mg	Amount found by present method ±SD*	Percentage of Label claim	%RSD	*t_{cal}
Tablet I	20	20.102±0.10	100.102	0.54	2.0513
Tablet II	20	20.104±0.05	100.104	0.25	4.6508

CONCLUSION

The calibration curve is linear up to 300 µg/ml indicating the suitability of the proposed method for the spectrophotometric determination of Risperidone in the range of 10 µg/ml to 300 µg/ml. The standard deviation values are found to be low showing high accuracy and reproducibility of the method. The calculated `t' values are less than the `t' theoretical values with 4 degrees of freedom at 95% level of significance. This indicates that there is no significant difference between the proposed method and the standard method. Further, there is no effect of additives and excipients such as starch, calcium lactose and glucose in the concentration of those present in general pharmaceutical preparations. Thus the proposed method can be conveniently adopted for the routine analysis and estimation of Risperidone in pharmaceutical formulations.

ACKNOWLEDGMENTS

The authors (ILP & NF) express their gratitude to the authorities of the Departments of Physics and Chemistry respectively of Rayalaseema University, Kurnool, and the Central Instrumentation Cell of Prof. T. Jayashankar, Telangana State Agricultural University, Hyderabad for providing necessary facilities to carry out the proposed work. One of the authors (ILP) acknowledges for the permission granted and encouragement by the Management of Tirumala Engineering College, Hyderabad.

REFERENCES

1. A. Maślanka, J. Krzek, and A. Patrzałek, "Determination of risperidone in tablets in the presence of its degradation products and placebo-derived constituents," Acta Poloniae Pharmaceutica—Drug Research, vol. 66, no. 5, pp. 461–470, 2009.
2. Tomar RS, Joseph TJ, Murthy AS, Yadav DV, Subbaiah G, KrishnaReddy KV. Identification and characterization of major degradation products of risperidone in bulk drug and pharmaceutical dosage forms. J Pharm Biomed Anal 2004; 36:231-35.
3. El said Hassan W. Extractive colorimetric method for the determination of dothiepin hydrochloride and risperidone in pure and in dosage forms. Chem. Pharm. Bull. 2008;56:1092–1096.
4. Song Z, Wang C. Sensitive chemiluminescence assay for risperidone in pharmaceutical preparations. J. Pharm. Biomed. Anal. 2004;36:491–494.
5. Fang, J., Bourin, M. & Baker, G. Naunyn-Schmiedeberg's Arch Pharmacol (1999) 359: 147. " Metabolism of risperidone to 9-hydroxyrisperidone by human cytochromes P450 2D6 and 3A4"
6. Locatelli I, Mrhar A, Grabnar I. Simultaneous determination of risperidone and 9-hydroxyrisperidone enantiomers in human blood plasma by liquid chromatography with electrochemical detection. J. Pharm. Biomed. Anal. 2009;50:905–910.
7. Mandrioli R, Mercolini L, Lateana D, Boncompagni G, et al. Analysis of risperidone and 9-hydroxyrisperidone in human plasma, urine and saliva by MEPS-LC-UV. J. Chromatogr. B. 2011;879:167–173.

8. Woestenborghs R, Lorreyne W, Rompaey F, Heykants J. Determination of risperidone and 9-hydroxyrisperidone in plasma, urine and animal tissues by high-performance liquid chromatography. J Chromatogra Bio Sci Appl 1992;583: 223-30.
9. Remmerie BM, Sips L, Vries R, Jong J, Schothuis A, Hooijschuur E. Validated method for the determination of risperidone and 9-hydroxyrisperidone in human plasma by liquid chromatography-tandem mass spectrometry. J Chromatogra Bio Sci Appl 2003;783: 461-72.
10. Subbaiah G, Singh S, Bhatt J, "Liquid chromatography/tandem mass spectrometry method for simultaneous determination of RIS and its active metabolite 9-hydroxy RISPERIDONE in human plasma" Rapid Communications in Mass Spectrometry, 2006, 20(14), 2109-2114.
11. D. Patel and J. Patel, "Development and validation of an RP-HPLC method for simultaneous estimation of Risperidone and Trihexyphenidyl hydrochloride in tablet dosage forms," International Journal of Pharmaceutical Sciences Review and Research, vol. 4, no. 3, p. 8, 2010.
12. M. F. Seyyed, Z. Afshin, S. Alireza, and K. Arash, "Rapid high performance liquid chromatographic determination of risperidone in human plasma," Iranian Journal of Pharmaceutical Research, no. 1, pp. 37–40, 2005.
13. Rabin C, Liang Y, Ehrlichman RS, Budhian A, Metzger KL, Majewski-Tiedeken C, et al. In vitro and in vivo demonstration of risperidone implants in mice. Schizophr Res 2008;98:66-78.
14. Rabin C, Liang Y, Ehrlichman RS, Budhian A, Metzger KL, Majewski-Tiedeken C, et al. In vitro and in vivo demonstration of risperidone implants in mice. Schizophr Res 2008;98:66-78.