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Der Pharmacia Lettre, 2015, 7 (3):221-227
(http://scholarsresearchlibrary.com/archive.html)

Der Pharmacia Lettre
Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Development and validation of RP-HPLC method for the estimation of risperidone in bulk and pharmaceutical dosage form

B. Lakshmi[1,*], K. Rama Krishna[2] and K. N. Jayaveera[3]

[1]Department of Chemistry, GITAM University, Hyderabad, AP, India
[2]Department of Chemistry, GIS, GITAM University, Visakhapatnam, AP, India
[3]Department of Chemistry, JNTU, Anantapur, AP, India

ABSTRACT

The aim of the present study was to develop and validate a simple RP-HPLC method for the estimation of Risperidone in bulk and pharmaceutical Dosage Forms. Seperation was achieved on Chromosil C18 (250×4.6mm)column with Methanol: Acetonitrile 75:25 v/v as a mobile phase at a flow rate of 1mL/min. The analyte was monitored with UV detector at a wavelength of 238 nm. Linearity was observed in the concentration range of 20-100µg/ml with correlation coefficient of 0.9988. The limit of detection and limit of quantification for Risperidone were found to be 0.03µg/ml and 0.10µg/mL respectively. The proposed method is simple,accurate, precise and robust therefore can be used for routine analysis of Risperidone in bulk drug and pharmaceutical formulations.

Keywords: Risperidone, RP-HPLC method,Linearity,validation.

INTRODUCTION

Risperidone is an antipsychotic drug,used to treat schizophrenia (a mental illness that causes unusual thinking, loss of interest in life, and inappropriate emotions), the mixed and manic states of bipolar disorder(a disease that causes episodes of depression,other abnormal moods) [1,4,5]. It is a second-generation atypical antipsychotic drug[2]. The drug was developed by Janssen-Cilag and first approved by the FDA in 1994 [3].

Risperidone is also used to treat behavior problems such as aggression, self-injury, and sudden mood changes in teenagers and children 5 to 16 years of age who have autism (a condition that causes repetitive behavior, difficulty interacting with others, and problems with communication). Risperidone provides no benefit in the treatment of eating disorders or personality disorders [6,7,].

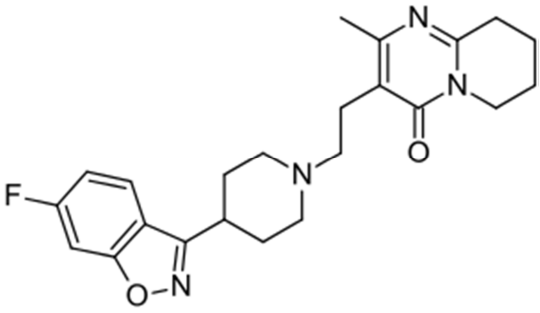


Figure 1: structure of Risperidone

The drug works by changing the activity of certain natural substances in the brain.It is believed that many psychotic illnesses are caused by abnormal communication among nerves in the brain and that by altering communication through neurotransmitters, risperidone can alter the psychotic state [8-10].

Literature survey revealed that many Analytical methods were developed for Risperidone in bulk and pharmaceutical formulation individually[11-14] and in combination with other drugs[15-16], HPLC-MS[17],Spectrophotometric[18-24] and LC-MS/MS[25-27].Some of the HPLC methods were not economical in terms of mobile phse,column,run time and .Hence there is a need for development of new method for the estimation of Risperidone in bulk drug and pharmaceutical formulations.

MATERIALS AND METHODS

2.1 Chemicals and Reagents

Analytically pure sample of Risperidone was a generous gift from Sun Pharmaceutical Industries, MS, and India. All other solvents like Methanol and acetonitrile (HPLC Grade) were purchased from E. Merck Ltd., Mumbai, India.

2.2 Instrumentation

PEAK LC7000 isocratic HPLC instrument was used for the analysis purpose with peak 7000 delivery system,rheodyne manual sample injector. UV 2301 Spectrophotometer was used to determine the wavelength of maximum absorbance. Samples were injected through a Rheodyne injector with a 20µl loop.

2.3. Preparation of standard and stock solution

Standard stock solution of Risperidone pure drug was prepared by accurately weighing about 1mg of drug in 10ml volumetric flask. The drug was dissolved with few ml of methanol, and sonicated to dissolve it completely and made up to the mark. From this stock solution selected concentrations were prepared by further dilutions.

2.4 Preparation of Formulation Solution

Marketed formulation of Risperidone 20 tablets were powdered with mortor and piston and 10mg of Risperidone was weighed and was dissolved in little amount of methanol and mixed well and then make up to 10ml with methanol.Then It was filtered using 0.45µm Nylon filter membrane.

2.5 Method development and Chromatographic conditions

The chromatographic separation was performed at room temperature on a Chromosil C18 (250×4.6mm)Column and the detection Wavelength was 238 nm. Mobile phase used for the estimation is Methanol: Acetonitrile 75: 25 (v/v) with flow rate 1ml/min.Optimized chromatographic conditions were shown in table-1. Standard and blank chromatograms were shown in figures-2 and 3.

Table-1: Optimized chromatographic conditions for estimation of Risperidone

Condition	Results
Mobile Phase	Methanol: Acetonitrile 75: 25 (v/v)
Wavelength	238nm
Column	kromasil C18 column (250 X 4.6 mm, 5µ)
P^H	5.1
Retention Time	3.83min
Run Time	8min
Area	260004
Th. Plates	11473
Tailing Factor	1.65
Pump Pressure	5.0±5MPa
Flow Rate	1ml/min

Figure-2: Standard chromatogram of Risperidone

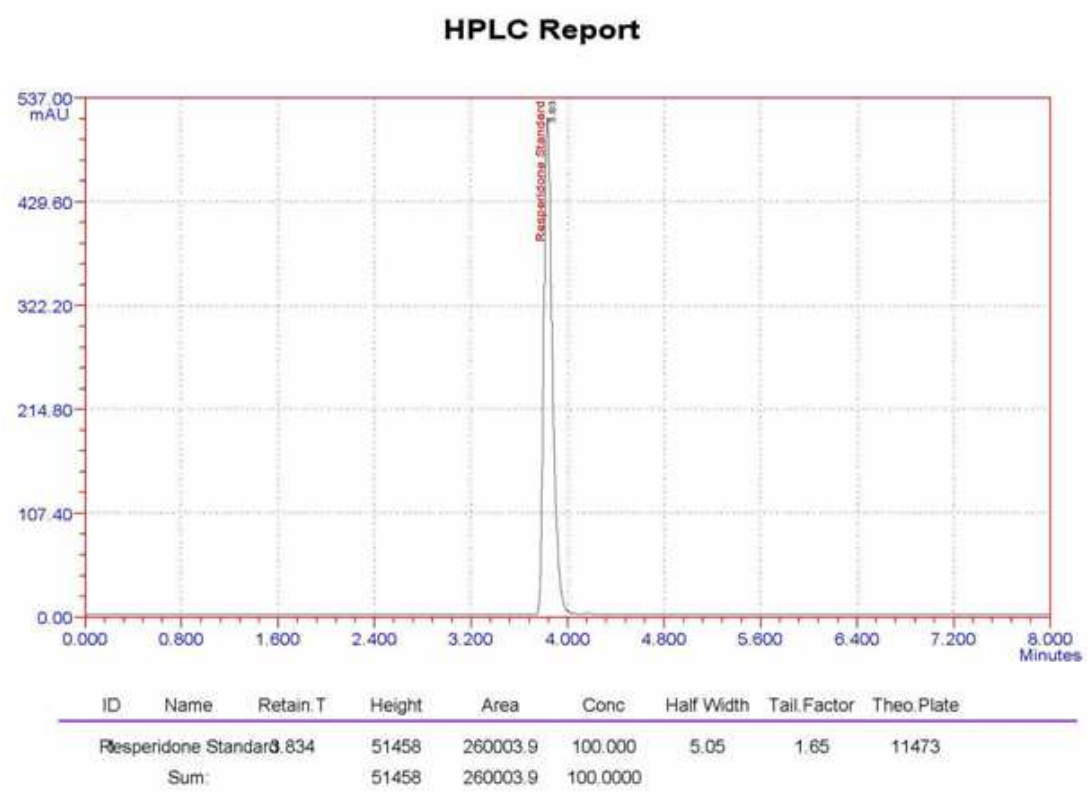
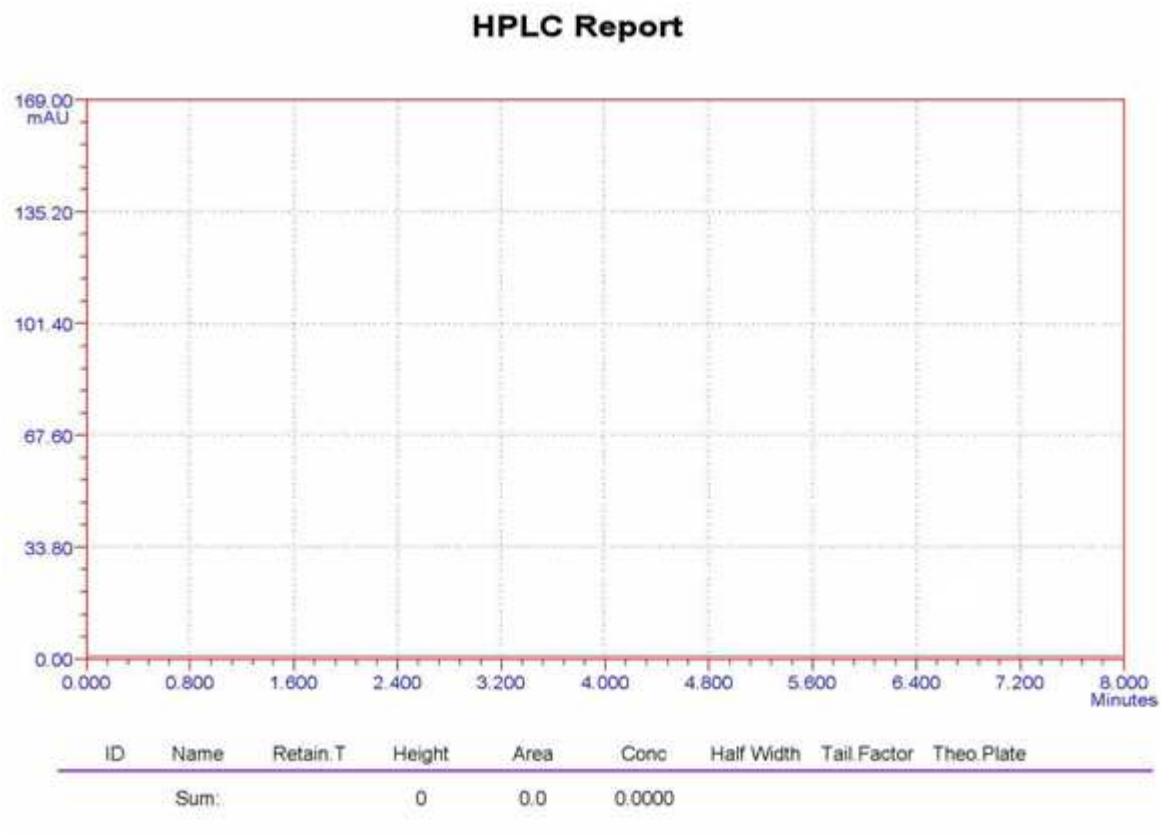


Figure-3: Blank chromatogram for Risperidone



2.5 Method Validation

The proposed method was validated according to the ICH guidelines.

2.5.1 System Suitability:

The RSD value for the two consecutive injections was < 2.0%,number of theoretical plates found as 11473,tailing factor was 1.65. This confirms that the proposed method obeys system suitable acceptance limit.

2.5.2 Linearity Curve (Calibration Curve):

Aliquots of standard Risperidone stock solution were taken in nine different volumetric flasks and diluted up to the mark with the diluent (Methanol) such that the final concentrations of Risperidone was 20, 30,40,50, 60,70, 80,90 and 100µg/ml. The regression equation of the calibration curve is y=3872.1x + 27979and co-relation coefficient found to be 0.9988.linearity data was shown in table 2 and calibration curve was shown in figure 4.

Table 2: Linearity results for Risperidone

S.NO	Concentration in µg/ml	Peak Area
1	20	107750
2	30	149019
3	40	181518
4	50	213431
5	60	260003
6	70	297734
7	80	337736
8	90	377681
9	100	417888
	Slope: 3872.1 Intercept: 27979 Correlation Coefficient:0.9988	

Figure 4: Calibration curve of Risperidone

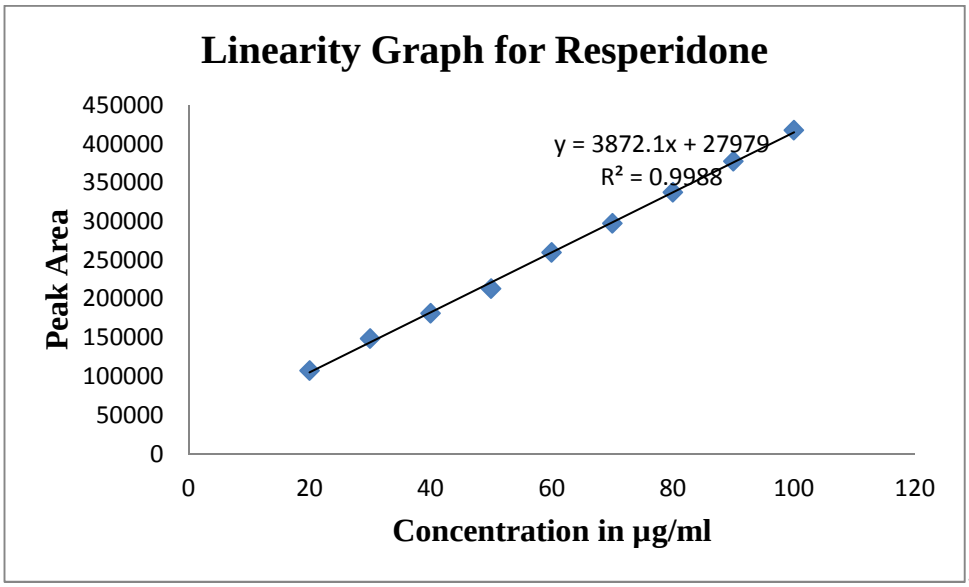


Table 3: Recovery results for the proposed method

Recovery	Target Conc., (µg/ml)	Spiked conc., (µg/ml)	Final Conc., (µg/ml)	Conc., Obtained	% of Assay	%RSD
50%	40	20	60	59.79	99.66	0.638
	40	20	60	59.04	98.40	
	40	20	60	59.43	99.05	
100%	40	40	80	78.748	98.43	0.528
	40	40	80	79.56	99.46	
	40	40	80	79.03	98.78	
150%	40	60	100	99.33	99.33	0.538
	40	60	100	99.08	99.08	
	40	60	100	98.31	98.31	

2.5.3 Accuracy: The accuracy of the method was determined by calculating percentage recovery. Recovery studies were carried out by applying the spiking method, known amount of Risperidone corresponding to 50, 100 and 150% was added (standard addition method) to the Risperidone sample. The recoveries were found in the range of 98.31-99.66. Data was shown in table 3.

2.5.4 Precision:

Precision of the Risperidone was tested by performing intra-day and inter-day studies.It was estimated in terms of percentage relative standard deviation (%RSD) and were shown in Table 4.

Table 4: Intra, Inter day precision results

S.NO	Concentration in µg/ml	Peak Area	Peak Area
1	60	260934	261382
2	60	260797	261368
3	60	260439	258886
4	60	260861	260759
5	60	259742	260064
6	60	259950	260181
	(Intra day)RSD: 0.19		**(Inter day)RSD: 0.36**

2.5.5 LOD and LOQ: The LOD and LOQ were determined using the signal-to-noise (S/N) method by comparing results of the test of samples with known concentrations of analyte to blank samples. A signal-to-noise ratio of 3:1 is used for LOD whereas a signal-to noise ratio of 10:1 is used for LOQ. The LOD & LOQ values for risperidone were found to be 0.03µg/ml and 0.10µg/ml respectively.

2.5.6 Robustness:

Robustness can be used to check the capacity of method which is unaffected by changing the chromatographic conditions like wavelength, pH of the system,mobile phase etc.Detection wavelength was changed in the range of 287 nm and 277 nm, pH was changed in the range of $\pm$0.5. Effect of these parameters was studied by injecting the sample,results were tabulated in table 5.

Table 5: Robustness results

S.NO	Parameter	Change	Area	% of Change
1	Standard	……	260003	……
2	MP 1	75: 25 (v/v)	259701	0.12
2	MP 2	75: 25 (v/v)	259971	0.01
3	pH 1	4.0	260646	0.25
4	pH 2	5.2	260377	0.14
5	WL 1	241nm	260358	0.13
6	WL 2	235nm	260368	0.14

2.5.7 Ruggedness:

It is performed by injecting 6 replicates(60µg/ml) of solution which were prepared and analyzed by different analysts. The % RSD was found to be 0.22,is in satisfactory range. Results were reported in table 6.

Table 6: Ruggedness results for the proposed method.

S.NO	Concentration in µg/ml	Peak Area
1	60	259562
2	60	259342
3	60	260027
4	60	259125
5	60	260621
6	60	260331
	RSD: 0.22	

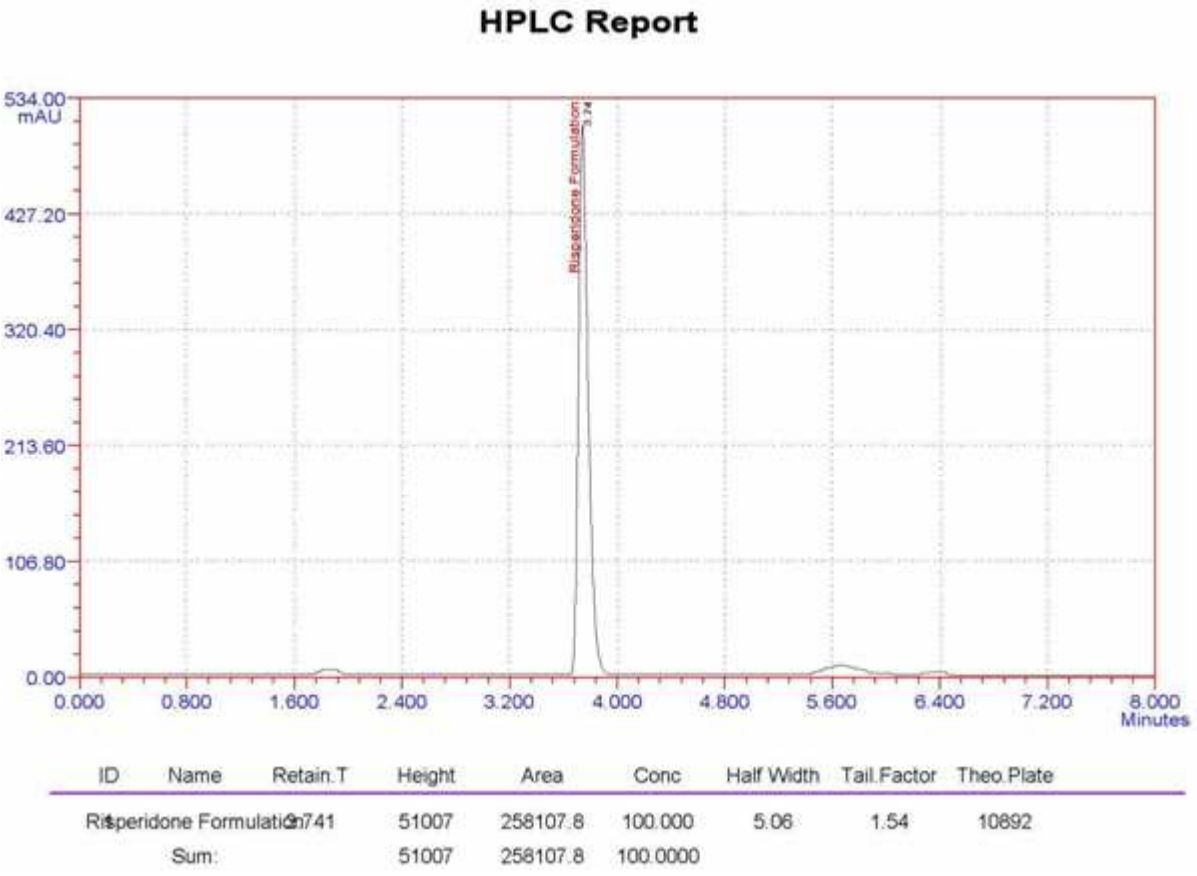
2.5.6 Assay of marketed formulation of Risperidone .

This method was applied for the commercial tablets of risperidone (Ridon-4mg) and peak area responses and % assay was calculated by using standard area value. The results have good agreement with the label claim. Results were given in table-7 and formulation chromatogram was shown in figure-5.

Table 7: Formulation analysis of Risperidone

S.NO	Brand name	Available form	Label claim	Concentration	Amount found	% Assay
1	Ridon	Tablet	4mg	60µg/ml	59.56µg/ml	99.27

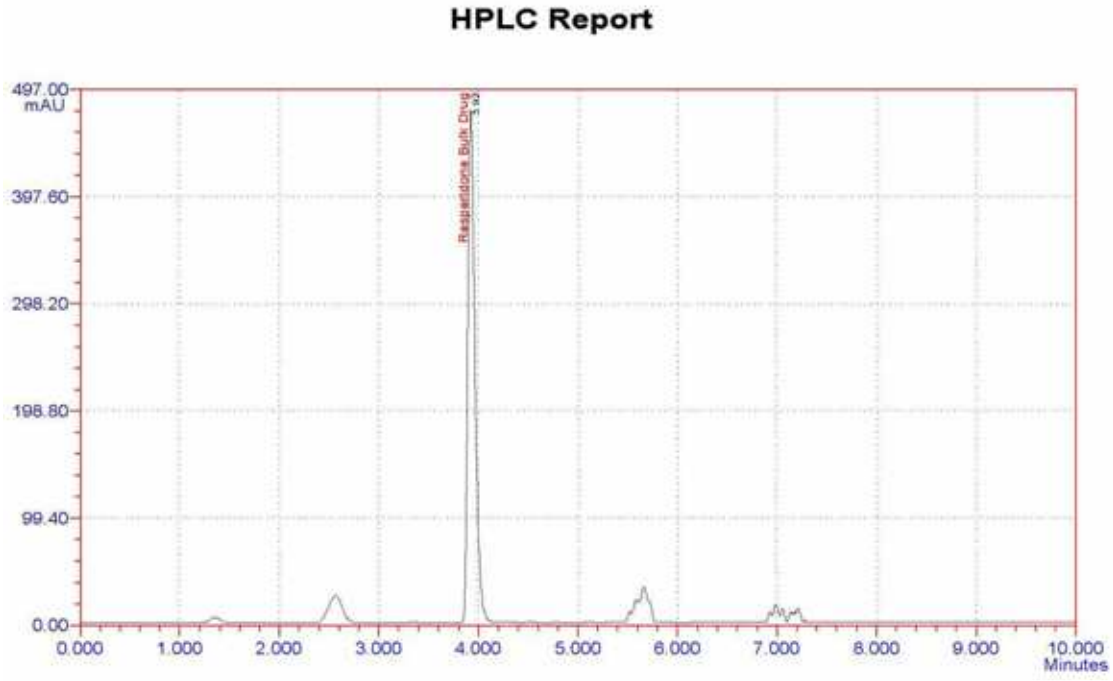
Figure 5: Formulation chromatogram for Risperidone



2.5.7 Estimation of Risperidone in Bulk drug sample:

The proposed method was applied for the estimation of drug in bulk samples. Bulk drug samples solution at a concentration of 60µg/ml was prepared and analyzed using the optimized conditions. % assay was calculated using the peak area of the resultant chromatogram. % assay was found to be 97.73. Results were found to be good argument with the standard values and hence the proposed method can be applied for the estimation of Risperidone in bulk drug samples also. The chromatogram of bulk drug analysis was shown in figure 6.

Figure 6: Chromatogram of bulk drug analysis



CONCLUSION

A simple isocratic RP-HPLC method has been developed for the estimation Risperidone. The method was validated as per ICH guidelines and the method was found to be simple, sensitive, accurate, rugged, robust and precise. Hence, the method can be successfully applied for the estimation of Risperidone in bulk and pharmaceutical Dosage Forms.

REFERENCES

[1] Truven, Health Analytics**, 2013**.
[2] Komossa K, Rummel-Kluge C, Schwarz S, Schmid F, Hunger H, Kissling W and Leucht S, "Risperidone versus other atypical antipsychotics for schizophrenia", The Cochrane database of systematic reviews, **2011,**1**.**
[3] WHO Model List of Essential Medicines. World Health Organization, **2014.**
[4] Respiridone, The American Society of Health-System Pharmacists, **2011.**
[5] Rattehalli RD, Jayaram MB and Smith M, Risperidone versus placebo for schizophrenia, In Rattehalli, Ranganath Cochrane Database Syst, **2010.**
[6] Maher AR and Theodore G,Summary of the comparative effectiveness review on off-label use of atypical antipsychotics, *J Manag Care Pharm*,**2012,**18**.**
[7] Risperdal Prescribing Information Label, Drugs@FDA: FDA Approved Drug Products, Jannsen Pharmaceuticals, Inc, **2014.**
[8] Brunton L, Chabner B and Knollman B, Goodman and Gilman's The Pharmacological Basis of Therapeutics, Twelfth Edition, McGraw Hill Professional; **2010.**
[9] Abou El-Magd RM, Park HK, Kawazoe T, Iwana S, Ono K, Chung SP, Miyano M, Yorita K, Sakai T and Fukui K, *Journal of Psychopharmacology*, **2010,**24,7**.**
[10] Hecht EM and Landy DC. *Schizophrenia Research*, **2013,**134(2–3), 202–6**.**
[11]A.P.Suthar, *International Journal of Pharm Tech Research*, **2009**, 1(3) 568-574.
[12] Mohammad Yunoos, Pragati Kumar B and Subhani, *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, **2010**,1(2), 165-171.
[13] Zarna R, *International journal of analytical chemistry*,**2011**
[14] Ashour Safwan and Kattan Nuha, *International journal of biomedical science*, **2013**,9(2), 91-7.
[15] Dhara patel , *international journal of pharmaceutical sciences review and research*, **2010**, 4(3), 85-88.
[16] S.Dharmaraj Santhosam, *HYGEIA Journal For Drugs And Medicines*, **2011**,3(1),29- 33.
[17] Ming-zhu Huang, *Journal of Zhejiang University Science* B, **2008**, 9(2), 114-120.
[18] Kathirvel S, Rao, G Devala and Satyanarayana S. V, *Asian Journal of Research in Chemistry*, **2010**, 3(1), 151-153.
[19] Hasan Moynul, Al Masud Abdullh and Ahmed Jamiuddin,*International Journal of Pharmaceutical Sciences and Research*, **2011**, 2(2), 378-382.
[20] Akachukwu, I.; Nwodo, N. J.; Mbah, C. J, *International Journal of Pharmacy*,**2013**, 3(4), 710-715.
[21] Deepakumari, Hemavathi Nagaraju; Revanasiddappa, Hosakere Doddarevanna, *Journal of Pharmaceutics* **2013.**
[22] Kutty, Sheeja Velayudhan; Babu, Yellinah Hari; Greeshma, S.; Vidhya, P. M, *Pharma Innovation*,**2013**, 2(2), 44-49.
[23] Archana S, Naga Prasanna Y, Pavitra P, Santhi Krupa D and Hema Sri M, *International Journal of Pharmaceutical Sciences and Research*,**2013**, 4(3), 1116-1119.
[24] Narayana B and Shetty Divya N, *Der Pharmacia Letter*, **2013**, 3(5), 104-109.
[25] Li Hongxia, Yang Dongjing, Fan Di, Wang Xueqin and Xing Xiangwei, Huaxi Yaoxue Zazhi, **2011**,26(4), 369-371.
[26] Jia Jingying, Zhang Mengqi, Lu Xiaopei, Lu Chuan, Li Shuijun, Liu Gangyi and Yu Chen, Zhongguo Linchuang Yaoxue Zazhi, **2010**,19(5), 279-282.
[27] Gao Kepan, Chen Jun and Chen Qinghua, Zhongguo Yiyao Gongye Zazhi,**2010**,41(5), 360-362**.**