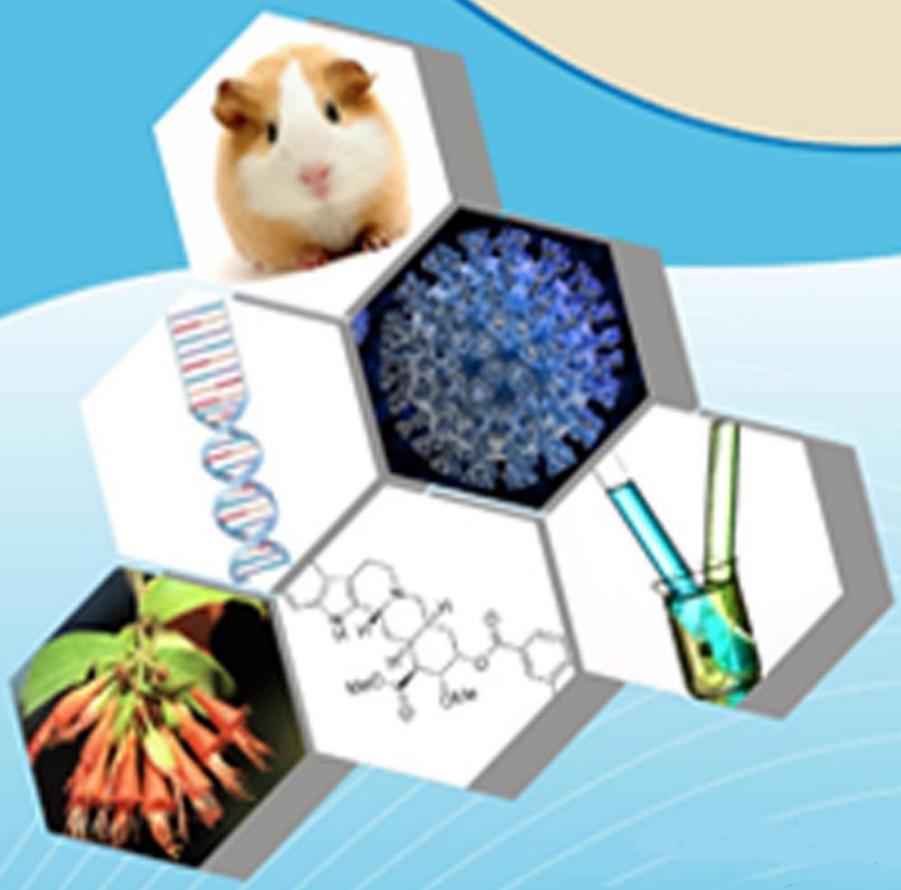
ISSN : 2347-2251

Indo-American Journal of Pharma and Bio Sciences



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Indo-American Journal of Pharma and Bio Sciences

Vol. 16, Issue 4, 2018

DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF RISPERIDONE IN PURE AND TABLET DOSAGE FORMS

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ABSTRACT

A straightforward and very accurate visible spectrophotometric technique is presented for the measurement of pure and solid dose forms of risperidone (RSP).

Using an oxidative coupling process, risperidone and MBTH are combined in the presence of dissolved ferric chloride in HCl to generate apple green chromogen, which has an absorption peak at 595.8 nm. A Beer-Lambert plot regression analysis revealed strong association in the concentration ranges of 10–80 µg/mL. The regression coefficient of 0.992 was discovered. The suggested approach is used on commercially available tablets, and recovery studies are used to statistically analyze and verify the outcomes. Both the drug's tablet dose form and its mass have been effectively analyzed using the suggested methodologies. After statistical analysis, the procedures were determined to be exact and correct.

I. INTRODUCTION

Risperidone 1 is an antipsychotic drug which is mainly used to treat schizophrenia (including adolescent schizophrenia), schizoaffective disorder, the mixed and manic states associated with bipolar disorder, and irritability in people with autism. Risperidone belongs to the class of atypical antipsychotics 2 . It is a dopamine antagonist possessing antiserotonergic, antiadrenergic and antihistaminergic properties. Many analytical methods like spectrophotophotometry 2-4 HPLC 5-10 , LC – MS 11, 12 , HPTLC 13 , polarography 14 and have been reported for the determination of Risperidone.

2. EXPERIMENTAL:

Instrument:

Elico double beam UV/Visible spectrophotometer (SL-210) with 1cm matched quartz cells, electronic Dona balance were used for all spectral measurements.

Reagents and Standards:

All the reagents used were of analytical grade and the solutions were freshly prepared. The reagents used in this method are triple distilled water, methanol, 0.1N HCl, MBTH (0.3%) and **FeCl3 (1%) . Stock Solution:**

The solution 1mg/ml (1000mcg/ml) was prepared by dissolving accurately about 0.1 g of drug in 100ml of distilled water.

Preparation of MBTH Reagent:

0.3gm of MBTH reagent was dissolved in 100ml distilled water and made up to the volume to 100ml.

Preparation of Ferric Chloride Solution:

1gm of FeCl3 was dissolved in 0.1N HCl and made up to the 100ml with 0.1N HCl.

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PROCEDURE:

Into a series of 10ml volumetric flask , 1ml of MBTH (0.3%) and 0.8ml FeCl3 (1%) and 0.1 – 0.8ml of working standard solution (1mg/ml) were added separately. The absorbance of apple green chromogen was measured at 595.8nm against reagent blank. The amount of risperidone present in the sample solution was computed from its calibration curve. The spectrum was shown in figure 1.

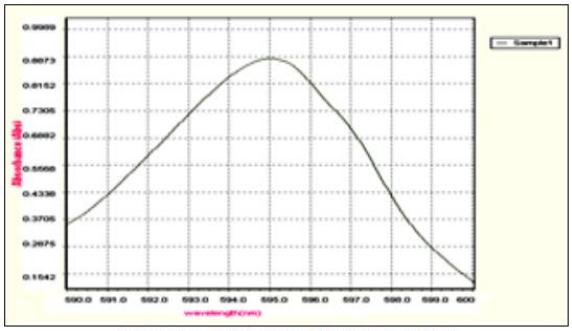

FIGURE 1: SPECTRUM OF RISPERIDONE

Preparation of Sample Solution: 20 tablets of commercial samples of risperidone were accurately weighed and powdered. The tablet powder equivalent to 50 mg of risperidone was dissolved in 5 ml of methanol and made up to volume with distilled water. The solution was filtered and analyzed as given under the assay procedure for bulk samples. None of the excipients usually employed in the formulation of tablets interfered in the analysis of risperidone by the proposed method. The standard graph was plotted by taking conc. of drug on x – axis and absorbance on y– axis and was shown in figure 2. Results of regression analysis was given in table 9.

Procedure for assay of drugs in Dosage Forms: Ten tablets of commercial samples of Risperidone were accurately weighed and powdered. An amount of powder equivalent to 50mg was weighed separately and made upto 50ml with distilled water. The solution was filtered and subjected to recommended procedure for the determination. The results were displayed in table 8.

Validation Parameters:

1. Linearity: The calibration curve was constructed in each case by considering the absorbance measured at eight concentration levels of Risperidone methanol (10-80 µg/ml) using the method of least squares, a line of best fit was taken and the correlation coefficient, slope and yintercept was calculated. The amount of drug was computed either from calibration curve or from regression equation, the results are given in table 1.

2. Accuracy: The accuracy of the method was determined by taking aliquots containing known quantity of risperidone & analyzed by proposed method & results are compared with results of reference method & tabulated in the table 2.

3. Precision: The precision of the method was studied by measuring 6 replications of sample containing 20µg/ml of risperidone. The % RSD & SD was calculated and presented in table 3.

4. Ruggedness: It is a measure of reproducibility of test results under normal expected operational condition from instrument to instrument & from analyst to analyst were reported in table 4 & 5.

5. Specificity: Absorbance of blank solution was measured and is found to be very negligible 0.0012 hence no interference with blank solution was observed. This indicates that the method for the drug is specific.

6. Robustness: The robustness of the method was followed by optimizing conditions with slight variation i.e. by altering detection wavelength (1nm) the results were reported in table 6 & 7.

3. RESULTS AND DISCUSSION

The presence of amino group in RSP enabled oxidative coupling with MBTH and FeCl3 to form green colored chromogen in this method exhibiting λmax at 595.8 nm. The Beer's law

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was obeyed for this method in the concentration ranges of 10-80 µg/ml respectively. The optical characteristics such as Beer's law limits (µg/ml), Molar extinction coefficient (L/mol.cm), Regression equation (y), Correlation coefficient was calculated and reported in Table 9. To evaluate the validity and reproducibility of the method, known amount of pure drug was added to the previously analyzed pharmaceutical preparation and the mixtures were analyzed by the proposed method. The percent recoveries are given in Table 2.

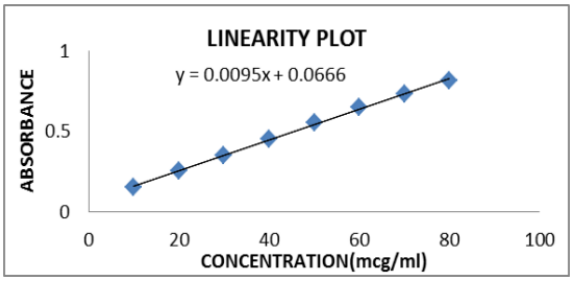

FIGURE 2: LINEARITY PLOT

TABLE 1: LINEARITY

S.NO	CONCENTRATION (µg/ml)	ABSORBANCE
1	10	0.155
2	20	0.255
3	30	0.351
4	40	0.452
5	50	0.556
6	60	0.648
7	70	0.731
8	80	0.815

TABLE 2: ACCURACY

Spike level	Amount present	Amount received	%recovered
80%	40mcg/ml	39.96	99.9%
100%	50mcg/ml	49.99	99.98%
120%	60mcg/ml	60.18	100%

TABLE 3: PRECISION

Concentration(µg/ml)	6 replicates
50	0.556
50	0.549
50	0.551
50	0.549
50	0.555
50	0.556
Average	0.5526
Std.deviation	0.003386
%RSD	0.6127

Ruggedness

TABLE 4: INSTRUMENT VARIATION

Concentration (µg/ml)	Instrumental-1	Instrumental-2
50	0.556	0.551
50	0.554	0.556
50	0.55	0.549
50	0.561	0.566
50	0.564	0.548
Average	0.555667	0.555167
Std.deviation	0.005955	0.007195
%RSD	1.071756	1.29599

TABLE 5: ANALYST VARIATION

Concentration (µg/ml)	Analyst-1	Analyst-2
50	0.556	0.548
50	0.554	0.543
50	0.55	0.537
50	0.549	0.546
50	0.561	0.538
50	0.564	0.552
Average	0.555667	0.544
Std.deviation	0.005955	0.005831
%RSD	1.071756	1.071866

Robustness

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1. **TABLE 6: 50mcg/ml :**

	Wavelength (nm)		
594.8	0.561	0.556	0.553
595.8	0.548	0.551	0.553
596.8	0.545	0.549	0.545
Average	0.551	0.552	0.550
Standard deviation	0.008505	0.003606	0.004619
%RSD	1.54	0.653	0.839

2. **TABLE 7: 60mcg/ml**

	Wavelength(nm)		
594.8	595.8	596.8	0.651
595.8	595.8	596.8	0.655
596.8	0.654	0.653	0.657
Average	0.650	0.650	0.654
Standard deviation	0.004583	0.002517	0.003055
%RSD	0.7050	0.387	0.467

TABLE 8: ASSAY OF RISPERIDONE TABLETS.

Sample (tablet)	Labeled amount mg	Amount obtained mg*	%Recovery by the proposed method**
1	50	49.98	99.96
2	50	49.88	99.76

*Average of three determinations; ** After spiking the sample

4. CONCLUSION

The created approach shows a good degree of precision and accuracy and is easy to use, quick, selective, and affordable. The current techniques include the creation of very stable colored species, which facilitates the regular identification of risperidone from pharmaceutical dose forms. There are no critical reaction conditions in the approach. The suggested approach may be used as a substitute for the standard RSP analysis of pharmaceutical formulations and pure drugs.

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