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DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF RISPERIDONE IN BULK DRUG AND PHARMACEUTICAL FORMULATION

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ABSTRACT

A simple, sensitive and accurate spectrophotometric method has been developed for the deterrmination of Risperidone in raw material and capsule. The λ_{max} of Risperidone was found to be 202nm. Risperidone obeys linearity within the concentration range of 2.5 to 20µg/mL and coefficient correlation was found to be 0.9991.The regression of the curve was Y= 0.0508X+0.0112. The %RSD value is below 2.0 for intraday and interday precision indicated that the method is highly precised. The percentage recovery value was higher than 100%, indicating the accuracy of the method and absence of interference of the excipients present in the formulation. The proposed method will be suitable for the analysis of Risperidone in bulk and pharmaceutical formulations.

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 H1 histaminergic receptors [1]. 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.

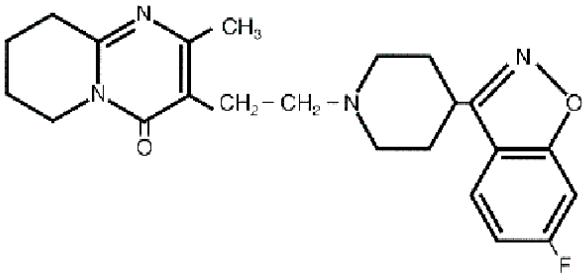

FIGURE 1: STRUCTURE OF RISPERIDONE

Literature survey revealed that various methods have been reported for estimation of Risperidone in biological matrices such as plasma with help of LC [2, 3], LC with diode array detection [4], LC with tandem mass spectrometry [5, 6, 7] and LC with electrochemical detection [8]. Few stability-indicating methods have been reported for determination of Risperidone in bulk powder and tablets in presence of its degradation products [9, 10].

However very few methods were reported for quantitation of Risperidone in tablet dosage forms in the literature. The objective of the present investigations was to develop a simple, accurate and economical spectrophotometric methods for estimation of Risperidone in tablet formulations.

MATERIALS AND METHODS:

Chemicals and Reagents: Risperidone was receieved as a gift sample from ACI Pharmaceutical Ltd, Bangladesh and Risperidone tablet manufactured by Orion Laboratories Ltd, Bangladesh were purchased from local market. Analytical grade Hydrochloric acid (0.1N HCL) used as solvent.

Instruments: UV-Visible double beam spectrophotometer (UV-1601 PC SHIMADZU Limited, Japan), Micropipette of Variable volume 10-1000 µL (Gene Pete Co.) and Digital balance (Citizen Co.)

Methods:

Selection of Wavelength: In order to ascertain the wavelength of maximum absorption (λ_{max}) of the drug, different solutions of the drugs (5µg/mL and 10µg/mL) in 0.1N HCl were scanned using spectrophotometer within the wavelength region of 200-380nm against methanol as blank. The resulting spectra showed characteristic absorption maxima at 202nm for Risperidone.

Preparation of Standard Solution for Calibration: 10 mg Standard Risperidone was accurately weighed and transferred to 100 mL volumetric flask and was dissolved properly and diluted up to the mark with 0.1N HCl. Then 5mL of this solution was diluted to 100mL with 0.1N HCl . Appropriate amounts of this stock solution were diluted with the same solvent, yields concentrations of 2.5µg/mL, 5µg/mL, 10µg/mL, 15µg/ml and 20µg/mL which were used for the construction of calibration curve.

Preparation of Sample Solution: Twenty tablets were weighed accurately and powdered. Powder equivalent to 10mg of Risperidone was weighed and transferred to a 100ml volumetric flask. About 40mL of 0.1N HCl was added and sonicated for 5 min for complete dissolution of drugs, the volume was made upto the mark with the same solvent and then the above solution was filtered through whatman filter paper. Now 5mL of the filtrate is transferred to a 100 mL volumetric flask and then the volume was made upto the mark with the same

solvent. After suitable dilution, the absorbance of final sample was recorded against the blank at 202 nm. All determinations were conducted in triplicate (**Table 1**).

The proposed method was validated according to ich guidelines for linearity, precision, accuracy, stability, lod, loq and stability [11] (**Table 2**).

Linearity: The linearity of this method was determined at five concentration levels ranging from 2.5μg/mL-20μg/mL . The plot of absorbance Vs respective concentration (**Fig. 2**) of Risperidone was found to be linear in the range of 2.5μg/mL-20μg/mL. Beer's law was obeyed over this concentration range. The regression equation was found to be Y =0.0508X + 0.0112 and the correlation coefficient (r) of the standard curve was found to be 0.9991 (Table 2).

Precision: The precision of the assay was determined by repeatability (intraday) and intermediate precision (inter-day) and reported as %RSD. For this, 5μg/mL concentration solution was measured three times in day and same was measured in next three days. Then the %RSD was calculated.

Accuracy (Recovery Studies): Recovery studies were performed to judge the accuracy of the method and were carried out by adding a known quantity of pure drug to the preanalyzed formulation and the proposed method was followed. From the amount of drug found, percentage recovery was calculated. Recovery study was carried out at three levels 80%, 100% and 120% for the formulation concentration of 5μg/mL (**Table 3**).

LOD & LOQ: LOD (k= 3.3) and LOQ (k= 10) of the method were established according to ICH definitions. LOD and LOQ of method are reported in **Table 2**. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve using the following equations;

$$LOD = 3.3\ S/M;\ LOQ = 10\ S/M$$

Where S is the standard deviation of the absorbance of the sample and M is the slope of the calibrations curve.

Stability Study: In order to demonstrate the stability of both standard and sample solutions during analysis, both solutions were analyzed over a period of 24 h at room temperature and % RSD of absorbance for both solutions was calculated.

RESULTS & DISCUSSION: The λ_{max} of Risperidone was found to be 202nm. From the optical characteristics (Table 2) of the proposed method, it was found that Risperidone obeys linearity within the concentration range of 2.5 to 20μg/mL and coefficient correlation was found to be 0.9991. The regression of the curve was Y =0.0508X+0.0112. The detection and quantization limits as LOD (k=3.3) and LOQ (k=10) were calculated and these were found to be 1.05μg/mL and 3.34μg/mL respectively.

The precision (measurements of intraday and interday) results showed (Table 2) good reproducibility with percent relative standard deviation (% RSD) is below 2.0. This indicated that method is highly precised. The percentage recovery value (table 3), which was higher than 100 %, indicating the accuracy of the method and absence of interference of the excipients present in the formulation.

The results of stability study showed that for both solutions, the absorbance remained almost similar (% R.S.D. less than 2.0) and no significant degradation within the indicated period, thus indicated that both solutions were stable for at least 24 h, which was sufficient to complete the whole analytical process. The proposed method

was also applied for the assay of Risperidone in tablet formulation (in triplicate) and the results are presented in Table 4. The results obtained were good agreement with the label claims.

TABLE 1: DATA FOR STANDARD CURVE

Concentration (µg/ml)	Absorbance
0.00	0.000
2.5	0.134
5	0.278
10	0.525
15	0.785
20	1.014

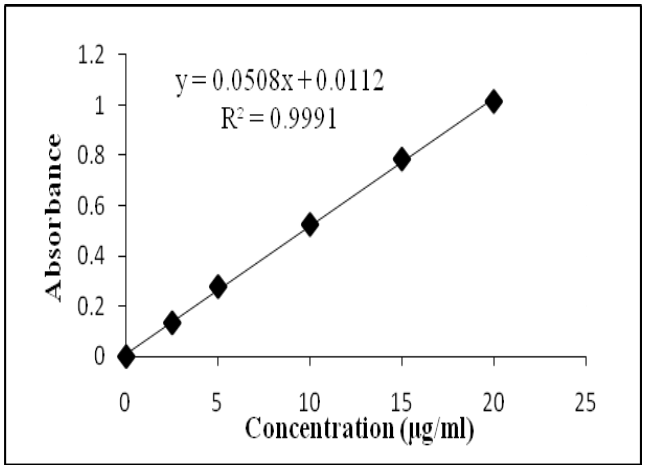

FIG. 2: STANDARD CURVE OF RISPERIDONE

TABLE 2: VALIDATION PARAMETERS

Parameters	Results	
Absorption maxima(nm)	202	
Linearity range (µg/ml)	2.5to 20	
Standard Regression equation	Y = 0.0508X + 0.0112	
Correlation coefficient	0.9991	
LOD (µg/ml)	1.05	
LOQ (µg/ml)	3.34	
Stability (hrs)	48	
Precision	Concntration	Intraday (%RSD) / Interday (%RSD)
	5(µg/ml)	0.385 / 0.313

TABLE 3: RECOVERY STUDY

Level of Addition (%)	Formulation (µg/ml)	Addition of pure drug (µg/ml)	% Recovery of pure drug	Recovery (%)±S.D.
80	5	4	100.5	
100	5	5	100.5	100.67±0.29
120	5	6	101.0	

TABLE 4: DETERMINATIONS OF ACTIVE INGREDIENTS IN TABLETS

Sample	Label claimed	Amount found	% Labeled Claim*
Risperidone	2 mg/tablet	2.01±0.008	100.5

* Average of three determinations

CONCLUSION: The proposed method was simple, sensitive and reliable with good precision and accuracy. The proposed method is specific while estimating the commercial formulations without interference of excipients and other additives. Hence, this method can be used for the routine determination of Risperidone in pure samples and pharmaceutical formulations.

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