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Development and Validation of UV Spectroscopic Method for Estimation of Ranolazine in Tablet Dosage Form

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ABSTRACT

To develop and validate simple, rapid, linear, accurate, precise and economical UV Spectroscopic method for estimation of Ranolazine in tablet dosage form. The drug is freely soluble in analytical grade methanol. The drug was identified in terms of solubility studies and on the basis of melting point which was done on melting point apparatus of Equiptronics. Ranolazine showed absorption maxima were determined in analytical grade methanol. The drug obeyed the Beer's law and showed good correlation of concentration with absorption which reflect in linearity. The UV spectroscopic method was developed for estimation of Ranolazine in tablet dosage form and also validated as per ICH guidelines. The drug is freely soluble in analytical grade methanol, slightly soluble acetonitrile and very slightly soluble in analytical grade water. So, the analytical grade methanol is used as a diluent in method. The melting point of Ranolazine was found to be 120-122°C (uncorrected). It showed absorption maxima 235 nm in analytical grade methanol. On the basis of absorption spectrum the working concentration was set on 8 µg/ml (PPM). The linearity was observed between 2-12 µg/ml (PPM). The results of analysis were validated by recovery studies. The recovery was found to be 98.75, 101 and 98.33% for three levels respectively. The % RSD for precision was found to be 0.6353% which was within acceptance criteria as per ICH guidelines. A simple, rapid, linear, accurate, precise and economical UV Spectroscopic method has been developed for estimation of Ranolazine in tablet dosage form. The method could be considered for the determination of Ranolazine in tablet dosage form in quality control laboratories.

Keywords: Ranolazine, UV Spectrophotometer, Melting Point, Assay Method, Validation, Accuracy, Linearity, Ruggedness, Precision.

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INTRODUCTION

Ranolazine Hydrochloride (RAN) is a piperazine derivative. Ranolazine is a strong base with pKa values of 13.6 [1]. On January 31, 2006, Ranolazine was approved for use in the United States by the FDA for the treatment of chronic angina [2]. Structurally it is N- (2, 6- dimethylphenyl) -2- [4-[2-hydroxy-3- (2- methoxyphenoxy) propyl] piperazin-1-yl] acetamide. RAN is believed to have its effects via altering the trans-cellular late sodium current [3]. Ranolazine is to inhibit late INa thus preventing sodium overload of the cell. As a consequence, Ranolazine prevents reverse mode sodium–calcium exchange and thus diastolic accumulation of calcium possibly resulting in improved diastolic tone and improved coronary blood flow. As a late INa inhibitor, Ranolazine was also shown to increase action potential duration and thus modestly QT interval by 2 - 5 ms. This effect, however, is not heart rate-dependent and cannot be exaggerated during bradycardia. Furthermore, Ranolazine does not induce early after depolarization and does not increase dispersion of repolarization across the left ventricular wall [4,5].

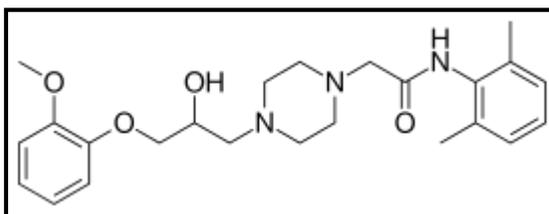


Figure 1: Chemical Structure of Ranolazine

RAN is indicated for the treatment of chronic angina. RAN may be used with beta blockers, nitrates, calcium channel blockers, antiplatelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers. RAN has antianginal and anti-ischemic effects that does not depend on reduction in heart rate or blood pressure [6, 7]. RAN has not appeared in any pharmacopoeia yet. Few spectrophotometric [8], HPLC [8, 9, 10], LC-MS [11, 17, 13] and LCMS- MS [12, 18] methods were reported in literature for determination of RAN. However, most of these reported in combination and most of these methods were related to the quantitative assay of RAN in human or dog plasma [7, 14, 15, 16]. This indicates that so far no UV method exists for the estimation and determination of Ranolazine in tablet dosage forms. The aim of the study was to develop a simple, precise, linear, economic and accurate UV method for determination of Ranolazine in tablet dosage forms.

MATERIALS AND METHOD

Instruments :

Shimadzu double beam UV-visible spectrophotometer 1700 Ultra with matched pair

Quartz cells corresponding to 1 cm path length and spectral bandwidth of 1 nm, Bath sonicator and citizen weighing balance. Melting point apparatus of Equiptronics were used.

Materials:

Ranolazine was obtained as a gift sample. Ranolazine tablets were procured from local pharmacy. Methanol used was of analytical grade. Freshly prepared solutions were employed.

Method development:

Determination of λ_{max}

Solution was prepared by dissolving 10 mg of Ranolazine USP standard in 100 ml of methanol to get concentration of 100 $\mu\text{g/ml}$ further Pipette out 4 ml from above stock and make upto the mark 100 ml with diluent. This solution was subjected to scanning between 200-400 nm and absorption maximum was determined [19, 20].

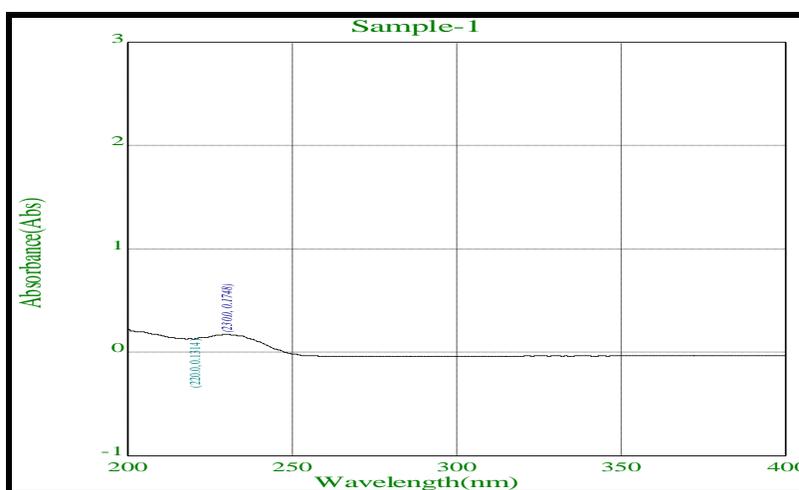


Figure. 2: Calibration Curve

Preparation of Working concentration

Preparation of Standard stock solution:

Standard solution was prepared by dissolving 20 mg of Ranolazine USP standard in 100 ml of diluent to get concentration of 200 $\mu\text{g/ml}$.

Preparation of Standard solution:

Pipette out 4 ml from standard stock solution and diluted up to 100 ml with analytical grade methanol to get concentration of 8 $\mu\text{g/ml}$ (PPM).

Procedure for UV reading

Blank Solution: (For Auto zero)

Fill the cuvette with analytical grade methanol. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Standard Solution:

Fill the cuvette with standard solution. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Sample Solution:

Rinse the cuvette using sample solution. Fill the cuvette with sample solution. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Procedure for sample preparations

For analysis of commercial formulations; twenty tablets are taken weighed it and powdered. The powder equivalent to 20 mg of Ranolazine was accurately weighed and transferred into the 100 ml of volumetric flask, added 60 ml analytical grade methanol, the solution was sonicated for 20 min. After sonication cool the flask and diluted upto 100 ml with analytical grade methanol. Filtered the solution through whatmann filter paper. Pipette out 4 ml of the above filtrate and diluted up to 100 ml with analytical grade methanol. The absorbance was measured at 235 nm [21, 22, 23, 24]. The absorbance was recorded.

Table 1: Absorbance of Dosage Form

Torrent Pharmaceutical Limited (500 mg)		
Sr. no.	Sample	Absorbance
1	Blank	0.0001
2	Standard	0.6532
3	Sample	0.6494

Table 2: Dosage Form Specifications

Type	Company	M.D.	E.D.	Batch No.	Average weight (g)	Assay (%)
1	Torrent Pharma LTD (500mg)	06/2017	07/2020	RN 50722	0.6027	98.5

Method of validation

The proposed method was developed by using linearity, accuracy, precision and ruggedness as per ICH guidelines, 1996 [21, 22, 23, 24].

Linearity:

The linearity of the proposed assay was studied in the concentration range 2 - 12 PPM at 235nm. The calibration data showed a linear relationship between concentrations.

Table 3: Linearity Studies

Sr. no.	Sample Concentration	Absorbance
1	2 PPM	0.1900
2	4 PPM	0.3378

3	6 PPM	0.4832
4	8 PPM	0.6517
5	10 PPM	0.8086
6	12 PPM	0.9953
Correlation coefficient		0.999

Accuracy:

To ensure the accuracy of the method, recovery study was performed by preparing 3 sample solutions of 80, 100 and 120% of working concentration and adding a known amount of active drug to each sample solution and dissolved in 100ml of volumetric flask with analytical grade methanol and measuring the absorbance at 235nm.

Table 4: Accuracy Studies

Accuracy (%)	Qty weighed (mg)	Qty found (mg)	Recovery (98-102%)
80	0.8	0.79	98.75
100	1	1.01	101.00
120	1.2	1.18	98.33

Precision:

The precision of the method was demonstrated by inter-day and intra-day variation studies. Five sample solutions were made and the %RSD was calculated.

Table 5: Precision studies

Sr. No.	Sample Solution	Absorbance
1	Sample Solution 1	0.6548
2	Sample Solution 2	0.6478
3	Sample Solution 3	0.6512
4	Sample Solution 4	0.6541
5	Sample Solution 5	0.6451
MEAN		0.6506
SD		0.0041
% RSD		0.6353

Ruggedness:

Ruggedness is a measure of the reproducibility of a test result under normal, expected operating condition from instrument to instrument and from analyst to analyst.

Table 6: Results for Ruggedness Studies

Sr. No.	Analyst	Results	Mean	% Assay	% RSD
1	Analyst 1	0.6488 0.6478	0.6513	98.7	0.2859
2	Analyst 2	0.6574 0.6541	0.6557	99.1	

RESULTS AND DISCUSSION

Solubility of Ranolazine

Solubility test was passed as per criteria.

Table 7: Results for solubility studies

Sr. no.	Title	Result
1	Analytical grade methanol	Soluble
2	Analytical grade Acetonitrile	Slightly soluble
3	Analytical grade Water	Very Slightly Soluble

Melting point of Ranolazine

The melting point of Ranolazine was found to be 120-122°C (uncorrected).

Results for linearity for assay method of Ranolazine

The linearity of method was determined at concentration level ranging from 2 to 12 µg/ml (PPM).

The correlation coefficient value was found to be (R^2) **0.999**.

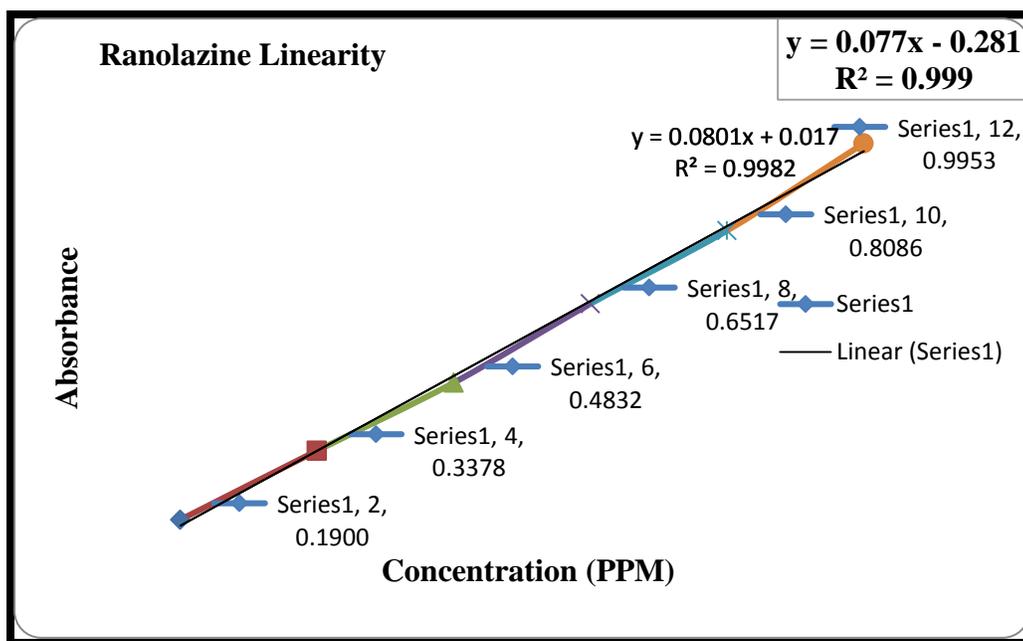


Figure. 3: Ranolazine Standard Curve

Results for accuracy for assay method of Ranolazine

The accuracy of the method was determined by recovery experiments. The recovery studies were carried out and the percentage recovery were calculated and represented in Table - 4. The high percentage of recovery indicates that the proposed method is highly accurate. Accuracy results were found within acceptance criteria that are within 98-102%.

Results for precision for assay method of Ranolazine

The % RSD for different sample of precision was found to be 0.6353 and it is within acceptance criteria represented in Table - 5.

Results for ruggedness for assay method of Ranolazine

The %RSD for different sample of ruggedness was found to be 0.2859 and it is within acceptance criteria represented in Table - 6.

CONCLUSION

A method for the estimation of Ranolazine in tablet form has been developed. From the spectrum of Ranolazine, it was found that the maximum absorbance was 235 nm in analytical grade methanol. A good linear relationship was observed in the concentration range of 2-12 µg/ml (PPM). The high percentage recovery indicates high accuracy of the method. This demonstrates that the developed spectroscopic method is simple, linear, accurate, rugged and precise for the estimation of Ranolazine in solid dosage forms. Hence, the method could be considered for the determination of Ranolazine in quality control laboratories.

ABBREVIATIONS

1. PPM - Parts per Million
2. RAN - Ranolazine
3. nm - Nanometer
4. HPLC - High Performance Liquid Chromatography
5. UV - Ultra violet
6. HBV - Hepatitis B virus
7. DNA - Deoxyribonucleic acid
8. HIV - Human Immunodeficiency Virus
9. ICH - International Council for Harmonization
10. RSD - Relative Standard Deviation
11. SD - Standard Deviation
12. Qty - Quantity
13. C - Celsius
14. M.D. - Manufacturing Date
15. E.D. - Expiry Date

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