A NOVEL SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF RANOLAZINE IN BULK DRUG AND IT'S FORMULATION

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ABSTRACT:
The simple, rapid, precise, accurate, robust and economical analytical method has been developed for estimation of Ranolazine in bulk and pharmaceutical dosage form. This study describes the validation of an UV Spectrophotometric method for quantitative determination of Ranolazine in pharmaceutical dosage form using acetate buffer (pH 4.4) as solvent. The maximum absorbance was found at 272 nm. The Linearity was found to be in range of 5 to 40µg/ml. The %RSD for Intraday and Interday precision studies was found to be 0.793 and 0.793 respectively. The % assay was found to be 99.6%±0.05. The average % recovery of ranoalazine was found to be in between 98.5-101.7%. LOD and LOQ was found to be 0.58 µg/ml and 1.75 µg/ml respectively. The results suggest that this method can be employed for routine analysis of Ranolazine in bulk and commercial pharmaceutical formulations.

KEY WORDS: Ranolazine, UV Spectrophotometric Method, Method Development and Method Validation.

INTRODUCTION:

The drug of choice for treating Angina Pectoris is Ranolazine.It is a piperazine derivative is a well-tolerated medication that selectively inhibits the late sodium current. It's IUPAC name is N-(2,6-dimethylphenyl)-4(2-hydroxy-3-[2-meth-oxyphenoxy]-propyl)-1-piperazine acetamide dihydrochloride (Fig.1) . [1-2] At clinically therapeutic levels, ranolazine inhibits sodium and potassium ion channel currents. Inhibition of the late phase of the inward sodium current during cardiac repolarization. Lowering that current causes intracellular calcium levels to decrease. As a result, the heart wall becomes less tense, which lowers the amount of oxygen needed by the muscles. [3-4] A white crystalline powder which is freely soluble in methanol, acetate buffer and dichloromethane. Sparingly soluble in ethanol, acetone and acetonitrile. Very slightly soluble in water.[5-7] According to a review of the literature, UV Spectrophotometric analytical methods were created at various conditions for the analysis of ranolazine in pharmaceutical tablet dosage forms, and bulk drug samples.[8-10] There are several dosage forms of ranolazine available in the market, including film-coated, oval-shaped, extended-release tablets. Ranolazine dose range is 500 mg to 1000 mg twice daily.[11-12] One of the methods used most commonly in pharmaceutical analysis is ultraviolet-visible spectrophotometry. Beer- Lambert law is the main principle governing Spectrophotometric quantitative analysis.[13-15] The goal of this research was to create a Spectrophotometric approach that was easy to use, precise, accurate, quick, repeatable, and economical for measuring Ranolazine at a quantitative level. With the help of the International Conference on Harmonization (ICH) Guidelines, we established a method in this approach for the measurement of Ranolazine in bulk drug samples and pharmaceutical dosage form.

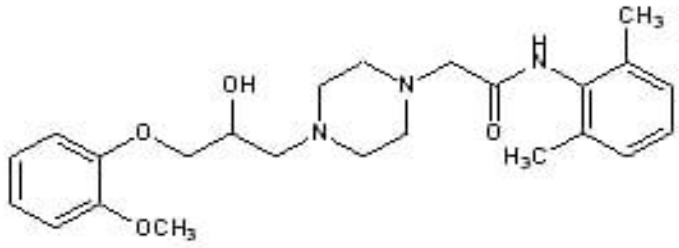

Fig.1: Chemical Structure of Ranolazine

MATERIALS AND METHODS:

Materials:

Ammonium acetate, glacial acetic acid, distilled water, ranolazine pure drug were procured from Research Lab Fine Chem Industry. Ranolazine extended release tablets(500 mg) were purchased from local pharmacy store.

Instruments Used:

UV-Visible spectrophotometer with UV Win software and make was PG-Instruments. Weighing balances and matching quartz cells with a 1 cm cell path length were utilized along with the mentioned equipment, which had automatic wavelength accuracy of 0.1 nm and pH meter.

METHOD DEVELOPMENT

Standard stock solution preparation:

A 10 µg/mL standard stock solution of ranolazine was prepared by dissolving 10 mg of compound in a 10 ml volumetric flask using acetate buffer at pH 4.4. Working standard solutions were then made by diluting this stock solution (1000 µg/ml) with the same acetate buffer[16-17].

Selection of wavelength for analysis of Ranolazine:

The stock solution was then scanned in UV region from 200- 400 nm to get λmax of 272 nm.

Selection of solvent :

Several trials were done to find out the right solvent system for dissolving the drug. The solvents like methanol, distilled water, different phosphate buffers, acetate buffer of different pH were tried depending on the solubility of the Ranolazine. The solvents such as methanol, phosphate buffer, acetate buffer were tried based on the solubility of the drug.

Method validation:

According to ICH Q2 (R1) and USP criteria, the suggested technique was validated for a number of parameters, including linearity, precision, assay, accuracy, robustness and limit of detection (LOD),limit of quantification (LOQ).[18-19]

Linearity:

Different concentrations of ranolazine solutions were prepared by using 100 µg/ml to give concentrations from 5 to 40µg/ml. The absorbance of these solutions is noted at wavelength of 272nm. The graph of concentration vs absorbance of linearity solutions was plotted.

Precision:

Intraday and Interday (between 2 days) precision study was carried out by using 20 µg/ml concentration of Ranolazine and analysed.

Preparation of sample solution for %assay:

Take ten tablets and weighed individually, made it into fine powder by using Mortar and pestle. From this powder weighed accurately a quantity of powder equivalent to 100 mg of Ranolazine. Transfer it into the 100 mL volumetric flask, add few mL acetate buffer to dissolve the powder and then volume was made up to mark with acetate buffer. Filter the solution through Whatmann filter paper and pipette out 1mL from the solution and diluted up to the 10 mL with acetate buffer to get concentration 100 µg/mL and it was further diluted to give 20µg/mL and measure the absorbance of six replicates at 272nm. Determine the amount of % Ranolazine in tablet according to the following formula.[20-21]

$$\% \text{ Assay} = \frac{\text{WS X AT X Sample D. F. X Avg. wt.}}{\text{AS X Standard D. F. X WT X LC}} \text{ X PS}$$

Where,

WS = Weight of standard

WT = Weight of Test

AT = Absorbance of Ranolazine in the test solution

AS = Absorbance of Ranolazine in the standard solution

Standard D.F = Standard dilution factor

Sample D.F. = Sample dilution factor

PS = Purity of working standard [%]

LC = Label claim of the Ranolazine

Accuracy:

Accuracy of the proposed method was determined using recovery studies. The recovery studies were carried out by adding different amounts (80%, 100%, and 120%) of the pure drug to the pre-analysed formulation. The solutions were prepared in triplicates and the %recovery was calculated.

Robustness:

Robustness was obtained by performing the analysis at two different wavelengths (±5 nm). The results were reported.

Limit of Detection and Limit of Quantitation:

The parameters LOD and LOQ were determined on the basis of response and slope of the regression equation. The limit of detection (LOD) and the limit of quantitation (LOQ) of the drug were derived by calculating using the following equations designated by International Conference on Harmonization (ICH Q2) guidelines[22-25].

$LOD = 3.3 \times \sigma/S$

$LOQ = 10\times \sigma/S$

Where,

σ = Standard deviation of the response, S = Slope of the calibration curve.

RESULTS AND DISCUSSION:

Linearity:

The linearity data of Ranolazine lies in between 5 to 40µg/ml was shown in table 1 . Absorbtion spectrum , Calibration curve were shown in below Fig.2 and 3 respectively. The optical characteristics (correlation coefficient, intercept and slope) were calculated for Ranolazine and results were shown in Table 2.

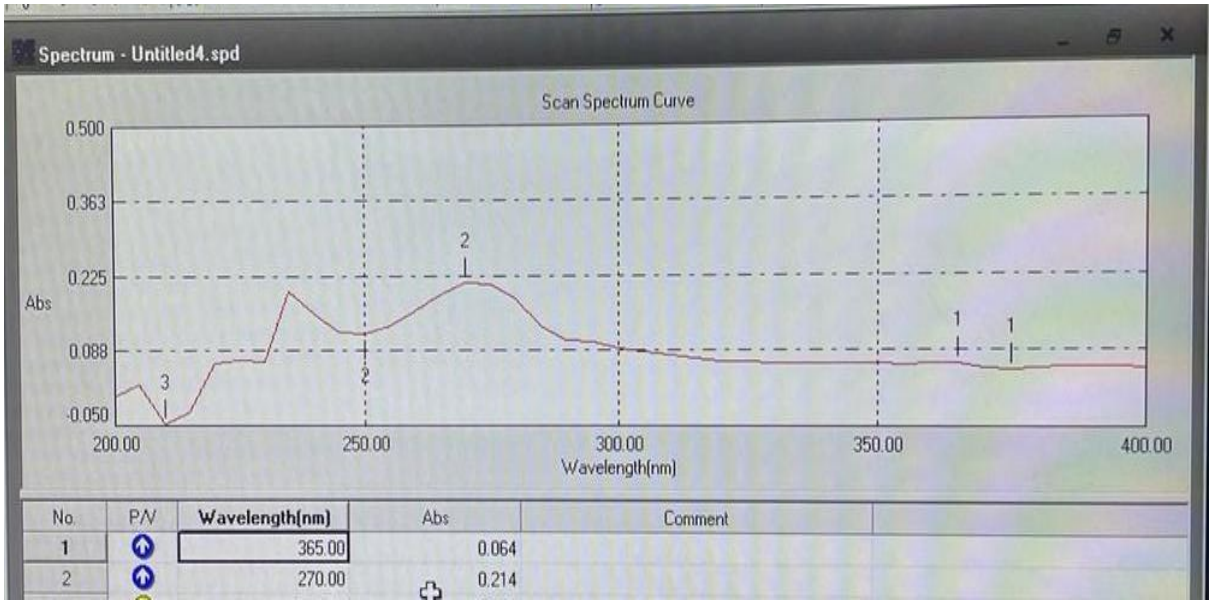

Fig.2 Absorbance Spectrum of Ranolazine at 272nm

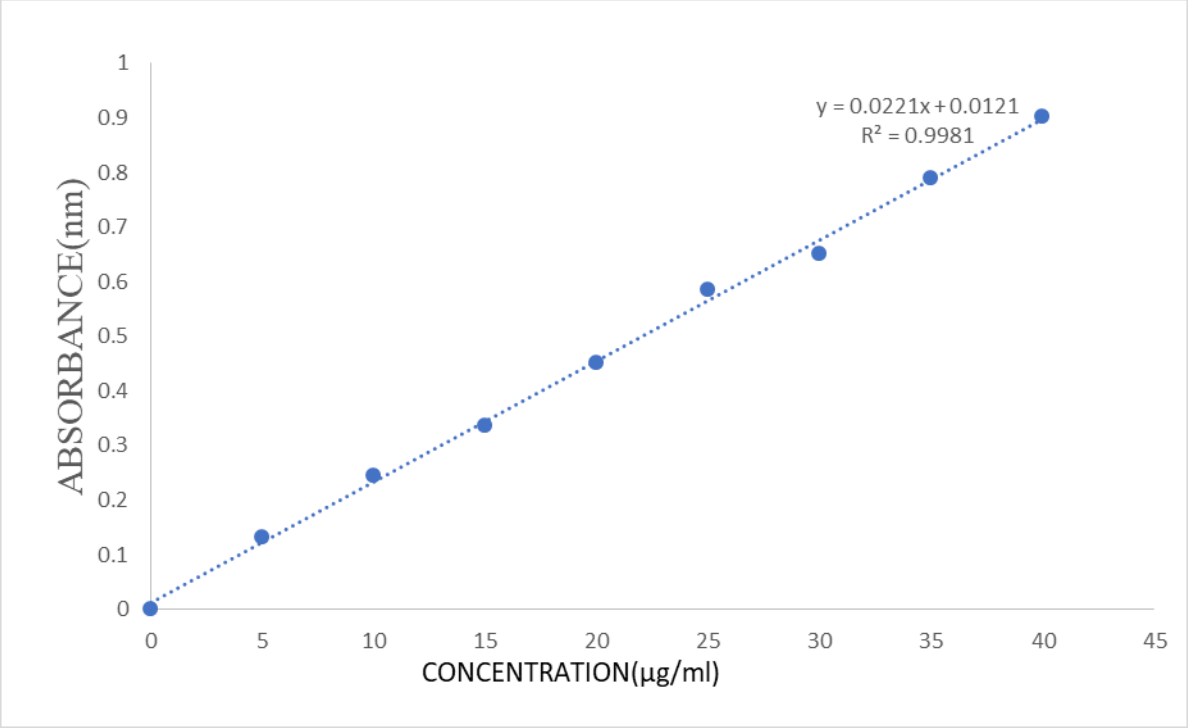

Fig.3 Calibration curve of Ranolazine at 272nm

Table-1: Linearity data of Ranolazine

Conc (µg/ml)	**Absorbance**
5	0.132
10	0.245
15	0.336
20	0.452
25	0.584
30	0.652
35	0.789
40	0.901

Table-2 Optical characteristics of Ranolazine

Parameters	**Ranolazine**
λmax	272
Slope	0.0221
Linearity	5 to 40 µg/ml
Correlation coefficient	0.998
Intercept	0.0121

Discussion: Calibration curve was plotted and correlation coefficient was found to be 0.998. So, there was a good correlation between absorbance and concentration.

Precision :

Intraday and Interday precision data was shown in Table-3 and 4 respectively.

Table-3 Intraday Precision data of Ranolazine

Conc (µg/ml)	**Absorbance**
20	0.449
20	0.447
20	0.455
20	0.448
20	0.445
20	0.446
Mean	0.448
SD	0.0035
%RSD	0.794

Table-4 Interday Precision data of Ranolazine

Conc (µg/ml)	**Day-1**	**Day-2**
20	0.449	0.460
20	0.447	0.460
20	0.455	0.460
20	0.448	0.459
20	0.445	0.462
20	0.446	0.460
Mean	0.448	0.460
SD	0.0035	0.000983
%RSD	0.793	0.213

Discussion: The %RSD for Intraday and Iinter day precision was found to be <2%. It indicates that the method was precise.

Assay :

Assay results of Ranolazine was shown in Table-5

Table–5 % Assay data of Ranolazine (n=6)

Label Claim	Amount Found	Assay% ± SD
500mg	498mg	99.6 ± 0.05%

Discussion: The % assay of Ranolazine was found to be 99.6 ± 0.05%. It shows that UV- Spectrophotometric method developed was successful in determining ranolazine from tablet dosage form.

Accuracy :

Accuracy was carried out by spiking the sample solutions with standard solution 80%, 100% and 120% for three replicates data was shown in Table-6

Table-6 Accuracy data of Ranolazine

(% level)	Amount taken (µg/ml)	Amount added (µg/ml)	Amount recovered	% recovered	Average Recovery
80 80 80	20 20 20	16 16 16	35.4 35.5 35.4	98.4% 98.8% 98.4%	98.5
100 100 100	20 20 20	20 20 20	39.80 39.9 39.88	99.5% 99.8% 99.7%	99.6
120 120 120	20 20 20	24 24 24	44.8 44.5 44.4	102% 102.3% 101%	101.7

Discussion: The average % recovery of Ranolazine was found to be in between 98.5-101.7% .

Robustness :

Robustness data was shown in Table-7

Table-7 : Robustness data of Ranolazine(n=3)

S.No	Wavelength	Absorbance Mean ± SD
1	272	0.462 ± 0.010
2	277	0.345 ± 0.005
3	267	0.411 ± 0.011

Discussion: There was no much variation in the absorbance with change in wavelength.

Limit of Detection and Limit of Quantification :

LOD and LOQ was calculated and shown in Table-8

Table-8 : LOD and LOQ data

Parameters	Ranolazine (µg/ml)
LOD	0.58
LOQ	1.75

Discussion: LOD and LOQ values for Ranolazine was found to be 0.58(µg/ml) and 1.75(µg/ml) .

CONCLUSION:

From the above experimental results and parameters it was concluded that, this developed UV-Spectroscopy method for the estimation of Ranolazine was found to be simple , precise, accurate, robust, economic and rapid makes this method more acceptable and cost effective and it can be effectively applied for routine analysis of Ranolazine in bulk and commercial pharmaceutical formulations.

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