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MULTIVARIATE TECHNIQUE FOR SPECTROPHOTOMETRIC ESTIMATION OF RANITIDINE HYDROCHLORIDE IN BULK DRUG AND PHARMACEUTICAL FORMULATIONS

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ABSTRACT

The main objective of the present research is to develop and validate a simple, precise, reliable, and convenient UV-visible spectroscopic technique for the estimation of ranitidine hydrochloride in accordance with ICH Q2 (R1) guidelines. Multivariate calibration technique uses linear regression analysis to determine the correlation between concentration and absorbance at five selected equidistant wavelengths. Ranitidine hydrochloride showed a maximum absorbance at 314 nm using water as a solvent. A linear plot was obtained with a regression coefficient of 0.9990 for the concentrations between 8-12 µg mL^{-1}. The % RSD for intra-day and inter-day precision were found to be 0.539 and 0.389, respectively. The assay was determined and found to be 99.99% and 100.08% w/w.

Keywords: Ranitidine hydrochloride, UV-visible spectrophotometry, Multivariate calibration, ICH guidelines

INTRODUCTION

Ranitidine Hydrochloride, chemically known as (E)-1-N'-[2-[[5-[(dimethylamino)methyl] furan-2-yl] methylsulfanyl]ethyl]-1-N-methyl-2-nitroethene-1,1-diamine; hydrochloride. The molecular formula and molecular weight were found to be $C_{13}H_{23}ClN_4O_3S$ and 350.87 g mol^{-1} respectively **[1]**. Ranitidine Hydrochloride **(Figure 1)** is an H_2-receptor antagonist with Antacid activity. They prevent parietal cells from producing both meal-stimulated acid release and

normal acid storage. Blocking H_2-receptors reduces acid accumulation by histamine in enterochromaffin-like cells via two channels. Acetylcholine and gastrin are two new inducers of acid release; however, they have a lower impact on parietal cells **[1]**. Literature surveys demonstrate various techniques for estimating Ranitidine hydrochloride, like UV-Visible Spectroscopy (UV) **[2-9]**, High Performance Liquid Chromatography (HPLC) [10-15], High Performance Thin Layer Chromatography (HPTLC) [16-20] and Electrophoresis **[21]**.

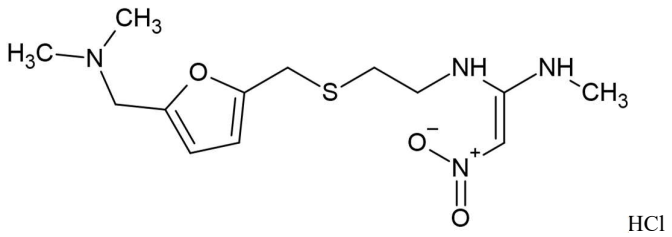

Figure 1: Chemical structure of Ranitidine hydrochloride

The suggested technique provides higher accuracy in results as it directly evaluates Ranitidine Hydrochloride with greater accuracy and precision than a classical UV-Visible method. This multivariate calibration method simplifies the result and converts to "m" value as a reliant variable. The absorbance of an analyte (X), i.e., Ranitidine hydrochloride, is scanned at 5 different wavelengths surrounding its absorbance maxima (λ = 310, 312, 314, 316, and 318 nm). The following formula can be expressed by,

$$A_{\lambda 310} = a\ X\ C_x + \ k_1 \text{ ---------- (1)}$$

$$A_{\lambda 312} = b\ X\ C_x + \ k_2 \text{ ---------- (2)}$$

$$A_{\lambda 314} = c\ X\ C_x + \ k_3 \text{ ---------- (3)}$$

$$A_{\lambda 316} = d\ X\ C_x + \ k_4 \text{ ---------- (4)}$$

$$A_{\lambda 318} = e\ X\ C_x + \ k_5 \text{ ---------- (5)}$$

Equation system from (1-5) represent the analyte's absorbance at specific wavelengths i.e., 310, 312, 314, 316, and 318 nm, linear regression slopes at (a, b, c, d, e), intercepts at (k_1, k_2, k_3, k_4, k_5), and concentration (C_x) respectively. A_T and K_T are the summations of absorbance from the regression equations at five selected wavelengths **[22-29]**.

$$A_T = a\ X\ C_x + \ b\ X\ C_x + \ c\ X\ C_x + \ d\ X\ C_x + \ e\ X\ C_x + \ K_T \text{ ---------- (6)}$$

The above equation can be further condensed to

$$A_T = C_x\ (a + b + c + d + e) + \ K_T \text{ --- (7)}$$

$$C_x = \frac{A_T - K_T}{(a + b + c + d + e)}$$

MATERIALS AND METHODS

Required chemicals and reagents

- Distilled water
- The marketed tablet formulation used was Rantac 150 mg

manufactured by J.B CHEMICALS AND PHARMACEUTICALS PVT.LTD, acquired from a local medical shop.

Instrumentation

- Ultra Sonicator
- UV-Visible double beam spectrophotometer [LAB INDIA 3092]
- Analytical balance
- Micropipette

Analytical method development

Solvent selection

Ranitidine Hydrochloride was found to be freely soluble in water. Further dilutions of the standard and sample solutions were made by using water as a solvent.

Standard stock solution

By dissolving 100 milligrams of the standard drug in water and then making up to the mark using the same solvent in a 100 ml standard flask, a standard stock solution of Ranitidine hydrochloride was prepared. This standard stock solution was used to make an aliquot of solutions with concentrations ranging from 8–12 µg mL^{-1}.

Determination of λ_{max}

The standard stock solution was diluted in water to obtain 10 µg mL^{-1}, scanned in the UV region from 200 to 400 nm, to identify the maximum absorbance. The λ_{max} was at 314 nm (Figure 2). The linear curve was obtained with a graph plotting the absorbance against the concentration range of 8–12 µg mL^{-1}. To minimise the instrument oscillations and enhance the correlation, the solutions were scanned over these wavelengths surrounding 314 nm, including 310, 312, 314, 316, and 318 nm, respectively.

Preparation of sample solution

Ten tablets of ranitidine hydrochloride were accurately weighed and pulverised. A weight equivalent to 100 mg was added to a 100 ml standard flask, it was further dissolved, diluted, and made up to the mark with water to get 100 µg mL^{-1}. The resulting solution is used for further analysis after filtering.

Method Validation

The above method has been evaluated in accordance with ICH Q2B guidelines for sensitivity, precision, accuracy, and linearity **[30]**.

Linearity

The standard stock solution of ranitidine hydrochloride was used to prepare different concentrations ranging from 8 to 12 µg mL^{-1}. To eliminate instrumental errors and enhance correlation these solutions were scanned over the wavelength range surrounding from

their respective absorbance maxima at 310, 312, 314, 316, and 318 nm. The absorbances were recorded, and a concentration versus absorbance graph was used to obtain the results. The limit of detection and

quantification were calculated using the formula below to determine the method's sensitivity **(Figure 3, Table 1)**.

Table 1: UV Calibration data at five distinct wavelengths

Concentration (µg mL^{-1})	Absorbance				
	310 nm	312 nm	314 nm	316 nm	318 nm
8	0.429	0.439	0.445	0.442	0.459
9	0.477	0.481	0.485	0.482	0.496
10	0.518	0.525	0.528	0.521	0.541
11	0.558	0.569	0.571	0.568	0.563
12	0.610	0.623	0.625	0.621	0.617

[#]**Average of 5 determinations; UV= Ultra Violet**

$$LOD = 3.3\ \sigma/S \quad \text{..... (8)}$$

$$LOQ = 10\ \sigma\ /S \quad \text{..... (9)}$$

Here, S stands for standard curve slope, and σ for the standard deviation (SD) of the lowest concentration.

Precision

10 µg mL^{-1} solution was scanned in the UV region from 200 to 400 nm six times in a short period of time on one day for intraday and six different days for interday to evaluate the precision studies.

Accuracy

The recovery study was assessed at 80%, 100%, and 120% using the standard addition technique**.** The standard and sample stock solutions were prepared. 0.5 ml of the standard solution was pipetted into three 10 ml volumetric flasks. 0.3, 0.5, and 0.7 ml of sample solution were added, respectively, and made up to 10 ml with water. These solutions were scanned in UV, and the % recovery was calculated.

Assay

By measuring the extracted tablet solution's absorbance at 314 nm, the amount of ranitidine hydrochloride that is present in the tablet dosage form has been determined.

RESULTS AND DISCUSSION

Using water as a solvent, the λ_{max} of Ranitidine Hydrochloride was found to be 314 nm **(Figure 2)**.

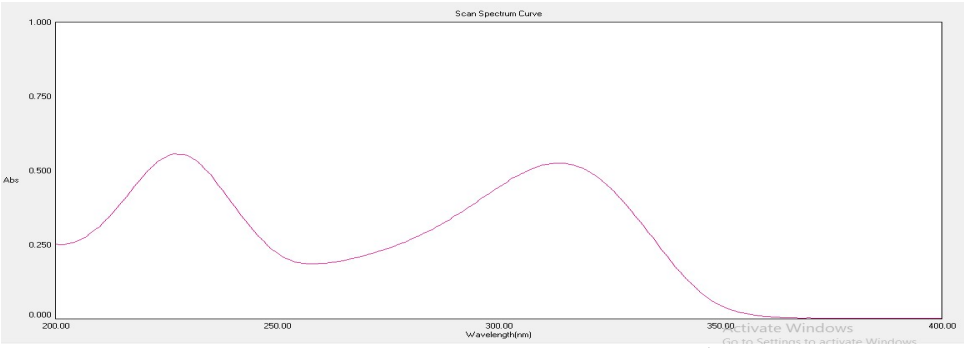

Figure 2: UV spectrum of Ranitidine Hydrochloride (10 µg mL^{-1}), λ_{max} at 314 nm

This approach is linear within the applied concentration range from 8 to 12 µg mL^{-1}. This linear regression analysis demonstrates a strong linear relationship with $R^2 = 0.9983$-0.9991 for all calibration plots. The % RSD for precision was found to be 0.539 and 0.389. The LOD and LOQ values were 0.2216 and 0.6717 g mL^{-1}, respectively. As a result, the obtained values were within the ICH validation parameter limits.

Linearity

Linearity at 310, 312, 314, 316, and 318 nm was recorded with concentration range from 8-12 µg mL^{-1} **(Figure 3)**, with low relative standard deviation values demonstrates the method accuracy and precision. LOD and LOQ were calculated. The calibration plots were shown in **Figures 4 to 8** and data is presented in **Table 2**.

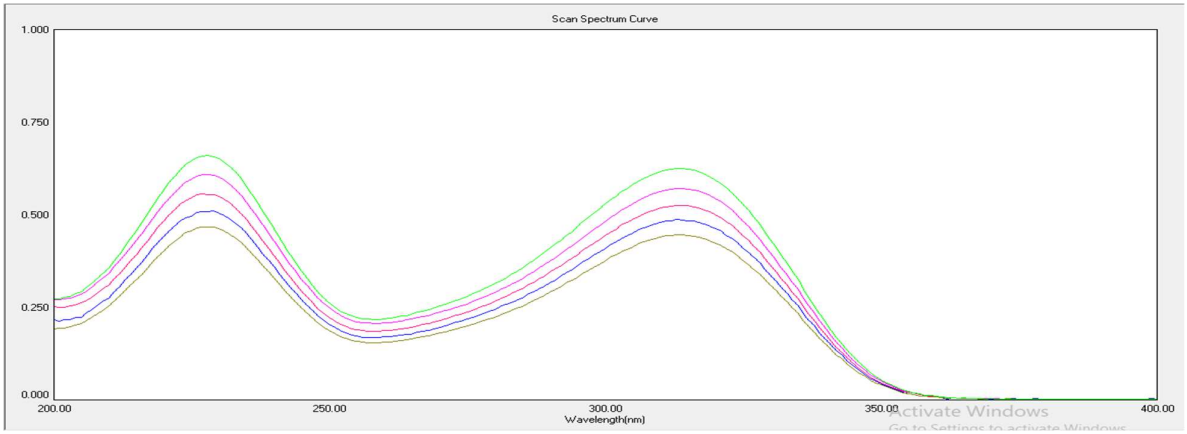

Figure 3: UV Spectrum of Ranitidine Hydrochloride showing linearity at 310nm

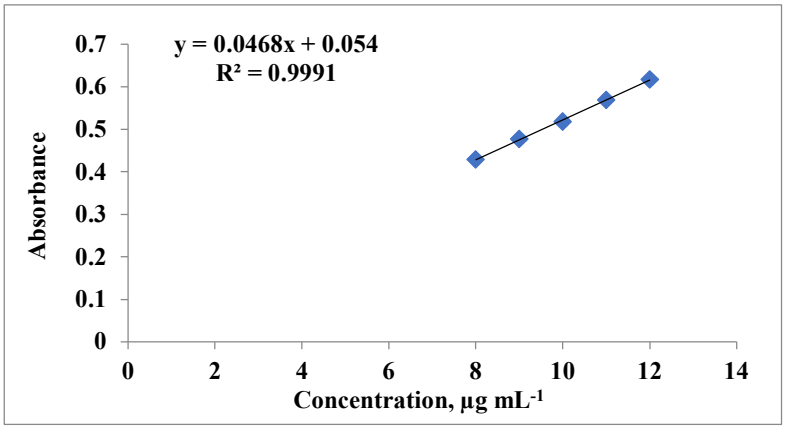

Figure 4: Calibration curve at 310 nm

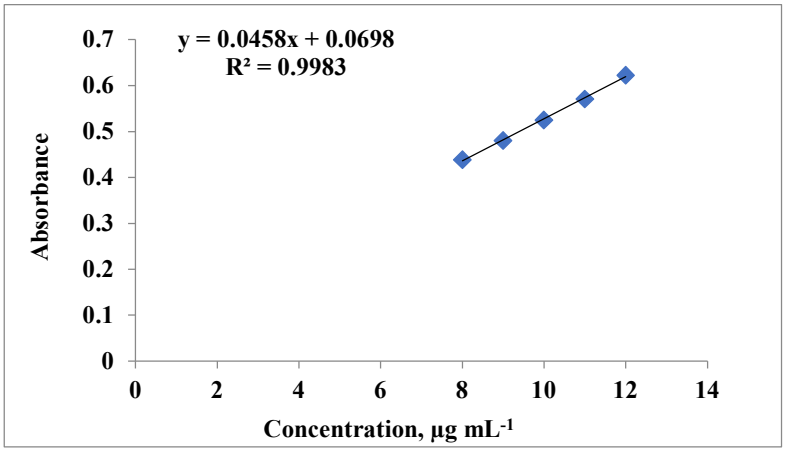

Figure 5: Calibration curve at 312 nm

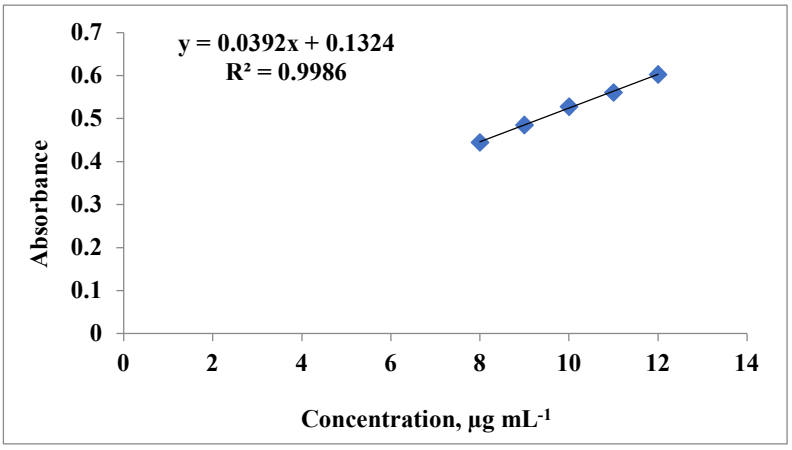

Figure 6: Calibration curve at 314 nm

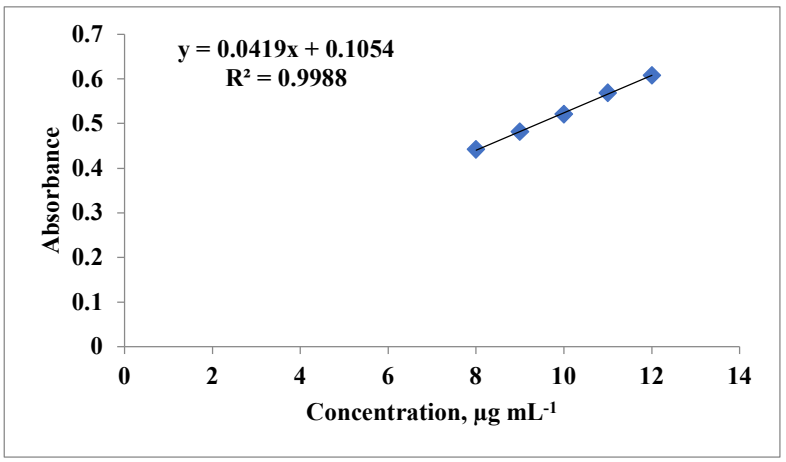

Figure 7: Calibration curve at 316 nm

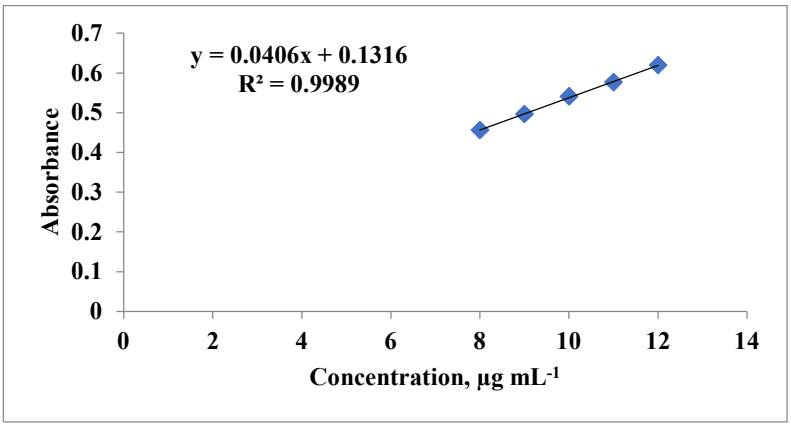

Figure 8: Calibration curve at 318 nm

Table 2: Linearity data with LOD and LOQ at selected five wavelengths.

Wavelength (nm)	Regression equation	R^2	LOD (µg mL^{-1})	LOQ (µg mL^{-1})	% RSD
310	y = 0.0468x + 0.054	0.9991	0.1892	0.5733	0.514
312	y = 0.0458x + 0.0698	0.9983	0.2509	0.7605	0.659
314	y = 0.0392x + 0.1324	0.9986	0.2216	0.6717	0.502
316	y = 0.0419x + 0.1054	0.9988	0.2088	0.6329	0.505
318	y =0.0406x + 0.1316	0.9989	0.2355	0.7138	0.538

*nm = nanometre; µg mL^{-1} = Microgram per millilitre

Precision

The low standard deviation values indicate that this technique is specific, and % RSD for the intra-day and inter-day precision were found to be 0.539 and 0.389, respectively. It lies within the limits of less than 2% at each wavelength. The low percentage value of relative standard deviation reveals that the suggested technique is accurate and precise **(Figure 9, 10)**.

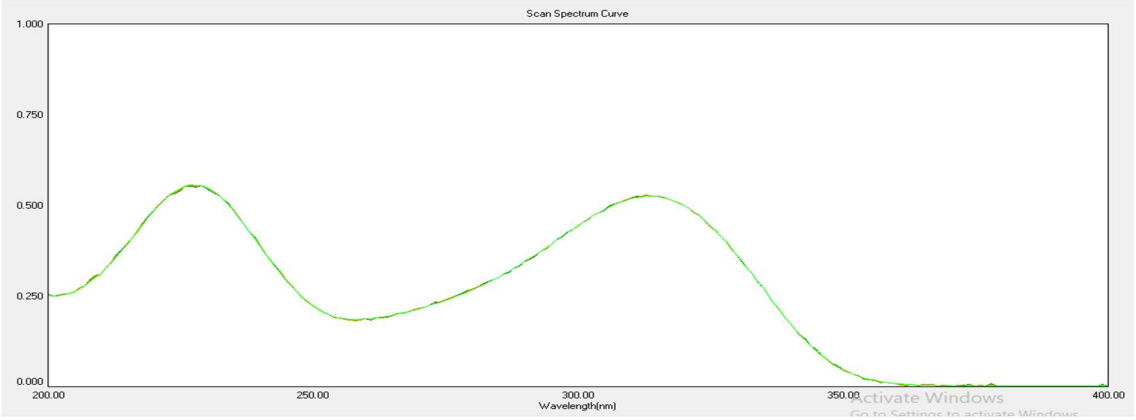

Figure 9: UV spectra showing intraday precision

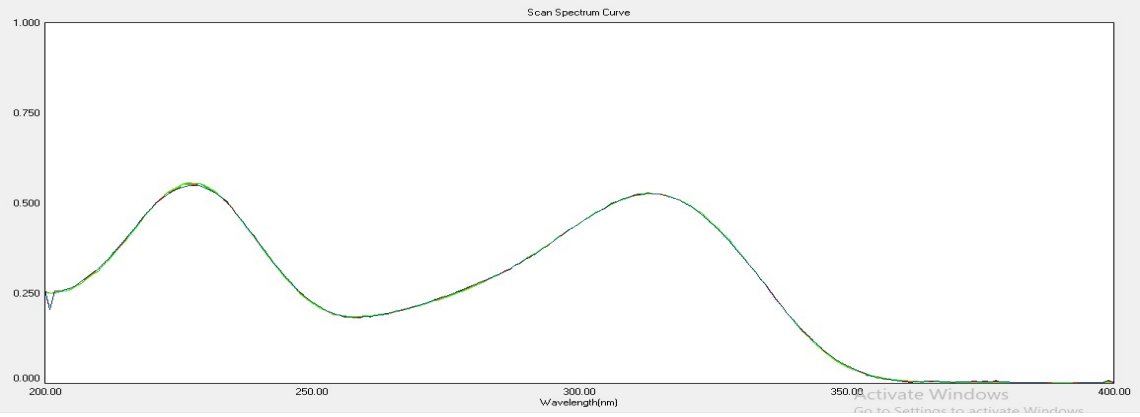

Figure 10: UV spectra showing interday precision

Recovery

The % recovery of Ranitidine Hydrochloride was from 99.38% to 101.90% w/w, as per ICH guidelines **(Figure 11, Table 3)**.

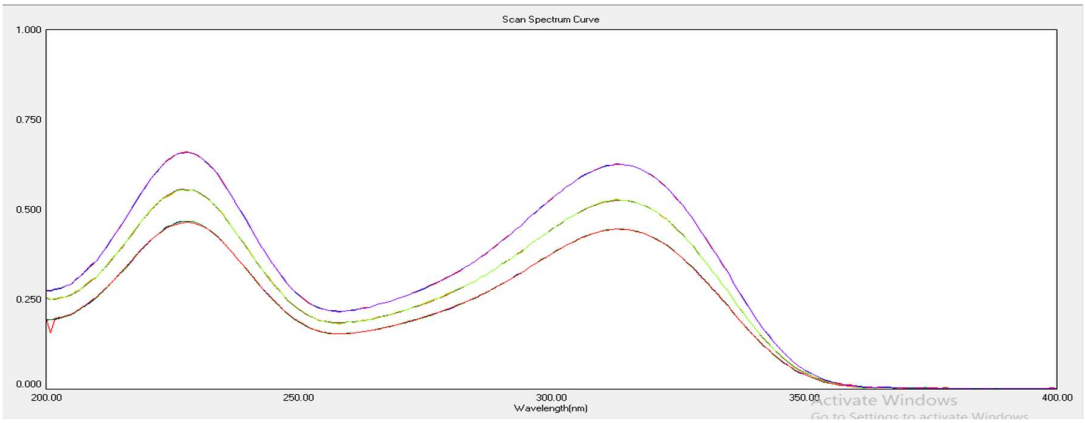

Figure 11: UV Spectrum showing accuracy of Ranitidine Hydrochloride

Table 3: Recovery Studies

Wavelength (nm)	Amount present (µg mL^{-1})	Amount added (µg mL^{-1})	Amount recovered (µg mL^{-1})	% Recovery
310 nm	5	3	7.95	99.38
		5	10.02	100.20
		7	12.21	101.75
312 nm	5	3	8.05	100.63
		5	10.12	101.20
		7	12.05	100.42
314 nm	5	3	8.12	101.50
		5	9.96	99.60
		7	12.05	100.42
316 nm	5	3	7.99	99.88
		5	9.97	99.70
		7	12.08	100.67
318 nm	5	3	8.14	101.75
		5	10.19	101.90
		7	12.02	100.17

Assay

The UV absorbance of the tablet formulation was recorded at 314 nm. The amount and assay results were 150.05 mg and 100.03% w/w, respectively with % RSD values as in **Table 4**.

Table 4: Assay of Ranitidine hydrochloride

Label claim (mg)	Amount obtained (mg)	% Assay
150	149.98	99.99
150	150.05	100.03
150	150.12	100.08
Average	150.05	100.03
SD		0.0467
% RSD		0.0467

CONCLUSION

This multivariate approach is more precise, accurate, sensitive, and cost-effective than a conventional UV-Visible spectrophotometry method for estimating Ranitidine Hydrochloride. This multilinear regression analysis has proven desirable for the testing standard drug and other dosage forms of Ranitidine Hydrochloride. This method is validated using ICH quality guidelines and found to be within the set limits of validation. In comparison to expensive and sophisticated techniques such as HPLC and HPTLC, this is a basic working procedure and can be used for routine analysis of Ranitidine Hydrochloride in bulk and pharmaceuticals.

ETHICAL STATEMENT

This study does not involve experiments on animals or human subjects.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article exists.

FUNDING SOURCES

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