Eurasian Journal of Analytical Chemistry

Eurasian J. Anal. Chem. 5(2): 170-176, 2010

Novel Reagent for the Spectrophotometric Determination of Ranitidine Hydrochloride

Badiadka Narayana*, Ashwini Krishnamurthy

Department of Post Graduate Studies and Research in Chemistry, Mangalore University, Mangalagangothri 574 199, India

Received: *26 October 2009****; Accepted:*** *23 December 2009*

Abstract

A simple method is presented for the determination of ranitidine hydrochloride (RNH). The method is based on the reaction of RNH with sodium periodate in acidic medium to liberate iodine. The liberated iodine then bleaches the dye crystal violet (CV). The dye shows absorption maximum at 600 nm. The calibration graph is found to be linear over the range 400.00-500.00 µg mL^{-1}. The molar absorptivity and sandell's sensitivity values are found to be 1.98×10^3 $Lmol^{-1}cm^{-1}$ and 0.17 µgcm^{-2} respectively. The proposed method is compared with the earlier spectrophotometric methods for the determination of ranitidine hydrochloride. The method is successfully applied for the determination of ranitidine hydrochloride in pharmaceutical preparations.

Keywords:

Ranitidine hydrochloride; Sodium periodate; Crystal violet

1. Introduction

Ranitidine hydrochloride, chemically N, N-dimethyl-5-[2-(1-methylamine-2-nitrovinyl)-ethylthiomethyl] furfurylamine hydrochloride is a H_2-receptor antagonist (Fig.1). Histamine is a natural chemical that stimulates the stomach cells to produce acid. The H_2-receptor antagonists are used to block the action of histamine on parietal cells in the stomach, decreasing the production of acid by these cells. H_2 antagonists are used in the treatment of dyspepsia, although they have largely been surpassed in popularity by the more effective proton pump inhibitors. They suppress the normal secretion of acid by parietal cells and the meal-stimulated secretion of acid. They accomplish this by two mechanisms, histamine released by ECL cells in the stomach is blocked from binding on parietal cell H_2 receptors which stimulate acid secretion, and other substances that promote acid secretion (such as gastrin and acetylcholine) have a reduced effect on parietal cells when the H_2 receptors are blocked. Like the H_1-antihistamines, the H_2 antagonists are inverse agonists rather than true receptor antagonists. The H_2-antagonists offer several advantages over antacids, including longer duration of action (6–10 hours vs 1–2 hours for antacids), greater efficacy and ability to be used prophylactically before meals to reduce the chance of heartburn occurring.

* **Corresponding Author**
E-mail: nbadiadka@yahoo.co.uk
ISSN: 1306-3057,

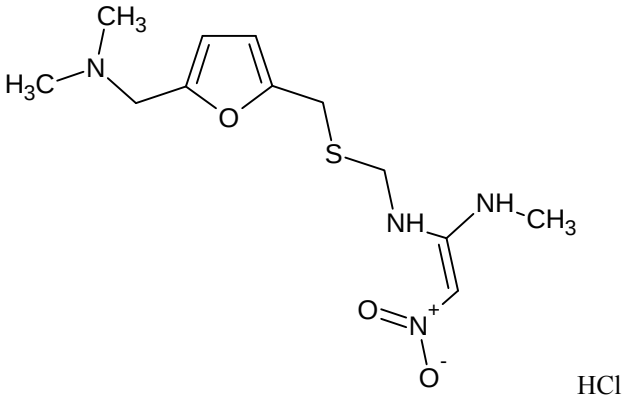

Fig. 1. Ranitidine hydrochloride

Ranitidine is widely used in short term treatment of duodenal ulcer and in the management of hypersecretory conditions [1]. It is commonly used in treatment of peptic ulcer disease and gastroesophageal reflux disease. Ranitidine is also used alongside fexofenadine and other antihistamines for the treatment of skin conditions such as hives.

Several spectrophotometric [2-10] methods have been reported for the determination of ranitidine hydrochloride in bulk, pharmaceutical dosage forms and/or biological fluids. The spectrophotometric method is one of the best methods for the assay of drugs because of its simplicity, sensitivity and rapidity. In the present investigation a simple method is described for the determination of ranitidine hydrochloride using sodium periodate and crystal violet.

2. Experimental

2.1 Apparatus

A Shimadzu UV-2550 PC UV-VIS Spectrophotometer with matched 1 cm quartz cells were used for all measurements.

2.2 Reagents and Solutions

All chemicals used were of analytical reagent grade. Sodium periodate (0.25 %), H_2SO_4 (2N) and crystal violet (0.05 %) were used. Ranitidine hydrochloride was obtained from CAD Pharma Ltd., Bangalore and used as such. A standard stock solution containing 100 mg mL^{-1} ranitidine hydrochloride was prepared by dissolving 100 mg of pure drug in water and diluting to the mark in a 100 mL calibrated flask.

2.3 Determination of Ranitidine Using Sodium Periodate

Different aliquots (400.00-500.00 μgmL^{-1}) of ranitidine were transferred into a series of 10 mL standard flasks using a micro burette. To this, 2 mL of periodate (0.25 %) was added followed by 2 mL of 2N H_2SO_4. The mixture was shaken well and heated to 50º C for 15 minutes until the appearance of yellow colour indicating the liberation of iodine. Then 1mL of 0.05 % crystal violet was added. The contents were shaken well and diluted up to the mark with distilled water. The absorbance of each solution was measured at 600 nm against the corresponding reagent blank prepared in the same manner without the analyte (Fig. 2).

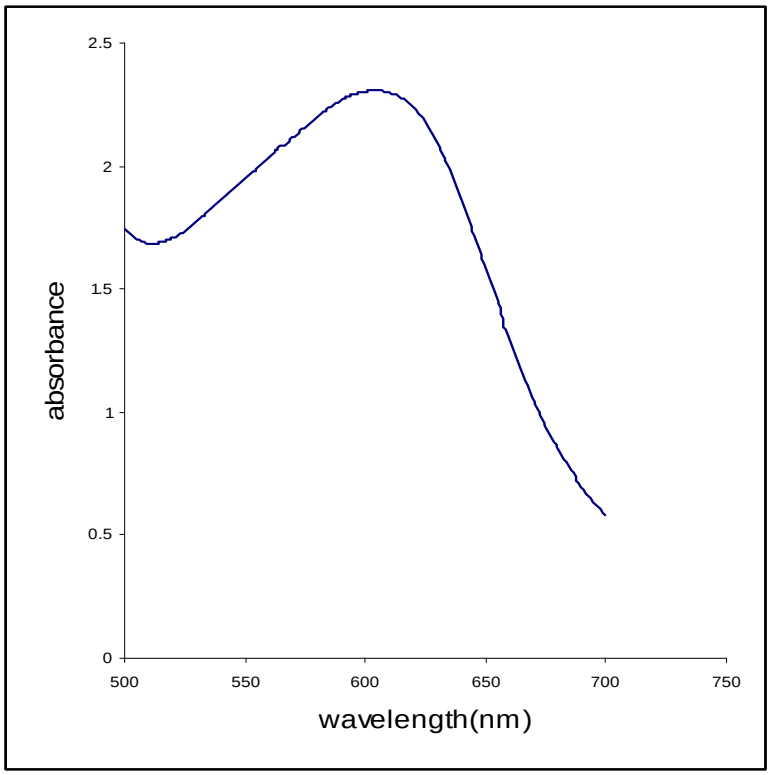

Fig. 2. Absorption spectrum of RNH-sodium periodate-CV system

2.4 Procedure for Tablet Formulations

Rantac -168 mg (Unique's Pharmaceuticals), Zinetac -168mg (Glaxo Smithkline Pharmaceuticals Ltd.) tablets were used in the investigation. Three tablets were taken and ground into a fine powder. Powder equivalent to 168 mg of ranitidine was weighed and transferred into a 100 mL calibrated flask by filtration and washing with distilled water. The solution was made up to the mark with distilled water. A suitable aliquot was then subjected to analysis by the proposed method.

3. Results and Discussions

The method is based on the reaction of ranitidine with sodium periodate in acidic medium to liberate iodine and the liberated iodine bleaches the violet colour of crystal violet which shows absorption maximum at 600 nm. The amount of periodate reacted corresponds to the ranitidine concentration. There was an increase in the concentration of liberated iodine when known excess of sodium periodate was added to an increasing concentration of ranitidine. When known volume of the dye was added to the same mixture it showed a decrease in the absorbance of the dye. The result could be observed by decrease in the absorbance with the increase in the concentration of ranitidine at the respective λ_{max}. The absorbance corresponding to the bleached colour which in turn corresponds to the analyte concentration was obtained by subtracting the absorbance of the blank solution from that of the test solution (Fig.3). To ensure the validity of the analytical procedure, the stability of the analytical solutions during the analytical procedure was studied and the colour was stable up to 2 hours. The comparison between the existing spectrophotometric methods and the proposed method is given in Table 1.

Table 1. A comparison table for the performance characteristics of the reported methods and the proposed method

Reagent	Range(μg mL^{-1})	λ_{max} (nm)	Molar absorptivity (L $mol^{-1}cm^{-1}$)	Reference
2,3-Dichloro-5,6 dicyanoquinone	20.00-140.00	467	2.431×10^3	[5]
p-Chloranilic acid	20.00-240.00	515	1.052×10^3	[5]
Perchloric acid+Crystal violet	10.00-70.00	570	2.2×10^3	[10]
Sodium periodate-Crystal violet	400.00-500.00	600	1.98×10^3	Present method

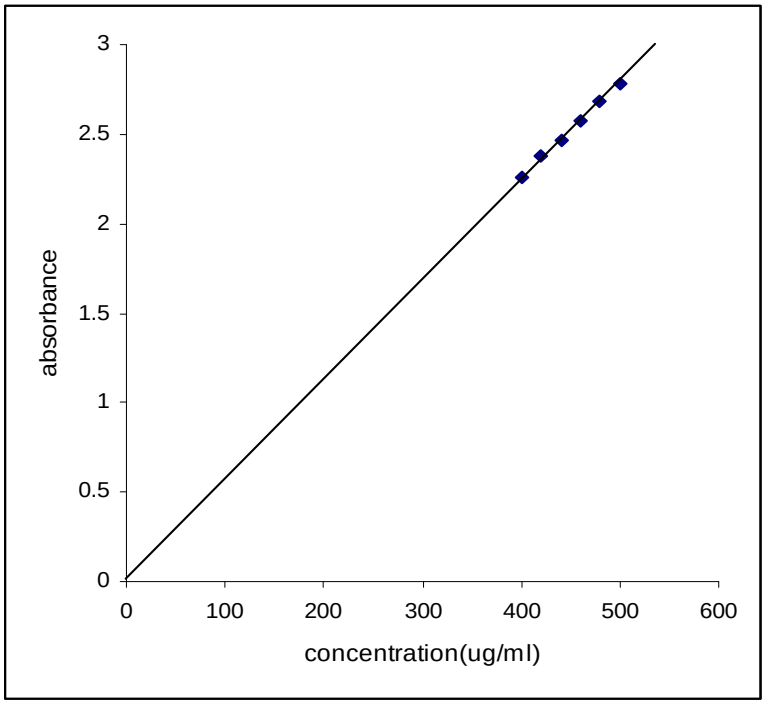

Fig. 3. Calibration curve for the system

3.1 Analytical Data

A linear correlation was found between absorbance at λ_{max} and concentration ranges given in Table 2. Sensitivity parameters such as molar absorptivity, Sandell's sensitivity, detection limit and quantification limit are presented in Table 2. Regression analysis of Beer's law data using the method of least squares was made to evaluate the slope (b), intercept (a), correlation coefficient (r) and is also given in Table 2.

3.2 Accuracy and Precision

The accuracy and precision of the method was established by analyzing the pure drug solution at 5 different levels (within working limits). The relative error (%) which is a measure of accuracy and RSD (%) a measure of precision are summarized in Table 3 and reveal the high accuracy and precision of the methods.

Table 2. Analytical parameters

λ_{max} nm	600
Beer's Law limit (μg mL^{-1})	400.0-500.0
Molar Absorptivity ($Lmol^{-1}cm^{-1}$)	1.9858×10^{3}
Sandell's Sensitivity (μg cm^{-2})	0.1767
Limit of Detection * *(μg mL^{-1})	0.3933
Limit of Quantification * *(μg mL^{-1})	1.1918
Regression Equation *	Y=a+ bX
Slope (b)	0.5186
Intercept (a)	0.1875
Correlation coefficient (r)	0.9994

* Y is the absorbance and X concentration in μg mL^{-1}.
* * Calculated according to ICH guidelines.

Table 3. Evaluation of accuracy and precision

Amount taken (μg mL^{-1})	*Amount found (μg mL^{-1})	RE (%)	SD(μgmL^{-1})	RSD (%)
400.00	401.20	0.30	0.2775	0.0691
420.00	421.20	0.28	0.6181	0.1467
440.00	439.40	0.14	0.2509	0.0571
460.00	459.40	0.13	0.1949	0.0424
480.00	477.40	0.54	0.6426	0.1346
500.00	499.40	0.12	0.1673	0.0335

* Mean value of five determinations
RE-Relative error; SD-Standard deviation; RSD-Relative standard deviation

3.3 Interference Study

In pharmaceutical analysis, it is important to test the selectivity towards the excipients added to the pharmaceutical preparations. Commonly encountered excipients such as glucose, starch, talc did not interfere in the determination of ranitidine hydrochloride.

4. Applications

The proposed method was successfully applied to determine ranitidine in tablets. The content of the tablet formulation was calculated by applying suitable dilution factor. The results for the tablets were compared statistically with those of the tabulated value at 95 % confidence level. The calculated student's t-test did not exceed the tabulated value. Table 4 gives the results of the determination from which it is clear that there is close agreement between the results obtained by the proposed methods and label claim.

Table 4. Results of assay of formulations for the proposed method

Brand name	Labeled amount(mg)	% Found* ± SD	t-test
Rantac[a]	168.00	100.38±0.241	0.94
Zinetac[b]	168.00	99.81±0.109	1.04

* Mean of 5 determinations
[a]Unique's Pharmaceuticals
[b]Glaxo Smithkline Pharmaceuticals Ltd.
Tabulated t-value at 95% confidence level is 2.77

5. Conclusion

Simple and rapid determination of ranitidine has been developed. The method is easy to perform and do not contain any stringent experimental variables which effect the reliability of the results. There is no interference from common additives and excipients. The method thus can be used in the determination of ranitidine in pure and dosage forms.

Acknowledgement

The authors acknowledge the receipt of pure ranitidine hydrochloride from CAD Pharma Ltd., Bangalore.

References

1. Remington J P, Remington Pharnaceutical Sciences, Mack Publishing Co., USA 17th Ed. (1985).
2. Perez R T, Martinez L C, Tomas V, Sanz A and Sahuquillo E (2001) Flow-injection extraction-spectrophotometric method for the determination of ranitidine in pharmaceutical preparations. J Pharm Biomed Anal 26:609.
3. Walash M, Khalid S M, Sayed M M and Shabana M R (2004) Kinetic spectrophotometric determination of ranitidine. J Chin Chem Soc 21:523.
4. Hassan E M and Belal M (2002) Kinetic spectrophotometric determination of nizatidine and ranitidine in pharmaceutical preparations. J Pharm Biomed Anal 27:31.
5. Walash M, Ei Din M S, Metwalli M E S and Redashabana M (2004) Spectrophotometric determination of nizatidine and ranitidine through charge transfer complexation. Arch Pharm Res 27:720.
6. Junior M, Luiz H, Filho F, Luiz C.S, Vieira H J and Orlando F F (2009) Flow injection spectrophotometric system for ranitidine determination in pharmaceuticals using Cerium(IV) and Ferroin. Curr Anal Chem 5:213.
7. Pillai S and Singhvi I (2007) Spectrophotometric simultaneous estimation of ranitidine hydrochloride and ondansetron hydrochloride from tablet formulation. Indian J Pharm Sci 69:201.
8. Ahmad A K S, Kawy M A and Nebsen M (1999) Spectrophotometric and spectrofluorimetric determination of famotidine and ranitidine using 1,4-benzoquinone reagent. Anal Lett 32:1403.
9. Basavaiah K and Nagegowda (2004) Determination of ranitidine hydrochloride in pharmaceutical preparations by titrimetry and visible spectrophotometry using bromate and acid dyes. Il Farmaco 59:147.

10. K.Basavaiah, P.Nagegowda and V.Ramakrishna (2005) Determination of drug content of pharmaceuticals containing ranitidine by titrimetry and spectrophotometry in non-aqueous medium. Science Asia 31: 207.