

Spectrophotometric Determination of Rantidine-HCl in Pharmaceutical Formulations

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Abstract

Spectrophotometric methods were developed for the determination of rantidine-HCl in pharmaceutical tablets. These methods were based on the reaction of DDQ and p-chloranil with rantidine-HCl, resulting in the formation of an orange-red and purple colored products which are quantified spectrophotometrically at 460 and 540nm in DDQ and p-chloranil, respectively. A graph of absorbance versus concentration show that Beer's law is obeyed in a concentration ranges of 20-160 and (30-120) $\mu\text{g/ml}$ with molar absorptivities of 2.631×10^3 and $1.052 \times 10^3 \text{ l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$ for DDQ and p-chloranil, respectively.

The optimum conditions for color development are described and the proposed methods were applied satisfactory to pharmaceutical preparations.

Introduction

Rantidine, is chemically known as N-[2-((5-dimethylamino) methyl)-2-furanyl]-methylthioethyl)-N-methyl-2-nitro-1,1 ethane diamine, and it is used therapeutically to inhibit the action of histamine on the H_2 receptors, So it is a histamine antagonist, reducing gastric acid and secretion under daytime and nocturnal basal condition. And also when it is stimulated by food, insulin, histamine or prostaglandin.(1)

The drug is used for the short-term treatment of an active duodenal ulcer and a benign gastric ulcer, for the treatment of pathogenic gastrointestinal hypersecretory conditions and to provide a short-term symptomatic relief of gastroesophageal reflux(1).

Several types of analytical procedures have been proposed for the analysis of rantidine in pharmaceutical formulations, These procedures include high-performance liquid chromatography (HPLC)(2-4), polarography(5-7), potentiometric methods(8,9) and spectrophotometry(10-12). Some of these procedures are not simple for routine analysis and required expensive or sophisticated instruments.

This paper reports spectrophotometric methods for the assay of rantidine using 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) and p-chloranil (p-Cl) as chromogenic reagents. The proposed methods were applied successfully to the determination of rantidine-HCl either in a pure form or in pharmaceutical formulations, with a good accuracy and precision.

Experimental

Apparatus:

A single beam UV-Vis spectrophotometer from Beckman Scientific Equipment model DU-65 with 1cm glass cells were used for absorbance measurements. pH meter model PW-9421 from Philips was used for all pH measurements.

Materials and Reagents

- All chemical which are used were of analytical reagent grade unless otherwise stated, rantidine-HCl standard powder was provided from the State Company for Drug Industries and Medical Appliances Samara-Iraq (SDI).
- DDQ ($2 \times 10^{-2} \text{M}$) solution is prepared by dissolving 0.4540gm in 100 ml of acetone by using a volumetric flask.
- P-Chloranil ($2 \times 10^{-3} \text{M}$) solution is prepared by dissolving 0.0122gm in 25 ml of acetonitrile by using a volumetric flask.
- Rantidine-HCl stock solution ($500 \text{ mg} \cdot \text{ml}^{-1}$)

It was prepared by dissolving 0.1 gm of rantidine – HCl in 20 ml distilled water, then the solution was rendered alkaline (pH=9.0) by a drop wise of 0.2N sodium hydroxide solution . The solution was quantitatively transferred into a 125-ml separating funnel and then the drug was extracted with 4x20 ml chloroform The extract was washed with 20ml water, filtered through anhydrous sodium sulphate into a 200ml volumetric flask and made up to volume by using chloroform.

Recommended Procedure

1-DDQ Method:

Into a series of 10 ml a calibrated flask transfers increasing volumes of rantidine-HCl ($500 \mu\text{g} \cdot \text{ml}^{-1}$) to cover the range of the calibration graph (20-160) $\mu\text{g} \cdot \text{ml}^{-1}$ in a final volume of 10 ml, adding 2.0 ml distilled water rendered alkaline (pH=9.0) by adrop wise of 0.2N sodium hydroxide solution, then adding 1.5 ml of DDQ solution, mixed well and dilute the solution to the mark with acetone and allow the reaction mixture to stand for 20 min at room temperature. The absorbance then was measured at 460 nm against reagent blank and prepared in the same manner except the addition of the drug.

2-p-Chloranil:

In to a series of 10 ml calibrated flask transfer, there is an increase of the volumes of rantidine-HCl ($500 \mu\text{g} \cdot \text{ml}^{-1}$) so as to cover the range of the calibration graph (30-120) $\mu\text{g} \cdot \text{ml}^{-1}$ in a final volume of 10 ml, we added 2 ml of distilled water, alkaline is rendered pH=9.0) by a dropwise of 0.2N sodium hydroxide solution, then we added 1 ml of the p-chloranil solution, mix well and dilute the solution to the mark with acetonitrile and allow the reaction mixture to stand for 20 min at room temperature. The absorbance then is measured at 540 nm against a reagent blank prepared in the same manner except the addition of the drug.

Procedure for pharmaceutical tablets:

Twenty tablets were washed from the color coat by using distilled water, dried, weighed and finely powdered, then an accurately weighed quantity equivalent to the drug concentration is mentioned in the preparation of standard solution was dissolved in 20 ml distilled water, and quantitatively transferred into a 125 ml separating funnel and rendered alkaline (pH=9.0) by a drop wise of 0.1 N sodium hydroxide, then the solution was extracted with 4 x 20 ml chloroform. The extract was washed with 20ml water, filtered through anhydrous sodium sulphate into 200ml volumetric flask and made up to volume using chloroform

A suitable aliquot of the drug solutions was treated as described under the preparation of calibration graphs.

Results and Discussion

The reaction of rantidine-HCl with DDQ results in the formation of an intense orange-red product which exhibit an absorption band maximum at 460 nm (Fig 1). The band may be attributed to the formation of a DDQ radical anion(13,14). The suggested mechanism for this reaction depends on the formation of an original donor-acceptor (DA) complex through the interaction between tertiary amine (Drug) as n-electron donor and DDQ as π - acceptor. The dissociation of DA complex was promoted by the high ionizing power of the solvent acetone which completes the electron transfer from the donor to the acceptor moiety that takes place. This is followed by the formation of the DDQ radical anions as a predominant chromogen(15).

On the other hand, the spectrum of p-chloranil solution in acetonitrile displayed a maximum absorption band at 480nm. Mixing the solution of rantidine - HCl with the solution of p-chloranil in acetonitrile resulted in the change of the yellow color of the p-chloranil to a purple chromogen that exhibits a strong absorption maximum at 540nm (Fig 2).

This band can be attributed to the formation of a charge-transfer complex between rantidine-HCl (n-donor) and p-chloranil (π -acceptor) followed by the formation of p-chloranil radical anion(15,16).

Optimization conditions

pH effect:

The effect of pH on the development of the colored complexes upon the reaction of rantidine-HCl and DDQ, p-chloranil is shown in Fig (3). The pH of the solution was adjusted to the required value with few drops of 0.1M HCl or 0.1M NaOH.

Maximum and constant absorbances were obtained at the pH= 9.0. The absorbance started to decrease at pH values above 9.0. Therefore a pH of 9.0 was used in all the subsequent experimental work.

Effect of amount of acceptors:

Various volumes of DDQ and p-chloranil were added to a fixed amount of a drug solution, 1.5ml of 2×10^{-2} M of DDQ and 1 ml of 2×10^{-3} M of p-chloranil were found enough to develop the color to its full intensity.

Effect of reaction time:

The color intensity reached a maximum after the drug reaction with DDQ or p-chloranil solution 20 min of at room temperature. Therefore 20 min development time was selected as an optimum for both general procedures. The color obtained was stable for at least 2 hours for DDQ and p-chloranil reactions with drug.

Calibration graph:

Employing the condition described under recommended procedure, linear calibration graphs for rantidine-HCl was obtained (Fig 4,5), which show that Beer's law was obeyed in the concentration range (20-160) and (30-120) $\mu\text{g.ml}^{-1}$ rantidine-HCl for DDQ and p-chloranil reaction respectively. The molar absorptivities of orange-red and purple formed products were found to be 2.63×10^3 and $1.05 \times 10^3 \text{ l.mol}^{-1}.\text{cm}^{-1}$, and the sandell sensitivities were found 0.133 and $0.333 \mu\text{g.cm}^{-2}$ for DDQ and p-chloranil reaction respectively.

Structure of complexes:

The stoichiometry of the reactions between rantidine-HCl and DDQ and p-chloranil were studied by mole ratio method; The results obtained (Fig 6 , 7) show that 1:1 rantidine-HCl to DDQ and p-chloranil complex were formed at 460 and 540nm respectively.

Precision and Accuracy:

Rantidine-HCl was determined at three different concentrations. The results are shown in (Table 1).

A satisfactory precisions and accuracies could be obtained with the proposed methods.

Analytical application:

Three types of drug containing rantidine-HCl were analysed and they gave good accuracies and precisions. (Table 2)

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Table (1): Accuracy and precision of the proposed method.

Amount of Rantidine-HCl taken (µg/ml)	Recovery %*	Average Recovery %	R.S.D %*
30	98.60		1.61
45	100.20	99.73	0.54
60	100.40		1.03

*for five determination

Table (2): The application of the proposed method for the determination of Rantidine-HCl in pharmaceutical tablets:

Tablet sample	w.t of Rantidine-HCl (mg)	Amount of Rantidine-HCl taken (mg)	*Recovery %	R.S.D %*
Ranitidine (a)	150	25	99.23	1.11
		35	99.01	1.74
Rinatadine(b)	150	25	103.91	1.40
		35	98.42	1.27
Rantisam(c)	150	25	98.18	0.90
		35	99.05	1.69

* for five determination.

a: marked by zorka pharma (Yugoslavia)

b: marked by Bal pharma LTD (India)

c: marked by Samara drug industries (Iraq)

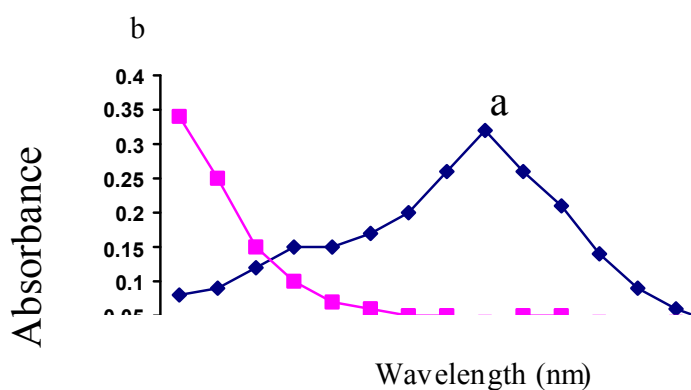


Fig (1): Absorption spectra of:
a. 40 µg/ml rantidine-HCl, 3×10^{-3} M DDQ at pH=9.0 against blank.
b. 3×10^{-3} M DDQ in acetone (blank) against distilled water.

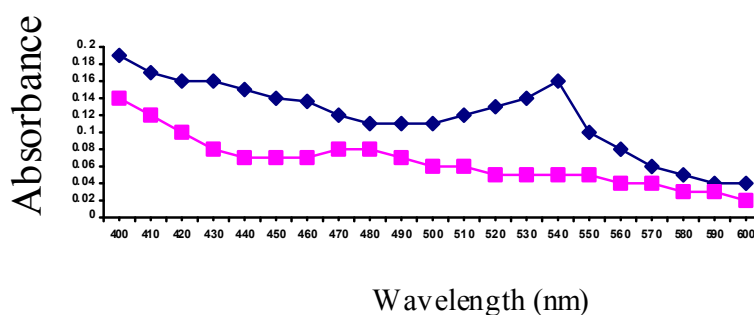


Fig (2): Absorption spectra of:
a. 50 µg/ml rantidine-HCl, 2×10^{-4} M p-chloranil (p-Cl) at pH=9.0 against blank.
b. 2×10^{-4} M p-Cl in acetonitrile (blank) against distilled water.

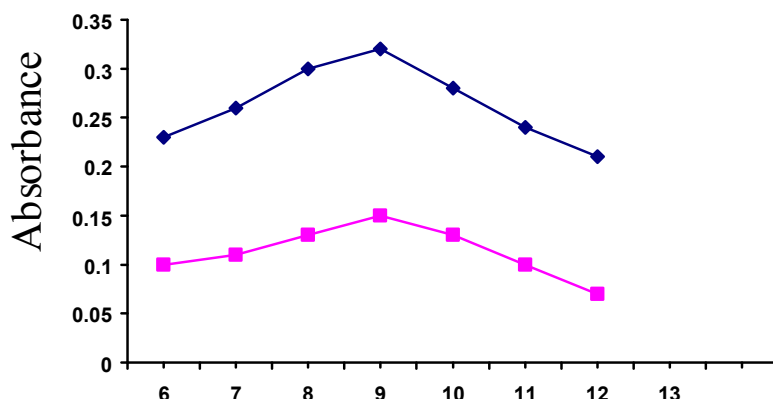


Fig (3): of pH on the absorbance of:
a. 40 µg/ml rantidine-HCl, 3×10^{-3} M DDQ at 460nm.
b. 50 µg/ml rantidine-HCl, 2×10^{-4} M P-Cl at 540nm.

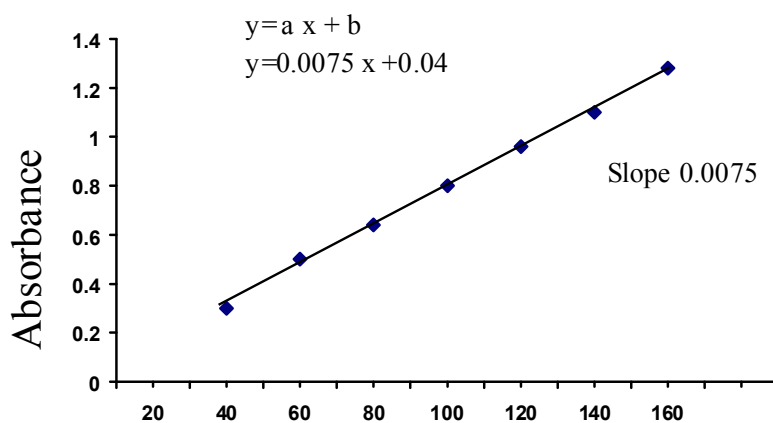


Fig (4): Calibration graph of rantidine-HCl with DDQ.

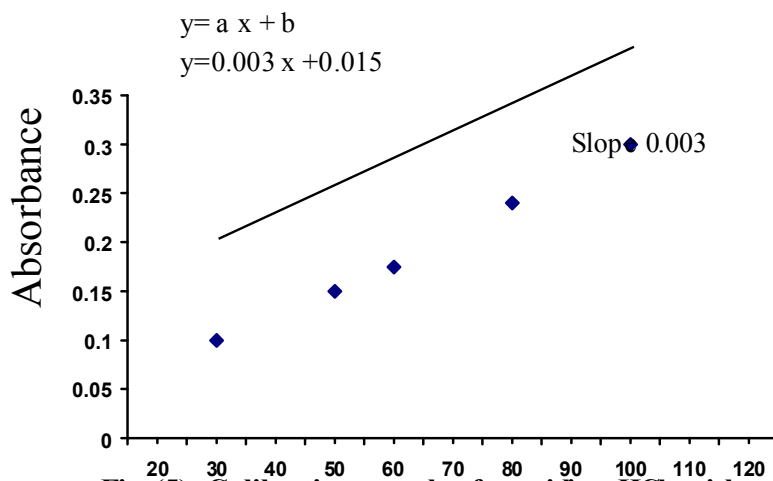


Fig (5): Calibration graph of rantidine-HCl with p-Cl.

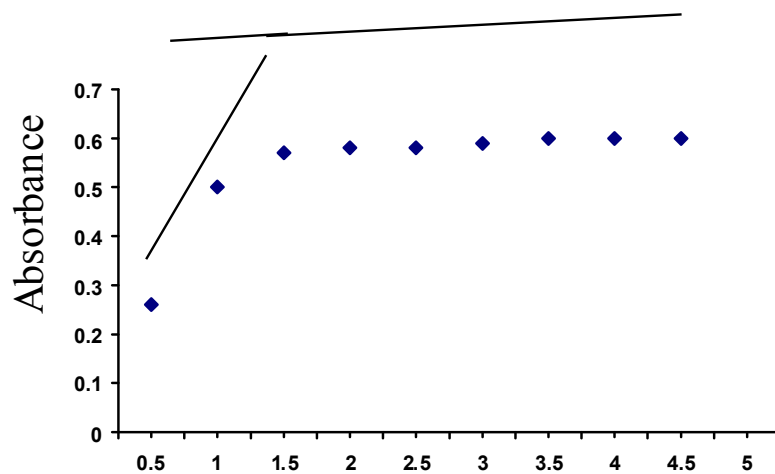


Fig (6): Mole ratio plot of 1.74×10^{-4} M rantidine-HCl with DDQ solution.

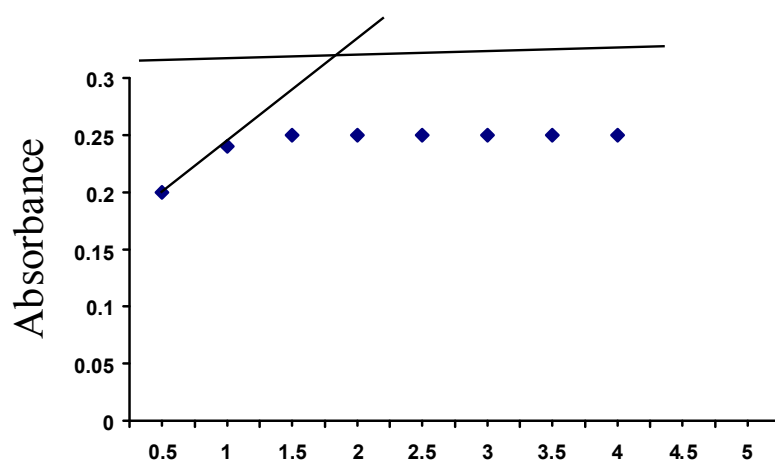


Fig (7): Mole ratio plot of 2.27×10^{-4} M rantidine-HCl with p-Cl solution..

التقدير الطيفي للرانتيدين-هايدروكلوريد في المستحضرات الصيدلانية

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الخلاصة

يتضمن البحث تطوير طريقة طيفية لتقدير الرانتيدين-هايدروكلوريد في الحبوب اللوائية. تعتمد الطريقة على تفاعل DDQ و p-Cl مع الرانتيدين-هايدروكلوريد لتكوين ناتج برتقالي محمر وقرمزي يعطي امتصاصية عند طول موجي قدره 460 و 540 نانومتر لكل من DDQ و p-Cl على التوالي. يشير الرسم البياني الخطي للاختصاص مقابل التركيز بان قانون بير ينطبق ضمن مدى التراكيز 20-160 و 30-120 مايكروغرام/مل مع امتصاصية مولارية مسلوكة الى 2.631 $\times 10^3$ و 1.052 $\times 10^3$ لتر. مول⁻¹. سم⁻¹ لكل من طريقة DDQ و p-Cl على التوالي. تمت دراسة الظروف المثلى للتفاعل وتطبيق الطريقة على المستحضرات الصيدلانية.