New spectrophotometric determination of Ranitidine Hydrochloride in different pharmaceutical samples

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Abstract

Simple ,rapid ,accurate and sensitive spectrophotometric method have been developed for the determination of ranitidine-HCl in pharmaceutical preparations. The method based on complex formation between Ranitidine-HCl and Copper(II) in acetonitrile solvent to yield a green colored complex with a maximum absorbance at 412 nm. Beers law is obeyed in the concentration range of (0.5-12) µg.mL^{-1}; The molar absorpitivity and sandell sensitivity are (8.772 *10^{3}) L . mole^{-1}. cm^{-1}, (0.04) µg. cm^{-2} respectively. Optimisation of the analytical parameters is achieved where; the optimum temperature is (12-50) ℃, and the optimum time to complex formation is 15 min. Standard deviation, relative standard deviation, limit of quantification LOQ, limit of detection LOD were found to be in the range of (1.2*10^{-3}), (0.324)%, (0.08) µg.mL^{-1}, (0.0264) µg.mL^{-1} respectively. The proposed method was successfully applied to the analysis of the studied drug in pure and pharmaceutical dosage forms with good accuracy,the recovery percentages R_e%, and relative error percentage E_{rel}% were found to be (101±0.58)%, (1.58)% for pure drug and (102±0.80)%,(2.58)% for pharmaceutical dosage.

Keywords: Ranitidine hydrochloride, copper(II), Spectrophotometry.

الخلاصة

تم التوصل الى طريقة طيفية تمتاز بالبساطة والدقة و الحساسية والسرعة لتقدير دواء الرانتدين في مستحضراته الصيدلانية. تضمنت الطريقة تكوين معقد بين الرانتدين ومحلول ايون النحاسيك في الاسيتونايترايل كمذيب مكون معقد مستقر اخضر اللون له اقصى قمة امتصاص عند412 نانومتر. وقد لوحظ مطاوعة قانون بير في مدى التراكيز (12– 0.5) مايكروغرام.مل$^{-1}$ وكانت قيم معامل الامتصاص المولاري ودالة ساندل هي (8.77 *10^{3}) لتر.مول$^{-1}$.سم$^{-1}$ ، (0.04) مايكروغرام.سم$^{-2}$ على التوالي ، وتم تثبيت الظروف المثلى للتفاعل وكانت افضل درجة حرارة هي (50–12)درجة مئوية وافضل زمن لاتمام التفاعل هو (15) دقيقة

وكانت قيم الانحراف القياسي، الانحراف القياسي النسبي، حد الكشف، والتقدير الكمي هي ($1.2*10^{-3}$) ، (0.324)%، (0.024) مايكروغرام.مل$^{-1}$، (0.08) مايكروغرام.مل$^{-1}$ على التوالي اما قيم الاسترداد المئوي و الخطا النسبي المئوي كانت (101±0.58)% ، (1.58)%على التوالي .طبقت هذه الطريقه بنجاح على بعض المستحضرات الصيلانية لتعين كمية الرانتدين فيها باسترداد مئوي وخطا نسبي مئوي (102±0.80)%، (2.58)% على التوالي .

الكلمات المفتاحية : رانتدين هايدروكلورايد، نحاس(II) ، طريقة طيفية.

Introduction

Ranitidine (Zantac) is a H2-receptor antagonist has the chemical name (N, N dimethyl-5-(2-(1-methylamine- 2 - nitrovinyl) - ethylthiomethyl)furfurylamine hydrochloride, figure(1) with the empirical formula R-HCl is ($C_{13}H_{22}N_4O_3S.HCl$). its molecular weight is 350.9 g.mol^{-1} ,it is a white or pale yellow , crystalline powder, easily soluble in water and methanol and some other organic solvent[1] .

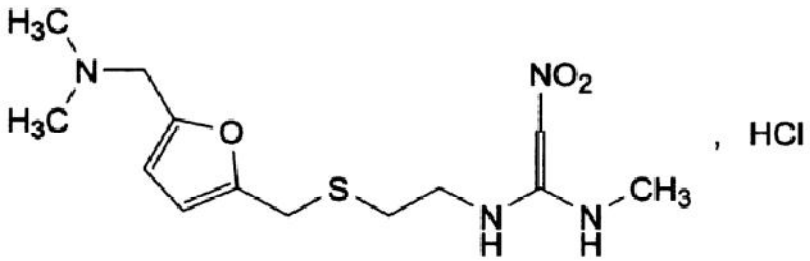


Figure 1: Chemical structure of ranitidine hydrochloride

Ranitidine is used for prevention and treatment of Peptic ulcer of the stomach and duodenum and the bleeding from the digestive tract. This drug reduces the amount of acid produced by the stomach, and so can heal the ulcers. It also reduces inflammation and bad feeling caused by inflammation of the esophagus accompanied the entry of fluids to it[2].

Various methods have been used for the determination of ranitidine in Pharmaceutical dosage, and biological fluids. These methods are Spectrophotometry[3-9], HPLC [10-13], colormetry [14], capillary electrophoresis[15], fluorimetry[16], Re-HPLC [17], voltammetry [18], potentiometry[19-21], polarography[22] and electrochemical methods[23].

The present determination is based on the reaction of ranitidine with copperic ion to form green colored complex tat has amaximum absorption at 412nm. The method describs a sensitive and simple method for the determination of ranitidine in pure form and in pharmaceuticals tablets by spectrophotometry.

Material and Methods

Apparatus

PH-metter Thermo circulator (Korea). Shimadzu uv-1800, double Beam U.V-Visible Spectrophotometer, , were used in this study.

Reagents

A Stock solution of (100 μg.mL^{-1}) ranitidine

This solution was prepared by dissolving (0.01) g of ranitidine powder with acetonitrile in 100mL volumetric flask and complete to the mark, from this solution, other standard solutions of lower concentration were prepared.

A Stock solution of (0.1M) copper ion

This solution was prepared by dissolving (2.3256) g of copper nitrate $Cu(NO_3)_2.2H_2O$ with a sufficient volume of methanol in 100mL volumetric flask, and the volume was completed by acetonitrile to the mark.

(0.01) M of ranitidine

Was prepared by dissolving (0.3509) g of ranitidine powder with acetonitrile in 100mL volumetric flask and complete to the mark.

General procedure

Different aliquots concentrations of ranitidine (0.5-12) μg.mL^{-1} were transferred into a series of 5mL volumetric flasks, (0.8)mL of (0.1)M copper solution was added. The contents were mixed, shaked and let to stand for (15) min. The solution was diluted to the mark with acetonitrile and mixed well. The absorbance of each solution was measured against the blank solution was prepared in the same manner but containing no rantidine at (412) nm.

Results and Disscusion

Spectral study was taken for ranitidine solution in acetonitrile in UV-Visible region was done, which gives two peak at (227)nm and (312)nm aganist aceto nitrile as blank figure (2 A).

The first result of preliminary study of the reaction of copper ion(II) with ranitidine-HCl ,froms green color solution which differ in natural with reactant substantces (rantidine and copper ion).

Figure (2C) shows the absorption spectrum for Ranitidine$-Cu^{2+}$ complex in acetonitrile solvent , which, gives a maximum wave length absorption (λ_{max}) (412) nm ,and this value differ from λ_{max} of ranitidine and Cu^{2+} in acetonitrile, Which, indicates the formation of the complex.

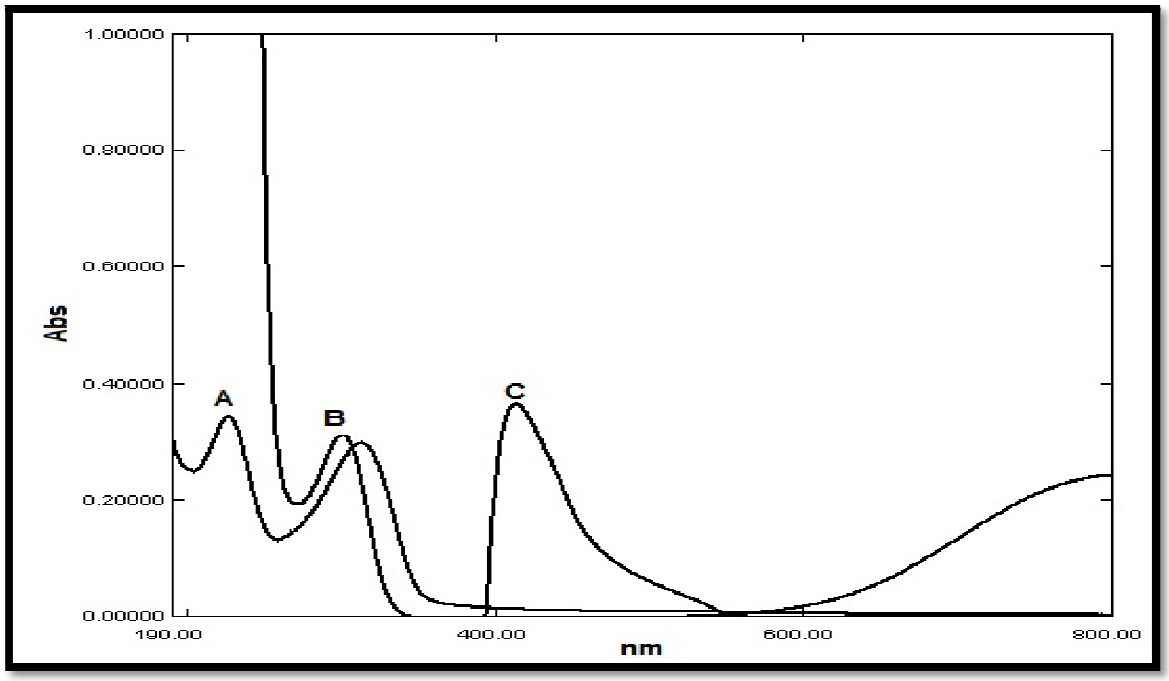


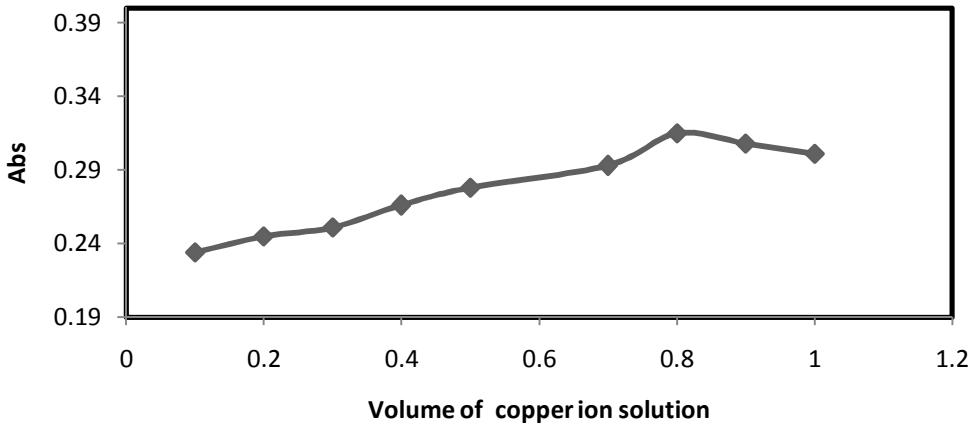
Figure (2) A- spectral absorption of (12) µg.mL^{-1} ranitidine solution, B- spectral absorption of (0.05) M copper solution, C-the absorption spectrum for Ranitidine–Cu^{2+} complex, in acetonitrile solvent.

Study the optimum conditions

The varius experimental affecting on the optical properties of the development and stability of the reaction prouduct are optimized by the following:

Effect of copper ion volume

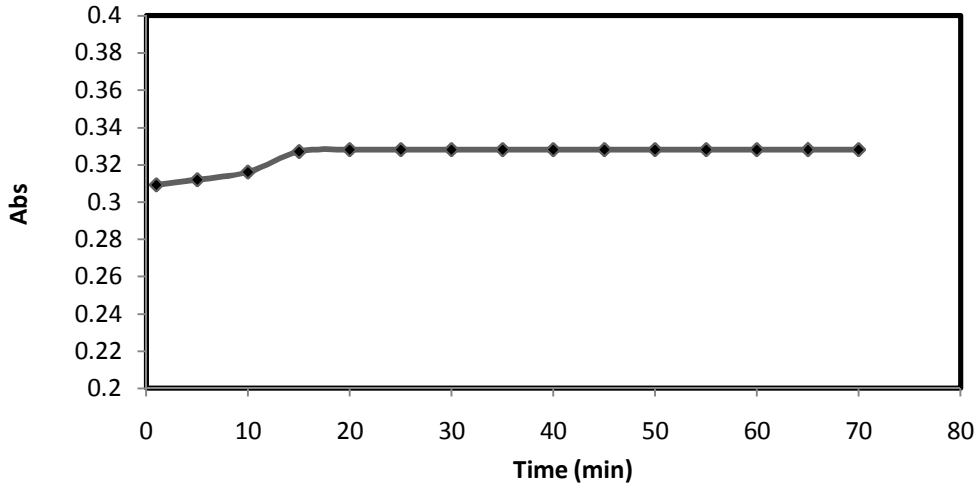
The effect of different volume on the absorbance has been studied with keeping the concentration of ranitidine constant (10) µg mL^{-1}. The results in figure (3) show that (0.8) mL of (0.1) mole L^{-1} Copper(II) was optimum and it was recommended for the subsequent experiments.



Figure(3) the effect of copper ion volume on the complex formed.

Effect of time

The time reaction required for the reaction completion was investigated. The results indicated that (15) min was needed to give complete reaction between rantidine-HCl and copper(II) as shown in figure (4).



Figure(4) Effect of time on absorption of complex.

Effect of temperature

The reaction prouduct was studied for the temperature range (4– 65) ℃ .The results indicated that the temperature between (12-50) ℃ is a suitable temperature to obtain the prefered absorption, after that, the absorption range was decreased due to evaporation of complex or dissociation. The colored complex wes stable at room tempreture is selected in this method as shown by figure (5).

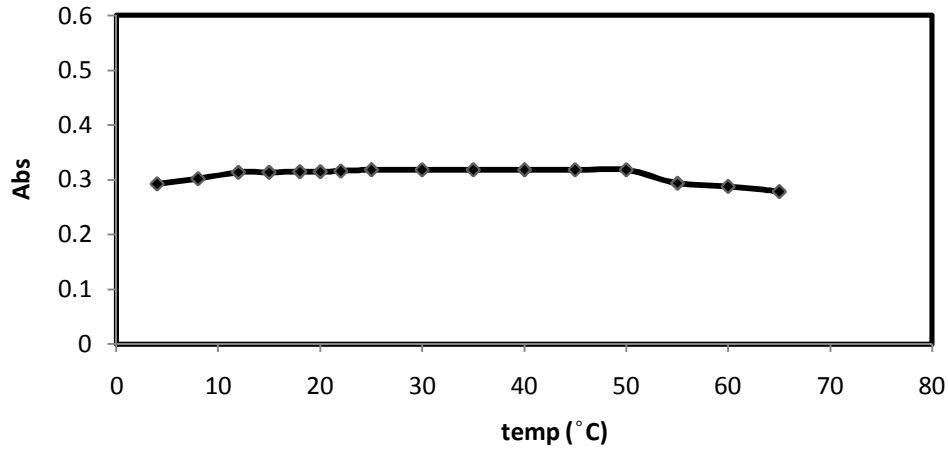


Figure (5) Effect of temperature on the absorption of the complex

Calibration curve

Under the recommended conditions described above, a linear calibration curve Figure (6) for ranitidine was obtained, which shows that Beers law is obeyed in the concentration rang (0.5-12) µg.mL^{-1} with a correlation coefficient of 0.999 . limit of ditection (LOD= 0.0246 µg mL^{-1}),limit of quantitiation (LOD= 0.08 µg.mL^{-1}) the molar absorpitivity and sandell sensitivity were found to be (8.772 *10^{3}) L. mole^{-1}. cm^{-1},(0.04) µg.cm^{-2} respectively.

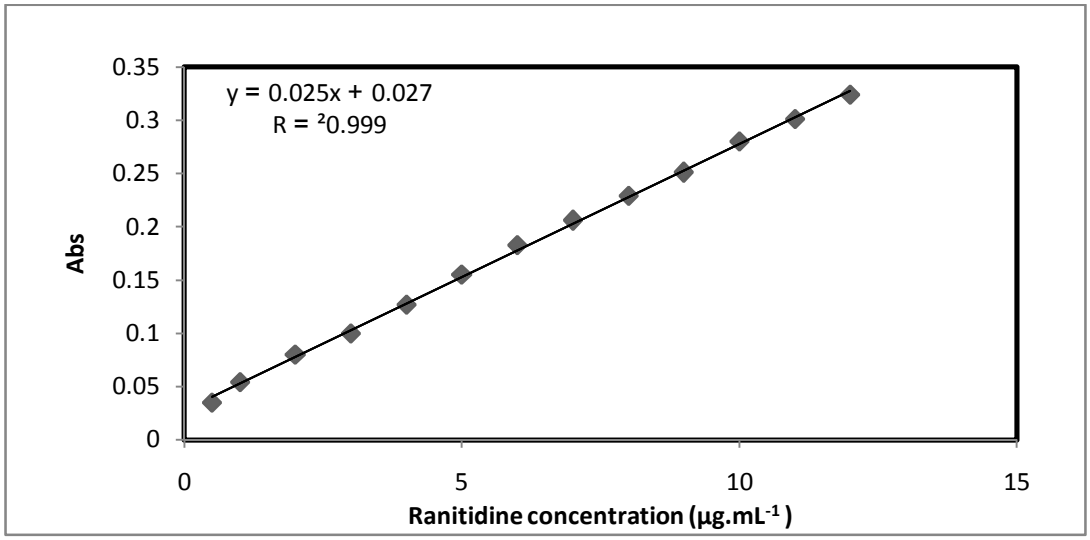
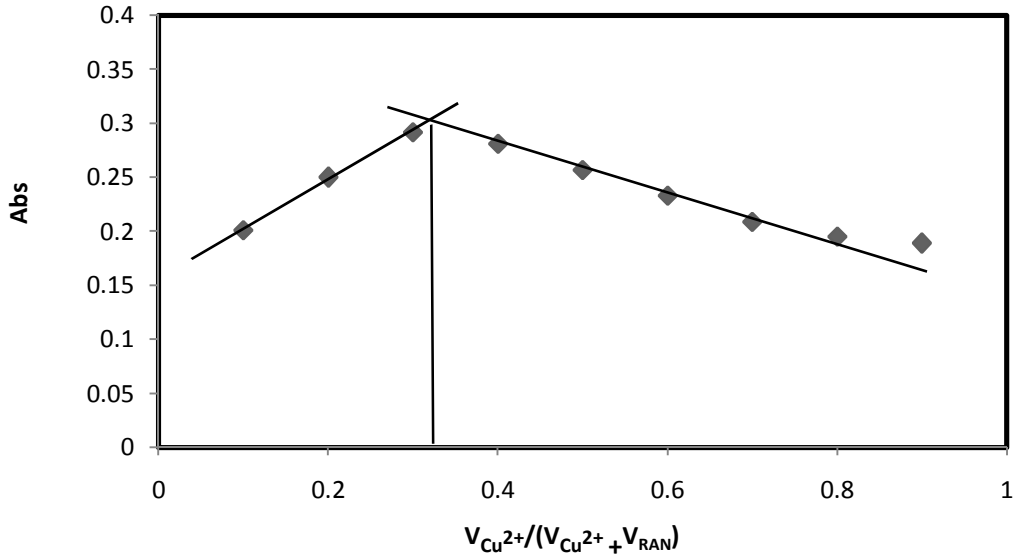


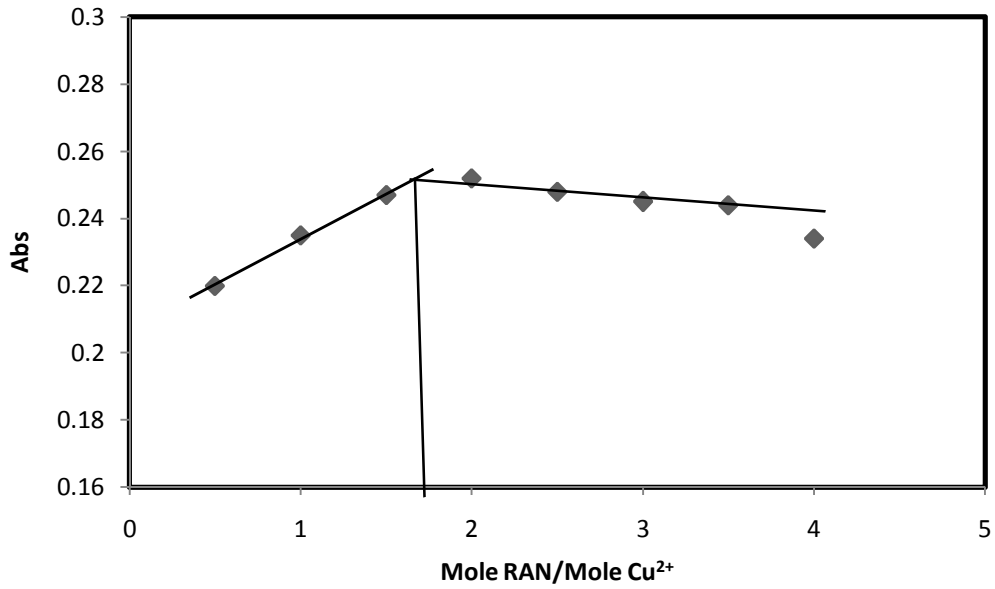
Figure (6) calibration curve of ranitidine.HCl.

Nature of complex

Figures (7) and (8) show continuous variations (Job*'s*) and mole ratio methods for the complex, which, from these figures can result the ratio between Cu^{2+} ion to rantidine is (1:2).



Figure(7) Continuous Variations (Job*'s*) plot.



Figure(8) Mole ratio method plot.

Stability of complex[24]

Dissociation degree and stability constant were calculated for the complex to be (0.103), (2.05×10^6) L^2mole^{-2} respectively. This indicates that the complex has high stability.

Precision and Accuracy

To determine the accuracy and precision of the method, ranitidine was determined in five replicates at three different levels, standard deviation, relative standard deviation (R.S.D%), the percent error ($\%E_{rel}$) and recovery ($\%R_e$) were calculated. The results were summarized in Table[1].

Table[1]: Evaluation of Accuracy and Precision for the proposed method.

Concentration of ranitidine (μg mL^{-1})		R_e%	E_{rel}%	SD	RSD%
Present	Found				
8	8.2	102.50%	2.50%	$1.4x10^{-3}$	0.416%
10	10.16	101.60%	1.60%	$1.2\ x10^{-3}$	0.310%
12	12.08	100.66%	0.66%	$1.0*10^{-3}$	0.246%
Range		101 ± 0.58	1.586%	$1.2*10^{-3}$	0.324%

Analytical applications

The method was applied on medicinal Product containing 150 mg of ranitidine of Indian,American and United Arab Emirates origin, where the 5 tablets of them were weighted , grinded and mixed, after that, a weight equivalent to 0.15 g of pure ranitidine has been taken from pharmaceutical preparations and dissolved by 50 mL of acetonitrile, so as to obtain the rantidine solution 3000 $\mu g.mL^{-1}$. then, from which, (8, 10, 12) $\mu g.mL^{-1}$. concentrations were prepared and applied the aproposed method on this concentrations. $R_e\%$, $E_{rel}\%$, SD, RSD% were calculated as in the table[2]. The results obtained are compared statically by the percent recovery, with those obtained by the official method which include potentiometric titration with NaOH[(2)]. The comparison was summarized in table [3].

Table[2]: Determination of ranitidine-HCl in different pharmaceutical preparations.

Drug factory	Concentration of ranitidine ($\mu g.mL^{-1}$)		$R_e\%$	$E_{rel}\%$	SD	RSD%
	Present	Found				
Indian	8	8.28	103.50%	3.50%	$1.9*10^{-3}$	0.566%
	10	10.32	103.20%	3.20%	$1.5*10^{-3}$	0.338%
	12	12.24	101.33%	1.33%	$1.3*10^{-3}$	0.320%
American	8	8.24	103.00%	3.00%	$1.8*10^{-3}$	0.541%
	10	10.28	102.80%	2.80%	$1.3*10^{-3}$	0.336%
	12	12.2	101.66%	1.66%	$1.2*10^{-3}$	0.295%
United Arab Emirates	8	8.32	104.00%	4.00%	$2.0*10^{-3}$	0.602%
	10	10.24	102.40%	2.40%	$1.2*10^{-3}$	0.310%
	12	12.16	103.33%	1.33 %	$1.1*10^{-3}$	0.295%
Range			102±0.80	2.58%	$1.47*10^{-3}$	0.400%

Table[3]: Comparison of the proposed method with the other official methods..

Drug factory	Re%		T-test	F-test
	Proposed method	Official method		
Pure ranitidine-HCl	101±0.58	99±0.75		
Indian	102±0.67	98±0.39	1.485917	0.993
American	102±0.48	98±0.80		
United Arab Emirates	103±0.24	98±0.90		

Effect of interferences

To order to assess the possible analytical applications of present proposed method.the interfering effects of excipients at various levels on the determination of 5 $\mu g.mL^{-1}$ of ranitidine-HCl for this study, solution contained ranitidine-HCl and each one of interference was taken separately in concentrations ten-times greater than that of rantidine-HCl and were analyzed to be the same procedure in the calibration curve .The result was given no interference with ranitidine-HCl as shown in Table[4].

Table[4] Effect of excipients on the determination of 5 $\mu g.mL^{-1}$ of ranitidine-HCl.

Excipient conc 50 $\mu g.mL^{-1}$	Conc of ranitidine $\mu g.mL^{-1}$ (found)	E_{rel}%	R_e%
Micro crystalline cellulose	5.08	1.6	101.6
Magnesium stearate	5.12	2.4	102.4
Titanium dioxide	4.96	-0.8	100.8
Theophyline	4.92	-1.6	98.4

Comparison of the proposed method with the other methods

Several previous analytical methods have been reported for determination of ranitidine-HCl in this paper table (4) summarizes some of these methods.

Table [5]: Comparison of the proposed method with the other reported methods.

S.No	method	Rang of determination	Re%	Reference
1	Spectrophotometry	50 to 350 $\mu g.mL^{-1}$	100.8%	3
2	HPLC	15-2000 $ng.mL^{-1}$	90.0%	12
3	Fluorimetry	40-1200 $ng.mL^{-1}$	98.97%	16
4	Re-HPLC	30-70 $\mu g.mL^{-1}$	100.5%	17
5	Potentiometry	10^{-6} - 10^{-2} $mol.L^{-1}$	98.65%	19
6	Polarography	$3.58*10^{-3}$-1.5 $mol.L^{-1}$	99.8%	22
7	Spectrophotometry	0.5-12 $\mu g.mL^{-1}$	101 ± 0.58	Proposed method

Conclusion

Spectrophotometric method has been proposed for the determination of ranitidine in pure and pharmaceutical dosage forms. It has been shown that the proposed method is more sensitive for assay ranitidine-HCl in pure form and pharmaceutical preparation (tablets).

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