Univariate and Simplex Optimization for the Spectrophotometric Determination of Cimetidine and Erythromycin ethylsuccinate Drugs Using Bromothymol Blue Via Ion-Pair Formation

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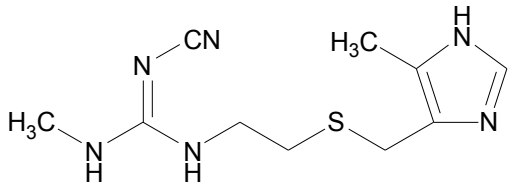
Abstract

The ion-pair formation method has been applied for the spectrophotometric determination of Cimetidine and Erythromycin ethylsuccinate, in bulk samples and in dosage form. The methods are accurate, simple, rapid, inexpensive and sensitive depending on the extraction of the formed ion-pair with brompthymol blue (BTB) as a chromogenic reagent in chloroform, use phthalate buffer of pH 5.5 and 4.0 for Cimetidine and Erythromycin ethylsuccinate respectively. The formed complexes show absorbance maxima at 427.5 nm and 414.5 nm for Cimetidine and Erythromycin ethylsuccinate respectively against reagent blank. The calibration graphs are linear in the ranges of 0.5-15 $\mu g.mL^{-1}$ with detection limit of 0.222 $\mu g.mL^{-1}$ for Cimetidine and 0.5-50 $\mu g.mL^{-1}$ with detection limit of 0.286 $\mu g.mL^{-1}$ for Erythromycin ethylsuccinate. The results show the absence of interferences from the excipients on the determination of these drugs. The proposed methods have been successfully applied for the determination of Cimetidine and Erythromycin ethylsuccinate (with two of its derivatives) in pharmaceutical preparations.

Keywords, Simplex, Spectrophotometric, Cimetidine, Erythromycin ethylsuccinate, Ion-pair.

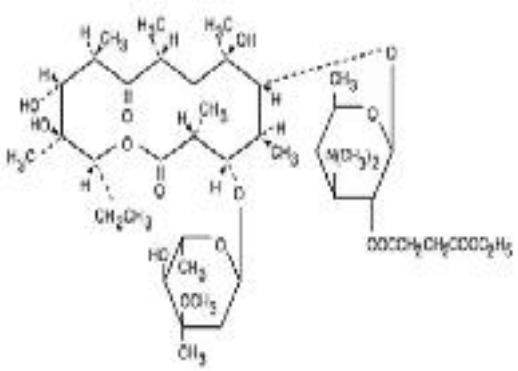
Introduction

Cimetidine was the first histamine H2-receptor antagonist approved by the Food and Drug Administration, USA, for the treatment of duodenal ulcers, Zollinger-Ellison syndrome, and othergastric hypersecretory states [1]. It's also indicated for the relief heartburn in peptic, duodenal ulcers and prevents rebleeding in patients which reduce the secretion of gastric acid[2], cimetidine, due to its effects on the immune system and as an H2-receptor antagonist, can inhibit growth of carcinogen-induced colonic tumors in rats, as well as the in vitro human colon cancer cell lines[1]. The Chemical structure of Cimetidine are given in (Scheme 1), which shows the imidazole ring on it.



Scheme 1: The chemical structure of Cimetidine

Erythromycin is the most employed macrolide antibiotic for treating a myriad of infections caused by gram-positive bacteria such as anthrax, tonsillitis, otits media and syphilis [2], it is often prescribed as an alternative for patient allergic to penicillin [2-3]. It has been also employed a as part of therapeutic cocktails together with amino glycoside antibiotics that covers gram-negative microorganisms [3]. The Chemical structure of Erythromycin is given in (Scheme 2), which shows the lactone ring on it.



Scheme 2: The chemical Structure of Erythromycin Ethylsuccinate

Several methods have been reported for the determination of Cimetidine and Erythromycin in bulk and pharmaceutical dosage forms, these methods include titrimetry[4], high performance liquid chromatography[5], high performance thin layer chromatography[6], liquid chromatography[7], capillary electrophoresis[8,9] and chemiluminesence[10].Some of these methods are time-consuming, tedious, and/or dedicated to sophisticated and expensive analytical instruments.

Spectrophotometry[11,12]and fluorimetry[13] are most convenient techniques because of their inherent simplicity, adequate sensitivity, low cost and wide availability in all quality control laboratories.

In experimental chemistry, the optimization of technical system is the process of adjusting the control variables to find the levels that achieve the best optimization. Usually, many conflicting response must be optimized simultaneously. In lack of systematic approaches the optimization is done by trial and error, or by changing one control variable at a time while holding the rest constant, such methods require a lot of experiments to be carried out.

Simplex optimization of experimental parameters was first introduced by Spendley[14], and then modified by Nelder[15] and Aberg[16]. A simplex is a geometric figure in which there are n +1 vertices, where (n) represents the number of variables [17], the method found a lot of applications in field of analytical chemistry [18-20], because it offers the capability of optimizing several factors simultaneously depending on a statistical design search to find out the maxima or minima of response, by rejecting the point producing the worst response and a replacement of it by the new point which is obtained statistically. The present work describes the utility of bromothymol blue (BTB) reagent for spectrophotometric determination of Cimetidine and Erythromycin in pure form as well as in these dosage form. In addition , the optimization of chemical dependent variables of affecting absorbance have been studied by using modified simplex method (MSM) via computer program.

Apparatus

A Cintra 5 spectrophotometer with 1 cm quartz cells was used for absorbance measurements. PH-meter DW-9421 from Philips instrument, a Sartorius BL 210S balance, and a Pentium 4 computer (DELL) was used for data processing.

Experimental

Material and Reagents:

All Chemicals used were of analytical reagent grad unless otherwise is mentioned, Cimetidine and Erythromycin ethylsuccinate standard powders (purity 99.8%) were kindly provided by the State Company for Drug Industries and Medical Appliances, Samara-Iraq (SDI).

Bromothymol blue(BTB) (Aldrich), 0.1% (w/v) solution is prepared by dissolving 0.1 g of the dye in 5 mL of methanol and then the solution was diluted to a final volume of 100 mL with distilled water. Working solutions were freshly prepared by subsequent dilutions.

Hydrochloric Acid (Aldrich), ~ 0.1 M , a 0.85 mL of concentrated hydrochloric acid (sp.gr1.18.37%) was added to 50 mL distilled water and diluted to the mark in a 100 mL calibrated flask .

Potassium Hydroxide (fluka), ~ 0.1 M, prepared by dissolving 0.56 g of potassium hydroxide in 25 mL distilled water and diluted to 100 mL in volumetric flask with distilled water.

Phthalate buffer 0.2M solution was prepared by dissolved 4.08 g of potassium hydrogen phthalate (MERCK) 25 mL distilled water and diluted to 100 mL in volumetric flask with distilled water, the pH was adjust to 5.5 by using few drops of 0.1M HCl and\or 0.1M KOH[21].

Standard drugs solutions:

Cimetidine stock solution (250 $\mu g.mL^{-1}$), was prepared by dissolving 25 mg of Cimetidine in 5mL methanol and diluting to 100mL in a volumetric flask with distilled water . Working solutions were freshly prepared by subsequent dilutions.

Erythromycin stock solution (250 $\mu g.mL^{-1}$), was prepared by dissolving an accurate weighed 25 mg of Erythromycin ethylsuccinate in 5 mL methanol and diluting to 100mL in a

volumetric flask with distilled water. Working solutions were freshly prepared by subsequent dilutions.

General Procedure

Assay procedure for pure Cimetidine

1 mL aliquots of Cimetidine standared solution containing (2.5-75) µg were transferred into a series of 50 mL separating funnels, to each funnel 0.5 mL of phthalate buffer of pH 5.5 and 1 mL of 0.038% BTB reagent solutions were added. The separating funnels were shaken vigorously with 5 mL chloroform for 6 mints. The two phases were then allowed for clear separation and the absorbance of the yellow colored organic phase was measured at 427.5 nm against a reagent blank prepared similarly without addition of Cimetidine. The calibration graph was constructed by plotting the measured absorbance of the organic phase against the drug concentration.

Assay procedure for pure Erythromycin ethylsuccinate

1 mL aliquots containing (2.5-250) µg Erythromycin ethylsuccinate were transferred into a series of 50 mL separating funnels and to each one, 0.5 mL of phthalate buffer of pH 4.0 and 1 mL of 0.02% BTB reagent were added. The separating funnels were shaken vigorously with 5 mL chloroform for 3 mints. The two phases were then allowed for clear separation and the absorbance of the yellow colored organic phase, measured at 414.5 nm against a reagent blank, was plotted against the concentration of the drug.

Analysis of Cimetidine and Erythromycin ethylsuccinate in pharmaceutical preparations

i. In tablets and capsules:

The content of 10 tablets or capsules were mixed well and a certain amount of fine powder was accurately weighted to give an equivalent to 200 mg for tablets and 250 mg for capsules was dissolve in 5 mL of methanol and diluted to 100mL in a volumetric flask with distilled water. The solution was filtered by using Whatman filter paper No.41 to avoid any suspended or un dissolved material before use. Working solutions were freshly prepared by subsequent dilutions with distilled water and analyzed by the recommended procedure.

ii. In Ampoules:

The volume of 10 ampoules were quantitatively transferred into 250 mL volumetric flask and diluted to the mark with distilled water. An accurately measured volume (2.5mL) was transferred into 100 mL volumetric flask and diluted to the mark with distilled water. Working solutions were freshly prepared by subsequent dilutions with distilled water and analyzed by the recommended procedure.

Results and Discussion

Extractive spectrophtometric procedures are popular for their sensitivity in the assay of drugs and hence, ion pair extractive spectrophotometry has received considerable attention for the quantitative determination of many pharmaceutical compounds [22-24].

Cimetidine and erythromycin ethylsuccinate reacts with BTB in acidic buffer to give yellow color chloroform soluble ion-pair complex, which exhibits absorption maxima at 427.5 and 414.5 nm respectively against their reagent blanks (Figure1). Under the experimental conditions the reagent blank showed in both cases negligible absorbance thereby permit good analytical conditions for quantitative determination of Cimetidine and Erythromycin ethylsuccinate in pharmaceutical dosage forms.

Optimization of experimental variables:

i. Univariable method:

The experimental variables affecting the development and stabilities of both ion-pair complexes were achieved through a number of preliminary experiments. Such factors include pH, reaction time, reagent concentration, order of mixing, shaking time and the type of organic solvent used for extraction. For this reason, a variable was modified while maintaining the other variables at their constant values, then by maintaining that variable at its optimized value, another was modified; all variables were optimized via this method.

Effect of pH

In order to establish the optimum pH range, Cimetidine and Erythromycin ethylsuccinate were mixed separately with specified volumes of BTB. The pH was then adjusted to a value between (4.5 -7.5) and (3-6.0) with few drops of 0.1M NaOH or 0.1M HCl for Cimetidine and Erythromycin ethylsuccinate respectively. It was noticed that maximum color intensities and constant absorbance values were found at pH 5.5 and 4.0 for Cimetidine and Erythromycin ethylsuccinate respectively (Figure 2). Low absorbencies were observed in solutions with higher or low pH than the optimum values for each drug. Hence, a pH of 5.5 and 4.0 was used in all the subsequent experimental work.

Effect of reaction time

The optimum reaction times for both drugs were determined by following the color development at ambient temperature (25±2). It was found that both reactions were instantaneous. Hence the products attained maximum and constant absorbancies immediately after the Cimetidine and Erythromycin ethylsuccinate have been mixed with BTB and the developed color, in each case, remained strictly unaltered for at least 24 hours.

Effect of reagent concentration

The influences of reagent concentration on the absorbancies of both complexes are illustrated in (Figure 3). 0.038% and 0.020% solutions of BTB were found to be optimum to develop the maximum color intensities for Cimetidine and Erythromycin ethylsuccinate ion-pair complexes respectively, after which no more increase in absorbance values was obtained; therefore, the cited concentrations of BTB solution were used.

Effect of the order of mixing:

The effect of order of addition of the reactant was also studied. It was found that best results were obtained in both cases by placing the cited drug, the buffer and finally the reagent instead of any other orders of addition.

Effect of shaking time

The optimum shaking times for the complete extraction of the formed ion pair complexes with chloroform were studied for the period of 1-8 minutes (Table 1). It was found that the minimum shaking times for complete extraction of Cimetidine and Erythromycin ethylsuccinate complexes, at room temperature, were 6 and 3 minutes respectively.

Effect of the extraction solvent

Several organic solvents, namely toluene, carbon tetrachloride, methylene chloride, 1, 2-dichloroethane, benzene in addition to chloroform, were examined for their ability to extract the drug-dye ion-pairs. The latter was found to be the most suitable solvent in terms of extraction efficiency (Table 2). On the other hand, it was observed that only a single extraction with 5 mL portion of chloroform was adequate to achieve a quantitative recovery of both complexes.

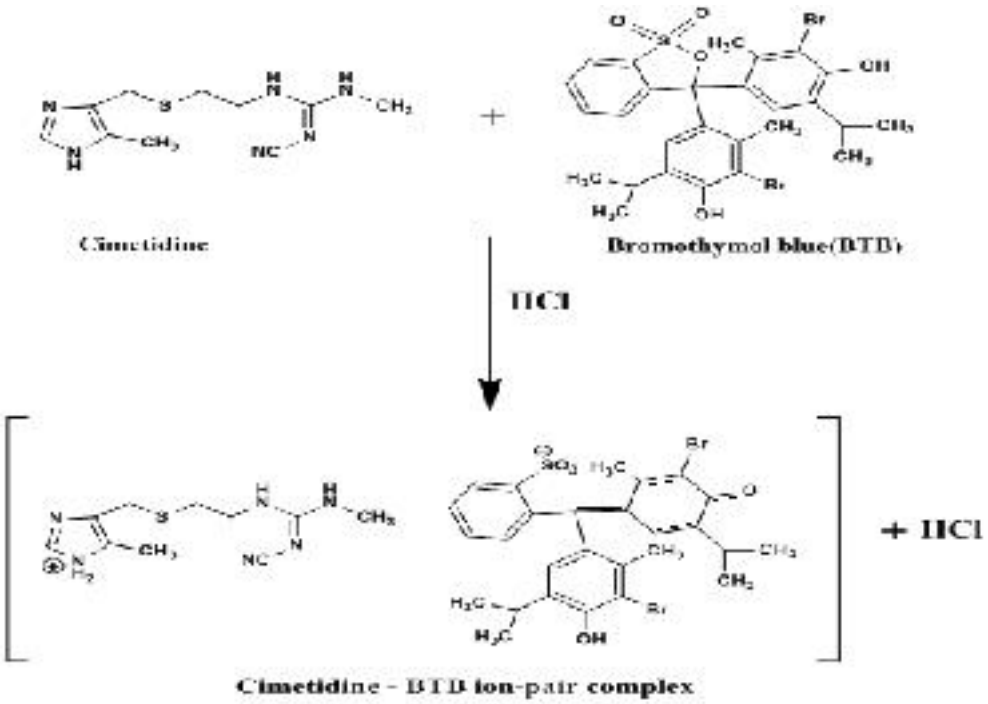
ii. Simplex method

Simplex method is used to confirm the optimum conditions, which were obtained by the univariate procedure. Three major parameters (pH, reagent concentration, and shaking time) were optimized by the simplex procedure, while the other minor parameters were obtained by the univariate method. To set simplex program for the three studied variables (Table 3), four arbitrary experimental conditions should be chosen. The values of these parameters were selected within specified boundaries for each at which they affected the measured absorption signal of the colored products.

The absorbencies of these four experiments were measured and the results were feed to the simplex program. Points (1 to 4) in Tables 4 and 5 represent the first four experiment cycle with their measured absorbencies. The Simplex program starts to reflect the worst point through the centroid of other points to obtain a new point 5. An experiment was then performed utilizing the variable setting as a reflected point; because this value was better than that at point 3, the latter was rejected and replaced by point 5. A measured absorption signal was feeding again to the program and the process is repeated successively until optimum conditions were obtained similarly to those obtained by the univariate method.

Stoichiometry of the complexes

To establish molar ratio between Cimetidine and Erythromycin ethylsuccinate with BTB, Job's method of continuous variation has been used (Figure 4). The results showed that 1:1 complexes were formed with BTB through the electrostatic attraction between the positive protonated Cimetidine and Erythromycin ethylsuccinate with the anion of BTB [25, 26]. The formation of the ion-pair complex can be represented by taking Cimetidine as an example (Scheme 3):



Scheme 3: Proposed reaction pathway between Cimetidine and BTB.

Calibration graphs

Employing the experimental conditions, linear calibration graph for Cimetidine and Erythromycin ethylsuccinate was obtained (Figure 5 A and B), which showed that Beer's law was obeyed in the concentration range of 0.5-15 and 0.5-50 $\mu g.mL^{-1}$ for Cimetidine and Erythromycin ethylsuccinate respectively.

Spectral characteristics of the proposed methods

According to the optimum experimental conditions of the proposed methods, the regression plots showed linear dependence of absorbance signals on the concentrations of the studied drugs in the range given (Table 6). The regression equations, correlation coefficients, molar absorptivities, detection limits and sandell sensitivities in addition to other parameters are given in Table 5.

Accuracy and precision

The accuracies of the proposed methods were confirmed by analyzing three replicate analyses of three different amounts of each drug (within Beer's law) by calculating the relative error percentage (Table 7). The results indicated good accuracies of the method for both cited drugs. The precision was determined in each case by calculating the percentage relative standard deviation (RSD %) for three determinations at each of the studied concentration level and were found to be in the range of 1.158-2.003% and 0.173-2.276% for Cimetidine and Erythromycin ethylsuccinate respectively.

The proposed method was compared statistically with other methods found in the literature and the results are shown in tables 10 and 11.

Interferences Study

The results showed that no interferences were found in the presence of 1000 µg of the studied excipients (lactose, sucrose, starch, glucose, magnesium stearate and sodium citrate) in the determination of Cimetidine and Erythromycin ethylsuccinate (Table 9).

Analysis of dosage forms

It is evident from the aforementioned results that the proposed method gave satisfactory results with the investigated drugs. Thus, their pharmaceutical dosage forms were subjected to analysis of their contents of the active ingredient by the proposed method (ion-pair formation). The results given in table 8 were satisfactory.

The recommended method was statistically compared with official, standard and other methods, no significant differences were found between the calculated and theoretical values of t- test at 95%and F- test at 99.5%, 99.5% and 95% (Tables 12 and 13).

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Table(1): Effect of shaking time on extraction of 5 µg.mL^{-1} Cimitidine; (0.038%BTB, pH5.5) and 10µg.mL^{-1} Erythromycin ethylsuccinate (0.02%BTB, pH 4)

Mixing Time/mint	Absorbance Cimetidine	Absorbance Erythromycin ethylsuccinate
1	0.272	0.247
2	0.274	0.249
3	0.268	0.255
4	0.269	0.243
5	0.294	0.242
6	0.298	0.242
7	0.264	0.241
8	0.264	0.240

Table (2): Effect of type of organic phase on extraction of 5 µg.mL^{-1} Cimetidine and 10 µg.mL^{-1} Erythromycin ethylsuccinate

Organic phase	Absorbance of Drug-BTB ion pair complex	
	Cimetidine	Erythromycin ethylsuccinate
Chloroform	0.298	0.255
Toluene	0.014	0.168
Carbontetrachloride	0.022	0.066
Benzene	0.002	0.185
1,2-Dichloro ethane	0.089	0.097
Dichloro methane	0.077	0.067

Table(3): Boundary conditions for the studied variables

Variable	Range for Cimetidine	Range for Erythromycin
pH	5.0-8.5	3-6
Reagent Conc.(%)	0.01-.038	0.01-0.025
Shaking time (min.)	1-8	1-5

Table (4): Multivariate experiments (Simplex) for determination of Cimitidine

Exp. No.	pH	%Reagent Conc.	Mixing Time	A
1	5.5	0.038	5	0.532
2	8.0	0.020	4	0.267
3	6.5	0.010	1	0.226
4	7.0	0.030	3	0.290
5	5.5	0.038	8	0.531
6	5.0	0.038	8	0.445
7	6.5	0.036	4	0.322
8	5.5	0.038	7	0.532
9	6.0	0.038	5	0.528
10	5.5	0.038	4	0.530
11	5.5	0.038	6	0.534
12	5.5	0.038	6	0.534

Table(5): Multivariate experiment (Simplex) for determination of Erythromycin ethylsuccinate

Exp. No.	pH	%Reagent Conc.	Mixing Time	A
1	4.0	0.010	1	0.164
2	5.5	0.020	2	0.229
3	6.0	0.015	4	0.023
4	3.0	0.025	3	0.226
5	6.0	0.025	5	0.239
6	6.0	0.020	5	0.200
7	4.5	0.025	4	0.246
8	5.0	0.025	5	0.235
9	4.0	0.025	5	0.254
10	3.0	0.025	5	0.210
11(8)	5.0	0.025	5	0.235
12	5.0	0.025	5	0.210
13(7)	4.5	0.025	4	0.246
14	3.5	0.025	5	0.240
15(7)	4.5	0.025	4	0.246
16(14)	3.5	0.025	5	0.240

Table (6): Spectral characteristics and statistical data of the regression equations for determination of Cimetidine and Erythromycin ethylsuccinate using ion–pair formation

Parameter	Cimetidine	Erythromycin ethylsuccinate
λ_{max} (nm)	427.5	414.5
Color	Yellow	Yellow
Linearity range ($\mu g.mL^{-1}$)	0.5 – 15.0	0.5 – 50.0
Molar absorpitivites ($l.mol^{-1}.cm^{-1}$)	13172	18103
Regression equation	A = 0.052 [Cim. $\mu g.mL^{-1}$] + 0.013	A = 0.021[Ery. $\mu g.mL^{-1}$] + 0.018
Calibration Sensitivity	0.052	0.021
Sandell's Sensitivity ($\mu g.cm^{-2}$)	19.157	47.620
Correlation of Linearity (R^2)	0.9970	0.9985
Correlation coefficient (R)	0.9984	0.9992
Detection limit ($\mu g.mL^{-1}$)	0.222	0.286

Table (7): Evaluation of accuracies and precisions of the two proposed procedure

Drug	Concentration ($\mu g.mL^{-1}$)		Relative Error %	R.S.D.* %
	Taken	Found*		
Cimetidine	2	1.971	-0.145	1.538
	4	3.972	-0.700	1.158
	10	9.936	-0.640	2.003
Erythromycin	5	4.921	-1.580	2.276
	20	19.858	-0.710	1.695
	40	40.272	+0.680	0.173

*Average of three determinations

Table (8): Spectrophotometric determination of Cimetidine and Erythromycin Ethylsuccinatein pharmaceutical compounds using Ion –Pair Formation

Sample	Amount (mg)		Concentration ($\mu g.mL^{-1}$)		Relative Error %	R.S.D.* %
	Labeled	Found	taken	Found*		
Tagadine (Cimetidine) 200mg/ tablet SDI/Iraq	200	204.840	5	5.121	+2.400	0.937
		200.760	10	10.038	+0.380	0.508
Cimedne^{R} (Cimetidine) 200mg/ tablet DAD Jordan	200	180.320	5	4.508	-9.840	0.615
		179.820	10	8.991	-10.090	0.316
Histale (Cimetidine Hydrochloride) 200mg/Ampoule IBH/Syria	200	199.000	5	4.975	-0.500	0.582
		198.840	10	9.942	-0.580	1.579
Erythrosam (Erythromycin ethylSuccinate) 250mg/ tablet SDI/Iraq	250	255.150	10	10.206	+2.060	0.970
		256.35	20	20.508	+2.540	0.353
Erythronin (Erythromycin ethylsuccinate) 250mg/ tablet NDI/Iraq	250	253.575	10	10.143	+1.430	0.473
		254.363	20	20.349	+1.745	0.359
Zithrorive (Azithromycin dehydrate) 250mg/ tablet R.P/Egypt	250	249.600	10	9.984	-0.160	1.202
		246.588	20	19.727	-1.365	0.487
Erythromycin Stearate (pure powder) SDI/Iraq	250	249.200	10	9.968	-0.320	1.204
		246.375	20	19.710	-1.450	0.639

*Average of three determinations

Table (9): Percent Recovary for 10 µg.mL^{-1}of Cimetidine and 20 µg.mL^{-1}of Erythromycin Ethylsuccinate in the presence of 1000 µg.mL^{-1}of Excipients

Excipients	Cimetidine Conc. Taken10 µg.mL^{-1}		Erythromycin Ethylsuccinate Conc. Taken20 µg.mL^{-}	
	Conc. Fundµg.mL^{-1}	%Recovery	Conc. Fundµg.mL^{-1}	%Recovery
lactose	9.928	99.280	19.829	99.145
Sucrose	9.934	99.340	19.842	99.210
starch	9.932	99.320	19.857	99.285
Glucose	9.929	99.290	19.857	99.285
Magnesium Stearate	9.935	99.350	19.839	99.195
Sodium Citrate	9.933	99.330	19.843	99.215

*Average of three determinations

Table(10): Analytical Parameters for the analysis of Cimetidine by the propsed and others methods

Ref. No.	methods	Linear range µg.mL^{-1}	ε L.mo^{1}.$^{-}$cm^{-} ^{1}	Correlation Coefficient (R)	Recoveries range%	RSD% range
-	Proposed method	0.5-15.0	13172	0.9984	98.550-99.36	1.158-2.003
12	Spectrophotometric	1-20		0.9994	98.3-102.6	
27	Spectrophotometric	8-30	6710		99.8-100.2	0.81-0.84
28	Spectrophotometric	2-16	13660	0.9989	99.8-100.7	0.74-0.92
6	H.P.TL.C.	5-50	-	-	100.39 ± 1.33	
29	H.P.L.C	0.25-83		0.998	99.2 - 100.8	
30	H.P.L.C	50-3000	-	-	71 -81	less than 6%
31	Spectrophotometric 1st derivative	25-150	-	-	100.27±0.679	-
	Spectrophotometric Complex formation	10-60	-	-	99.84±0.858	-

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Table(11): Analytical Parameters for the analysis of Erythromycin Ethylsuccinate by the propsed and others methods

Ref. No.	methods	Linear range $\mu g.mL^{-1}$	$\varepsilon L.mo^{l-}.cm^{-1}$	Correlation Coefficient (R)	Recovery %	RSD%
-	Proposed method	0.5-50	18103	0.9992	98.4-100.6	0.17-2.27
32	Spectrophotometric Direct UV 1st Derivative	3-15	37.43	0.9836-0.9892	97.6	0.48
		3-15	44.03	0.9917-0.9967	106.5	0.65
11	Spectrophotometric Ion-Pair	2-61	-	-	98.4-103.6	1.4-4.4
33	high-pressure L.C.	60-120	-	-	99.9	Lees than1%
34	Extraction	0.4-56	-	-		1.,3
35	Charge transfer	1.724-129.3	8500		98.3	
36	Spectroflurimetric	0.0426-1.2	-	-	98.3-100.8	0.014-0.058
37	Charge transfer	5-60	11410	-	98	0.82
38	Charge transfer	0-80	9910	-	97	-

Table(12): t- and F- Values for analysis of Cimetidine in Pharmaceytical Copmpounds

Cimetidine					
Proposed Method, (S.D.I)	T-Values[a]	F-values[b]	Other Methods (N=5)	S.D	Ref. No.
Ion-Pair	0.671	157.692	Official	0.640	27,39
N=3	0.567	357.692	Other	0.930	28
S.D = 0.051	0.177	1.727	Stander	0.167	40

* a Theoretical values for t-test at 95% confidence limit were N=6 (2.447).
b Theoretical values for F-test at 99.5% (199.25), 99.9%(999.25) and 95% (19.274) confidence limit respectively, were N=(4,2).

Table(13): t- and F- Values for analysis of Erythromycin Ethylsuccinate in Pharmaceytical Copmpounds

Erythromycin Ethylsuccinate					
Proposed Method, (S.D.I)	T-Values[a]	F-values[b]	Other Methods		Ref. No.
			N	S.D	
Ion-Pair	0.388	200	(N=9)	1.400	11
N=3	1.735	13.151	(N=8)	0.359	35
S.D = 0.099	2.832	2	(N=6)	0. 140	38

* a Theoretical values for t at 95% confidence limit were N=10(2.228), 9(2.262) and 7(2.365)respectively b Theoretical values for F at 99.9%were N=(8,2)(999.31), 95% were N=(7,2)(19.353) and 95% were N = (5,2)(19.296) confidence limit respectively.

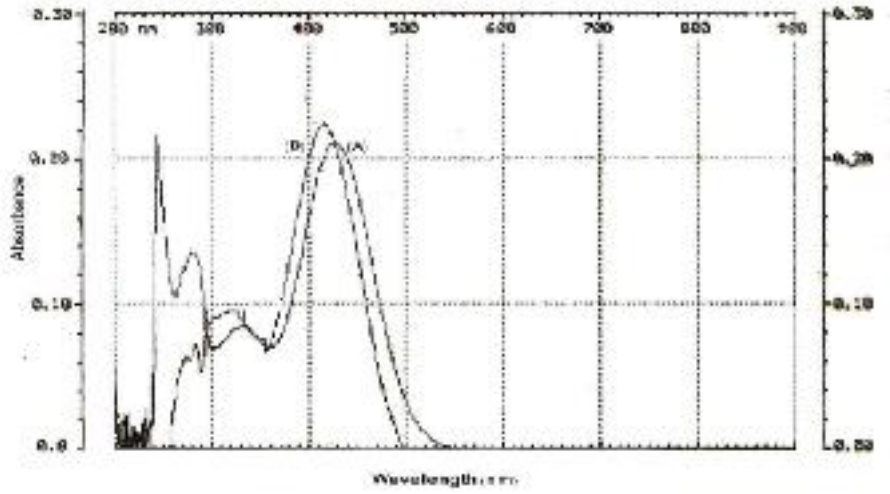

Fig.(1): Absorption spectra of (A) 4 µg.mL^{-1} Cimetidine-BTB ion-pair complex, (B) 10 µg.mL^{-1} Erythromycin ethylsuccinate-BTB ion-pair complex.

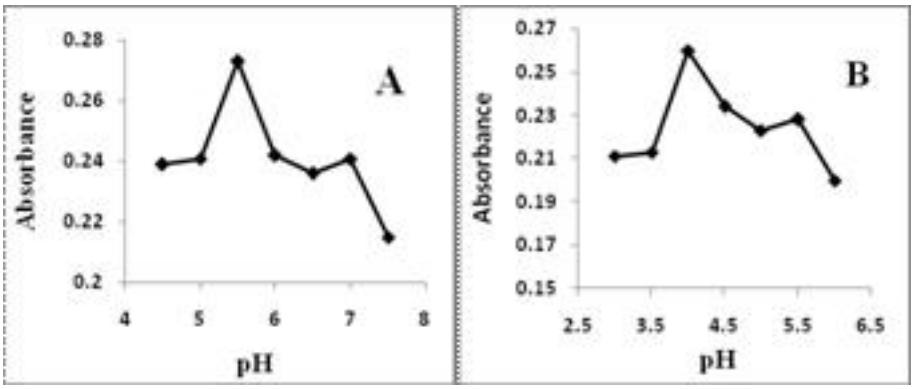

Fig.(2): Effect of pH on the Absorbance of: (A) 5 µg.mL^{-1} Cimetidine; 0.04% BTB. (B) 10 µg.mL^{-1} Erythromycin ethylsuccinate ; 0.04 % BTB.

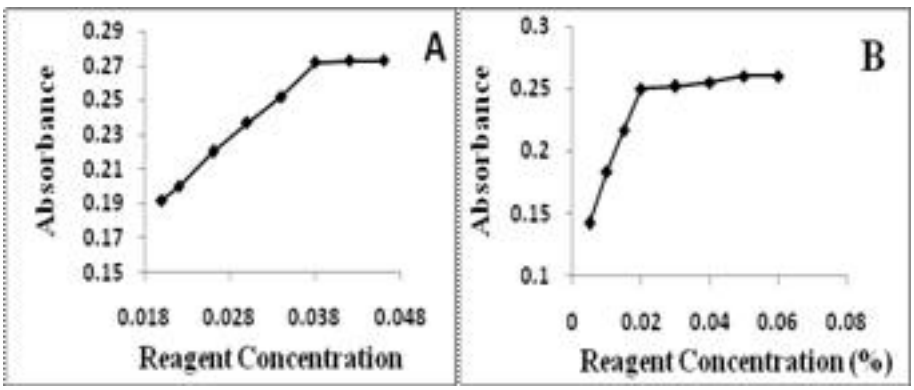

Fig.(3): Effect of Reagent Concentration on the Absorbance of: (A) 5 µg.mL^{-1} Cimitidine pH 5.5, (B) 10 µg.mL^{-1} Erythromycin ethylsuccinate pH 4.

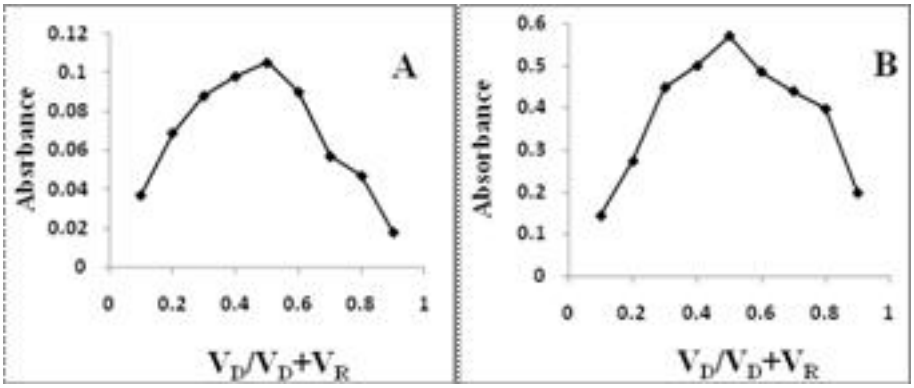

Fig. (4): Continuous Variation of (A) $9.907*10^{-5}$ M Cimetidine, $9.907*10^{-5}$ M BTB (B) $1.740*10^{-4}$ M Erythromycin ethylsuccinate, $1.740*10^{-4}$ M BTB.

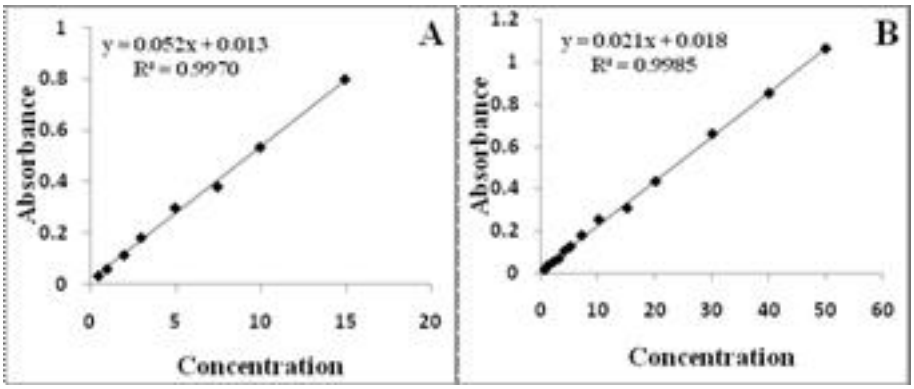

Fig.(6): Calibration graph of (A) Cimetidine, (B) Erythromycin ethylsuccinate; underder optimum experimental conditions.

مجلة ابن الهيثم للعلوم الصرفة والتطبيقية المجلد23 (3) 2010

ايجاد الظروف المثلى بدراسة المتغيرات الاحادية وبطريقة السمبلكس لتقديردوائي السمتيدين

والارثرومايسين ايثايل سوكسينيت بأستخدام الكاشف بروموثايمول الازرق بتكوين معقدات الازدواج الايوني

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الخلاصة

لقد استخدمت طريقة طيفية بالاعتماد على تكوين معقدات أزدواج ايوني لتقدير السمتيدين والارثرومايسين ايثايل سوكسينيت في عينات نقية ومستحضرات صيدلانية. كانت الطريقة دقيقة ،و بسيطة ، وسريعة، وغير مكلفة ،وحساسة تعتمد بالاساس على استخدام الكلوروفورم في استخلاص معقدات الازدواج الايوني المتكونة بين العقارين قيد الدراسة مع الكاشف بروموثايمول الازرق من وسط مائي وبدوال حامضية 5.5 و4.0 للسميتيدين والارثرومايسين ايثايل سوكسينيت على التوالي. لقد اظهرت المعقدات المتكونة للسميتيدين والارثرومايسين ايثايل سوكسينيت اعظم امتصاص لها عند الاطوال الموجية 427.5 نانومتر ،و414.5 نانومتر على التوالي مقابل محاليل الخلب لها. واظهرت منحنيات المقايسة علاقات خطية في المديات من(0.5 – 15) مايكروغرام / مل، و(0.5 – 50) ميكروغرام/ مل وبحدود كشف 0.222 مايكروغرام/ مل، و 0.286 مايكروغرام/ مل للعقارين المذكورين على التوالي. أظهرت الدراسة أيضآ أن الطريقتين المقترحتين خالية من تأثير المتداخلات المعروفة التي تتواجد غالبا في المستحضرات الصيدلانية لهذين العقارين، وقد أمكن تطبيق الطريقتين بنجاح لتقدير السمتيدين والارثروةمايسين ايثايل سوكسينيت (مع أثنين من مشتقاته) في بعض المستحضرات الصيدلانية.