بسم الله الرحمن الرحيم

An-Najah National University

Faculty of Graduate Studies

Extractional Spectrophotometric Determination of New Substituted Tricyclic Pyridopyrimidines

By

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3- Dr. Raqi M. Shubietah Assistant Prof. Of Analytical Chemistry An-Najah National University.	

Dedication

To my Parents

my brothers, my sisters

and .. my wife

with love and respect

Acknowledgments

I would like to express my profound thanks and indebtedness to Prof. Ali Z. Abu-Zuhri for his supervision, encouragement, guidance and inspiration throughout this study.

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Abstract

A simple and sensitive method was developed for the extractional spectrophotometric determination of new substituted tricyclic pyridopyrimidine compounds **(I)** (7-chloro-2,3-trimethylene-pyrido [1.2-a] pyrimidine-4-one), **(II)** (7-bromo-2,3-tetramethylene-pyrido [1,2-a] pyrimidine-4-one) and **(III)** (7-methyl-2,3-tetramethylene-pyrido [1,2-a] pyrimidine-4-one). The method was based on the formation of ion-pair complexes between compounds **I, II** and **III** with bromothymol blue (BTB). The absorbance of the produced ion-pair complexes were measured at 414, 418, and 418 nm for I-BTB, II-BTB and III-BTB respectively.

Beer's law was obeyed over the concentration ranges 0.04 -5.10, 0.12-5.58 and 0.76-6.82 μg/ml for compounds **I, II** and **III,** respectively. Molar absorptivities for compounds **I, II** and **III**, were found to be 8.0×10^3, 8.0×10^3 and 1.2×10^4 L mol^{-1} cm^{-1} ,respectively.

All factors affecting the sensitivity and reproducibility of the method were studied such as pH, shaking time, concentrations of BTB, amount of buffer, type of solvent, number of extraction times and stoichiometry. The method was applied for spectrophotometric determination for compounds **I, II** and **III.**

بسم الله الرحمن الرحيم

• يرفع الله الذين آمنوا منكم والذين أوتوا العلم درجات •

صدق الله العظيم

1.1 Biological Significance of Tricyclic pyridopyrimidines

Compounds **(I)** (7-chloro-2,3-trimethylene-pyrido [1.2-a] pyrimidine-4-one), **(II)** (7-bromo-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one) and **(III)** (7-methyl-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one) have shown the analogous of pydidopyrimidines high appreciable activity against some kinds of bacteria. These compounds would be expected to show high significance as antimitotic agents and anti-allergic agent.[12] ,3-substituted compounds , 2-phenyl-1,8-naphthyridin-4-ones **(IV),** showed significant cytotoxic effects of growth inhibition against a variety of human tumors including cells derived from solid tumors such as non-small cell lung, colon, central nervous system (CNS), metanomar, ovarian, prostate and breast cancers .[1,5]

Kuo and Lee evaluated 1,6,7,8-substituted phenyl-4-quinolones **(V)** and **(VI)** as cytotoxic compounds and as antimiotic agents interacting with tubulin.[2] Guirk and Jefson prepared and evaluated 6-fluoro-7-diazzbicyclo-alkyl quinolones **(VII)** for antibacterial activity against a wide range of important veterinary pathogenic bacteria. [3]

Qun Li showed that the 2-pyridones (**VIII**) have been shown to be excellent DNA gyrase inhibitors, most notably they were active against resistant bacteria such as MRSA (methicillin-resistant staphylococcus aureus. [4].Ke Chen and Sheng-Chu Kuo *et al* used the 2-phenyl-1,8-naphthyridin-4-ones (**IX**) as cytotoxic in vitro against six tumor cell lines, including human carcinoma of the nosophyarynx lung carcinoma, ileocecal carcenoma, melanoma and medulloblastoma as well as one murine leukemia cell line .[1]

Li Sun et al shown that 5-oxo-5H-[1] benzopyrano-[2,3-b] pyridine-3-carboxylic acid (**IX**) was used as anti-allergic.[6,7]

Fumios, S and Takeshi showed that 2-alkyl pyridiones as 6H-6-oxo-pyrido [1,2-a] pyrimidine (**VIII**) were active against Staphylococcus Aurous and Streptococcus Pneumonia .[8]

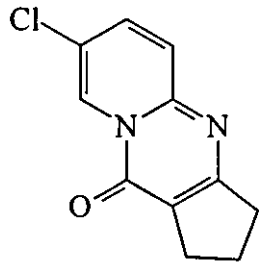
Leping Li and Hui-Kang shown that 2-phenyl-4-quinolones as 7-pyrrolo-2-[4-methoxyphenyl]-4-quinolone (**X**) can be used as anti-mitotic, anti-tumor and anti-tubulin polymerization .[9,10] Martin et al showed that the polyfluoralkeynal amidazo [1,2-a] pyridine (**XI**) showed fungicidal activity .[11,12]

From this information we noticed that pyridopyrimidines have approved biological significance.

1.2 Aim of the work

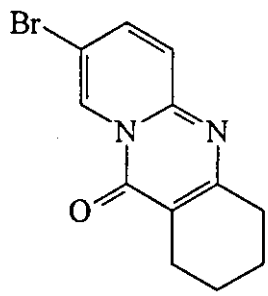
Pyridopyrimidines and their analogous have important biological activities. Our literature survey showed that no work has been done on quantitative determination of these compounds. The aim of this work is to develop new spectrophotometric methods for the determination of compounds **I, II** and **III** as their ion-pair complexes with bromothymol blue (BTB)

In this work we used new synthesized compounds **I, II** and **III** which have no previous reports concerning their spectrophotometric analysis. In this work a simple and sensitive spectrophotometric method was developed for the extraction and spectrophotometric determination of these compounds. The method is based on the formation of an ion-pair complex between the drug and bromothymol blue (BTB) dye. The produced yellow ion-pair complex was extracted to the organic phase using chloroform for compound **I** and dichloromethane for compounds **II** and **III**.



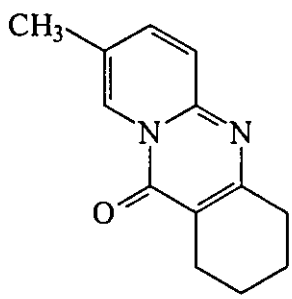
I

7-chloro-2,3-trimethylene-pyrido [1.2-a] pyrimidine-4-one



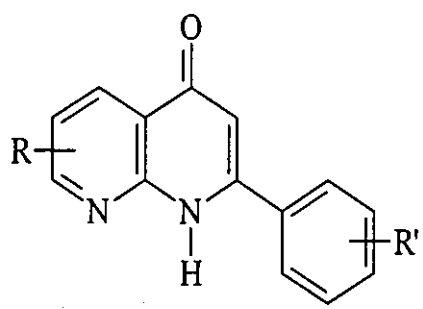
II

7-bromo-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one



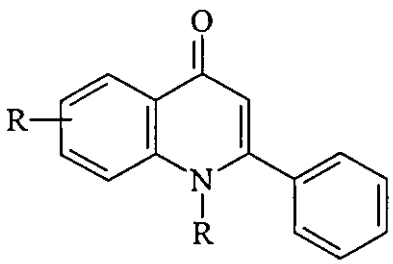
III

7-methyl-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one

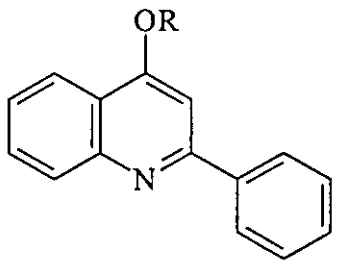


IV

2-phenyl-1,8-naphthyridin-4-one

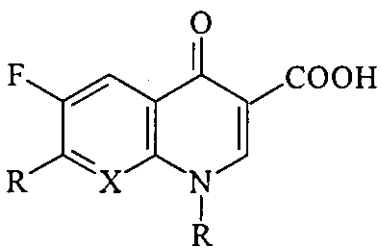


V



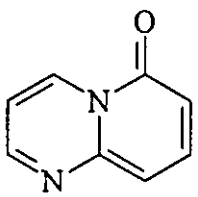
VI

1,6,7,8-substituted phenyl-4-quinolones



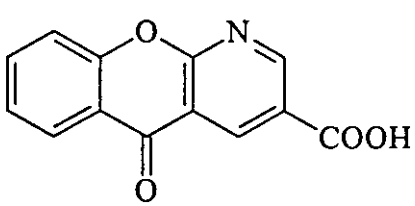
VII

6-fluoro-7-diazzbicyclo-alkyl quinolones



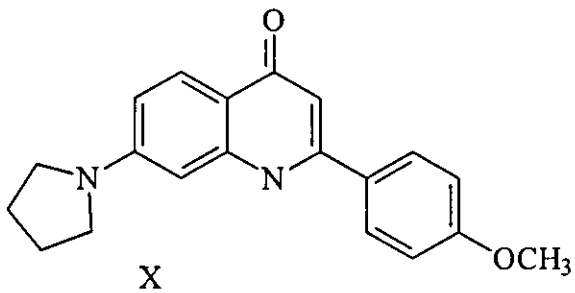
VIII

6H-6-oxo-pyrido [1,2-a] pyrimidine



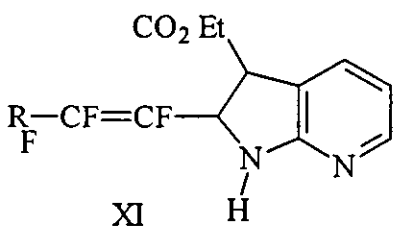
IX

5-oxo-5H-[1] benzopyrano-[2,3-b] pyridine-3-carboxylic acid



X

7-pyrrolo-2-[4-methoxyphenyl]-4-quinolone



XI

polyfluoralkeynal amidazo [1,2-a] pyridine

Chapter Two

Experimental

Chapter Two

Experimental

2.1 Reagents and solutions

Throughout the experimental work, doubly distilled water was used. Compounds **I** (m.p=151^{0}C), **II** (m.p=146^{0}C), and **III** (m.p=112^{0}C), prepared at An-Najah National University laboratories as described by Yasin R.[13]. Solvents and all other chemicals were of analytical grade.

2.1.1 General procedure for the preparation of compounds I, II and III

Polyphosphoric acid (3gm) was weighed out and transferred into 50 ml flask, ethyl 2-oxocyclopentane carboxylate or ethyl 2-cyclohexanone carboxylate or ethyl 2-cyclohexanone acetate was added followed by 2-amino-5 substituted pyridine[13]. The mixture was mixed manually and heated to 120 ^{0}C reflux and condense for 2 hours. The reaction was monitored periodically by (TLC). After completion, the flask was cooled in an ice bath, and the mixture was dissolved in an ice water, then the solution was neutralized by saturated NaOH, while cooling in an ice bath. The white to yellow precipitate was filtered using a glass sintered funnel and washed with distilled water[13]

2.1.2 7-chloro-2,3-trimethylene-pyrido [1.2-a] pyrimidine-4-one stock solution (1.0×10^{-3} M), (compound I).

This compound was prepared by dissolving exactly 0.0210 gm in ethanol, the solution was transferred to a 100 ml volumetric flask, and the volume was completed to the mark with ethanol in a volumetric flask.

2.1.3 7-bromo-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one stock solution (1.0×10^{-3} M)), (compound II).

This compound was prepared by dissolving exactly 0.0279 gm in ethanol, the solution was transferred to a 100 ml volumetric flask, and the volume was completed to the mark with ethanol in a volumetric flask.

2.1.4 7-methyl-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one stock solution (1.0×10^{-3} M)), (compound III).

This compound was prepared by dissolving exactly 0.0189 gm in ethanol, the solution was transferred to a 100 ml volumetric flask, and the volume was completed to the mark with methanol in a volumetric flask.

2.1.4 Preparation of Britton – Robinson (BR) Buffer

A mixture of acetic acid, boric acid, and phosphoric acid which has 0.04 M each was prepared by mixing equal volumes of 0.012 M of each acid, different pH values were prepared by adding 0.2 M sodium hydroxide solution.

2.1.5 Preparation of bromothymol blue (BTB) solution (1.0×10^{-3} M)

A 0.0624 gm of BTB was dissolved in 2 ml of 0.1 M sodium hydroxide. 20 ml of ethanol (96%) was added and the volume was completed to 100 ml using BR buffer of suitable pH.

2.2 Apparatus

A UV-2 UNICAM UV-Visible spectrophotometer was used for all spectrophotometric measurements. All measurements were carried out using quartz cells (10 mm), at room temperature. pH measurements were carried out using HANA pH meter of model 8521.

2.3 Recommended procedure for spectrophotometric determination of compounds I,II,III

A 1.0 ml of 1.0×10^{-3} M BTB solution was pipetted into a 100 ml separatory funnel. 1.0 ml of BR buffer of pH's 5.0,4.0 and 4.0 for compounds **I, II** and **III,** respectively were added, followed by a calculated amount of each compound, a 20-ml portion of chloroform was added for compound **I** and 20 ml of dichloromethane was added for compounds **II** and **III.** The mixtures were shaken out vigorously for 30, 30 and 150 seconds for compounds **I, II** and **III,** respectively. The solutions were allowed to stand for 20, 20 and 1 minutes for compounds **I, II** and **III** respectively. The organic layer was transferred into a 25- ml volumetric flask and completed to the mark with appropriate solvent. The blanks were prepared following the same procedure. The absorbancies were measured at 414,418 and 418 nm for compounds **I, II** and **III,** respectively against a reagent blank.

Chapter Three

Results and Discussion

Results and Discussion

3.1 Absorption spectra

The absorption spectra of compounds **I, II** and **III** ion-pair complexes with BTB were studied in the organic phase. Extraction of the yellow ion-pair complex from aqueous medium with selected solvent was investigated. The ion-pair formed was found to be extracted into chloroform for compound **I,** and dichloromethane for compounds **II** and **III.** The absorption spectrums of the ion-pair complex against the blank (containing BTB) and the absorption of the blank against the organic solvent were shown. The absorption spectrum were studied over the range 350-550 nm for compounds **I, II** and **III,** the results obtained are presented in figures 1, 2 and 3, respectively.

It was found that, the absorption spectrum for all ion-pairs extract exhibit an absorption peak at ~ 420 nm. The effect of different experimental parameters affecting the ion-pairs spectrum, for example pH, amount of buffer, equilibrium time, reagent concentration, type of organic solvent, amount of dye and shaking time were investigated.

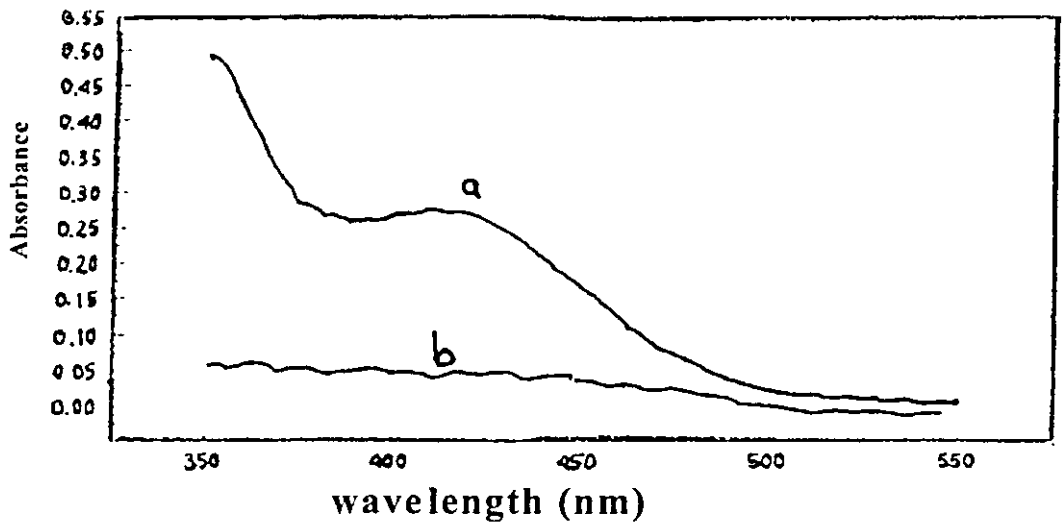


Figure 1 : Absorption spectra of (a) : compound **I** – BTB ion-pair against a reagent blank at pH=5.0, (b) : reagent blank against chloroform. Volume of aqueous phase = 12.0 ml, Volume of organic phase = 25.0 ml, temperature = 22±1 ^{0}C.

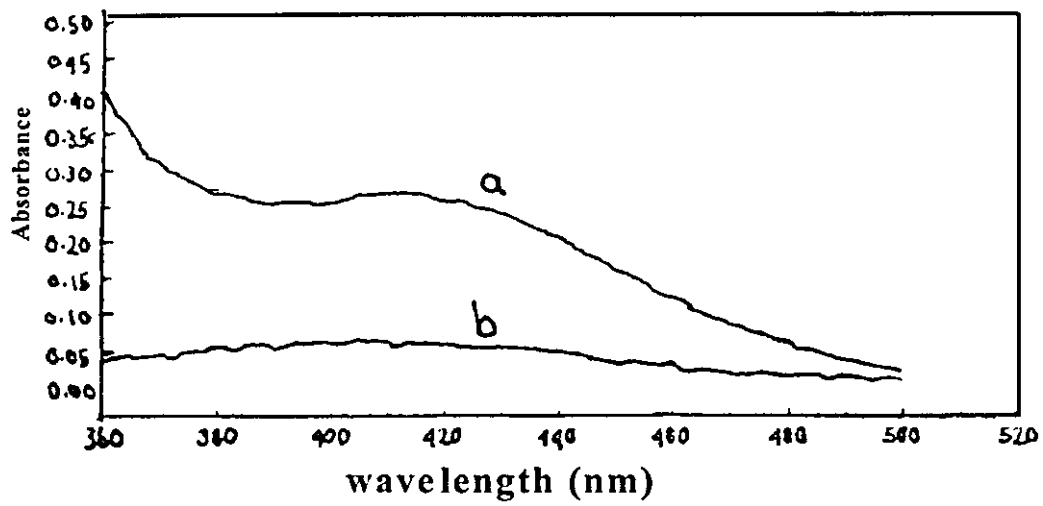


Figure 2 : Absorption spectra of (a) : compound **II** – BTB ion-pair against a reagent blank at pH=4.0, (b) : reagent blank against chloroform. Volume of aqueous phase = 12.0 ml, Volume of organic phase = 25.0 ml, temperature = 22±1 ^{0}C.

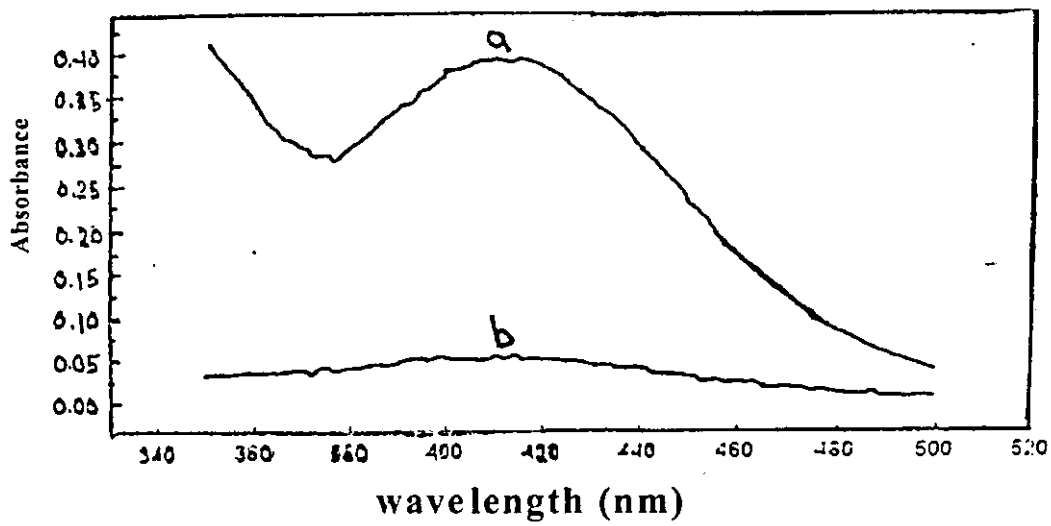


Figure 3 : Absorption spectra of (a) : compound **III** – BTB ion-pair against a reagent blank at pH=4.0, (b) : reagent blank against chloroform. Volume of aqueous phase = 12.0 ml, Volume of organic phase = 25.0 ml, temperature = 22±1 ^{0}C.

3.2 Effect of pH

The effect of pH on the absorbance of the organic phase was studied over the pH range 2.0-8.0 for the three ion-pair complexes. It was found that the absorbance of all ion-pairs increase gradually with increasing pH from 2.0 to 5.0, any further increase in the pH affects a gradual decrease in the absorbance up to pH 8.0.

The results indicate that the quantitative extraction of compounds **I, II** and **III** is optimum at pH 5.0, 4.0 and 4.0, respectively. Hence, all the extractions were carried out at these pH values.

Table 1 : Effect of pH on the absorbance of compounds **I,II** and **III** ion-pair complexes. [BTB] = [compound] = 1.0×10^{-3} M

pH	Absorption of complexes		
	I at λ=414 nm	**II** at λ=418 nm	**III** at λ=418 nm
2.0	0.22	0.20	0.39
3.0	0.23	0.36	0.44
4.0	0.24	0.38	0.49
5.0	0.25	0.38	0.41
5.5	0.23	0.36	0.40
6.0	0.17	0.32	0.37
7.0	0.15	0.31	0.34
8.0	0.14	0.28	0.05

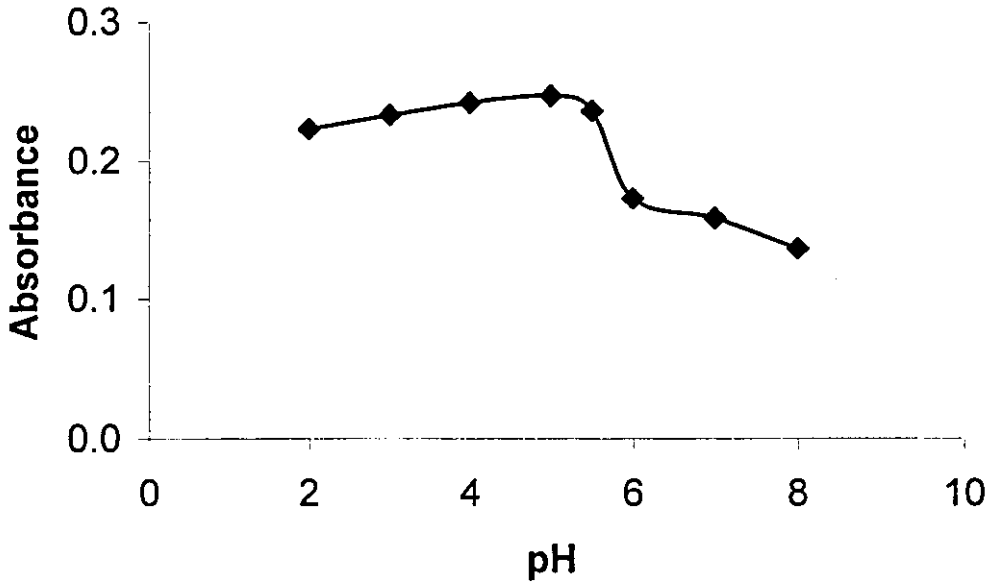


Figure (4) : effect of pH on the absorbance of compound **I** ion-pair complex, [BTB]=[compound I] =1.0×10^{-3} M, λ=414 nm, Volume of aqueous phase = 12.0 ml, Volume of organic phase = 25.0 ml, temperature = 22±1 ^{0}C.

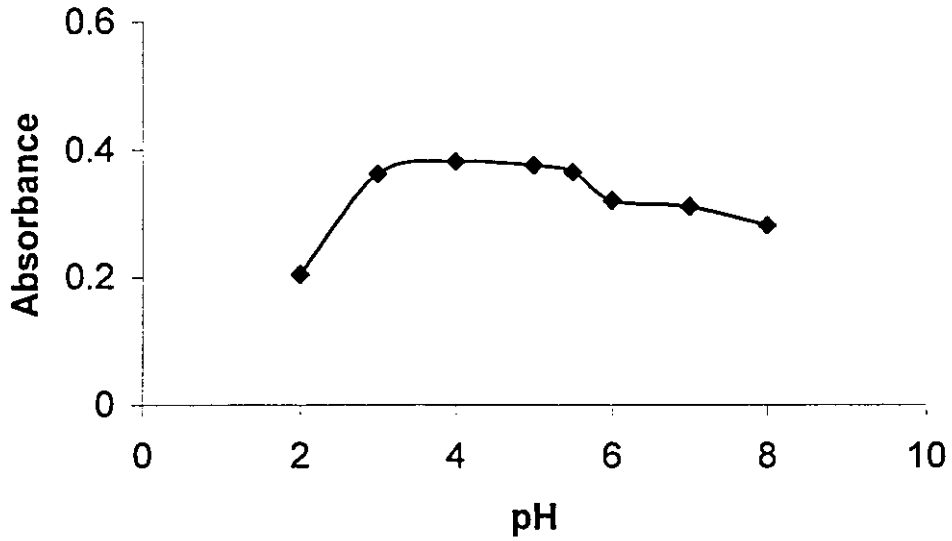


Figure (5) : effect of pH on the absorbance of compound **II** ion-pair complex, [BTB]=[compound **II**]=1.0×10^{-3} M, , λ=418 nm, Volume of aqueous phase = 12.0 ml, Volume of organic phase = 25.0 ml, temperature = 22±1 ^{0}C.

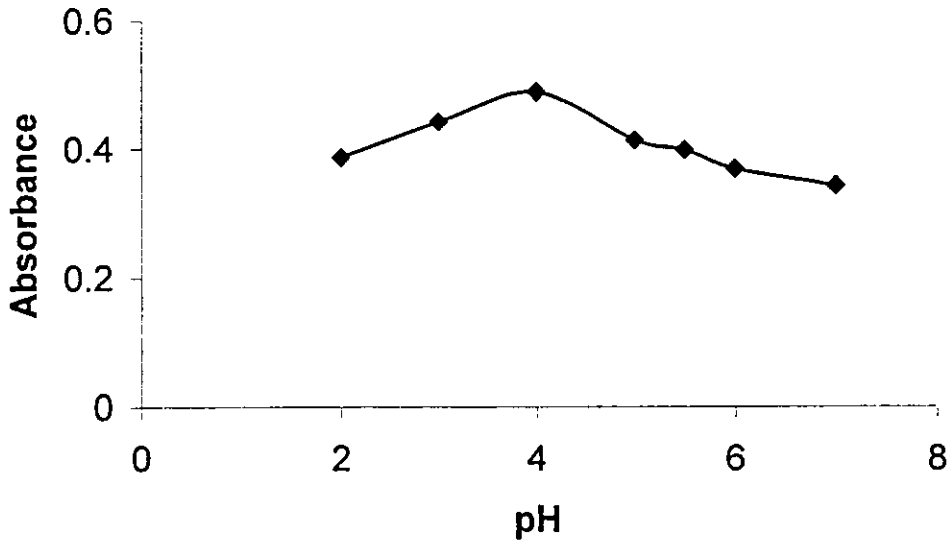


Figure (6) : Effect of pH on the absorbance of compound **III** ion-pair complex, [BTB]=[compound **III**]=1.0×10^{-3} M, , λ=418 nm, Volume of aqueous phase = 12.0 ml, Volume of organic phase = 25.0 ml, temperature = 22±1 ^{0}C.

3.3 Effect of amount of buffer

The effect of the amount of BR buffer was investigated for the three compounds **I, II** and **III** at 414, 418 and 418 nm (maximum absorbance) respectively (other variables were kept constant). The maximum absorbance of ion – pair complex for the three compound were decreased by increasing the amount of buffer. The best buffer amount was taken for the three compounds is found to be 1.0 ml.

Table 2 : Effect of amount of buffer solution on the absorption maxima at 414, 418, 418 nm for compounds **I, II** and **III**– BTB ion-pair respectively [BTB] = [compounds] in the aqueous phase = 1.0×10^{-3} M, at the optimum pH values

Amount of Buffer (ml)	Absorbance		
	I at λ=414 nm	**II** at λ=418 nm	**III** at λ=418 nm
0.5*	0.42	0.40	0.43
1.0	0.35	0.39	0.36
2.0	0.33	0.31	0.30
3.0	0.33	0.30	0.26
4.0	0.33	0.28	0.23
6.0	0.28	0.23	0.17
8.0	0.10	0.10	0.12
10.0	0.08	0.09	0.10

* slow extraction was shown.

3.4 Effect of type of organic solvent

Several water- immiscible organic solvents were examined for extraction of the ion-pair complex These include chloroform, dichloromethane, toluene, carbon tetrachloride and diethylether.

For compound **I** chloroform was found to be amongst those examined the best solvent for since it gave maximum extraction while dichloromethane was found to be the best for extraction in case of compound **II** and **III** as shown in table 3. On the other hand the extraction was found to increase by increasing the amount of solvent, so 20m1 of solvent were considered suitable for further work.

Table 3 : Effect of type of solvent on the absorption maxima at 414, 418, 418 nm for compounds **I, II** and **III** as BTB ion-pairs respectively [BTB] = [compounds] = 1.0×10^{-3} M, at the optimum pH values.

Type of solvent	Absorbance		
	I at λ=414 nm	**II** at λ=418 nm	**III** at λ=418 nm
Chloroform	0.40	0.34	0.37
Ethanol	0.35	0.27	0.28
n-hexane	0.01	0.01	0.01
Dichloromethane	0.19	0.41	0.40
Carbontetrachloride	0.36	0.12	0.19
Toluene	0.22	0.33	0.30

3.5 Effect of shaking time

The effect of shaking time on the extraction of the ion-pairs was studied. The range was studied between 0-150 sec. It was found that absorbance remained constant, when the shaking period was ≥30 sec. for compound **I** and **II** and 150 sec for compound **III**, as listed in Table 4.

Table 4 : Effect of shaking time on the absorbance of compounds **I, II** and **III** as BTB ion –pair complexes, **[I, II ,III]** = [BTB] in the aqueous phase = 1.0×10^{-3} M, at the optimum pH's.

Shaking time (s)	Absorbance		
	I at λ=414 nm	**II** at λ=418 nm	**III** at λ=418 nm
0	0.23	0.12	0.21
30	0.31	0.33	0.48
60	0.30	0.32	0.50
90	0.27	0.33	0.51
120	0.28	0.33	0.56
150	0.32	0.32	0.56

3.6 Effect of equilibration time

The equilibration time for extraction of the three complexes was varied between 15 sec and 50 min. No detectable effect on equilibration time was found up to 20 min.

3.7 Effect of number of extraction times on absorbance

Two methods were used for the extraction process. First, 20 ml of the organic solvent was used and the volume was completed to 25 ml with the solvent. Second, the process was done twice (10 ml each time) and collected together in the same volumetric flask and was completed to 25 ml with the same solvent. It was found that the absorbance of the three ion-pairs complexes did not change by interchanging the number of extraction times. In the present work one extraction with 20 ml organic phase was recommended for further work.

3.8 Effect of dye concentration

The effect of dye concentration on absorbance was studied for three systems at the optimum conditions. It was found that increasing the concentration of dye affect a gradual increase in the absorbance up to a dye:drug molar ratio of 1:2. Any further increase in the dye concentration did not show any effect on absorbance up to at least 1:1. The results obtained are presented in figures 7,8 and 9.

3.9 Stability of complex

The effect of time on the absorption maxima was studied for all the ion-pairs prepared as described in the general procedures, the results obtained showed that full color development was attained instantly and the intensity of the color stayed constant for at least 48 hour after extraction as show in Table 5.

Table 5 : Effect of time on the stability of compounds **I, II** and **III** as dye complexes. [Compounds] = [BTB] in aqueous phase = 1.0×10^{-3} M, pH = 5.0, 4.0 and 4.0 for compounds **I, II** and **III,** respectively.

Time(min)	Absorbance of complexes		
	I at λ=414 nm	**II** at λ=418 nm	**III** at λ=418 nm
0	0.36	0.38	0.38
5	0.36	0.36	0.38
10	0.36	0.35	0.38
15	0.36	0.33	0.38
20	0.36	0.34	0.38
25	0.36	0.34	0.38
30	0.36	0.34	0.38
35	0.36	0.34	0.38
48 hour	0.36	0.34	0.38

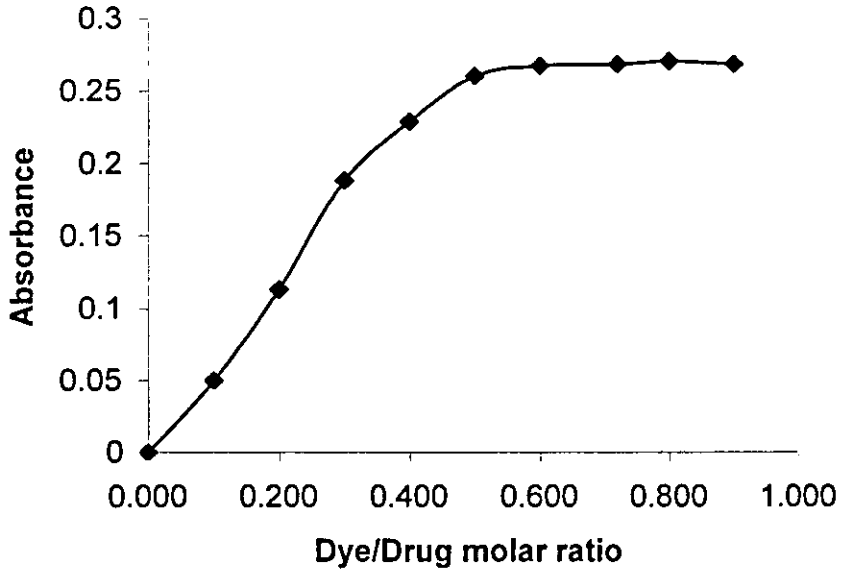


Figure 7 : Molar ratio method for compound I (drug) – BTB complex, λ_{max} = 414 nm, pH = 5.0, [compound I] in aqueous phase = 1.0×10^{-3}M.

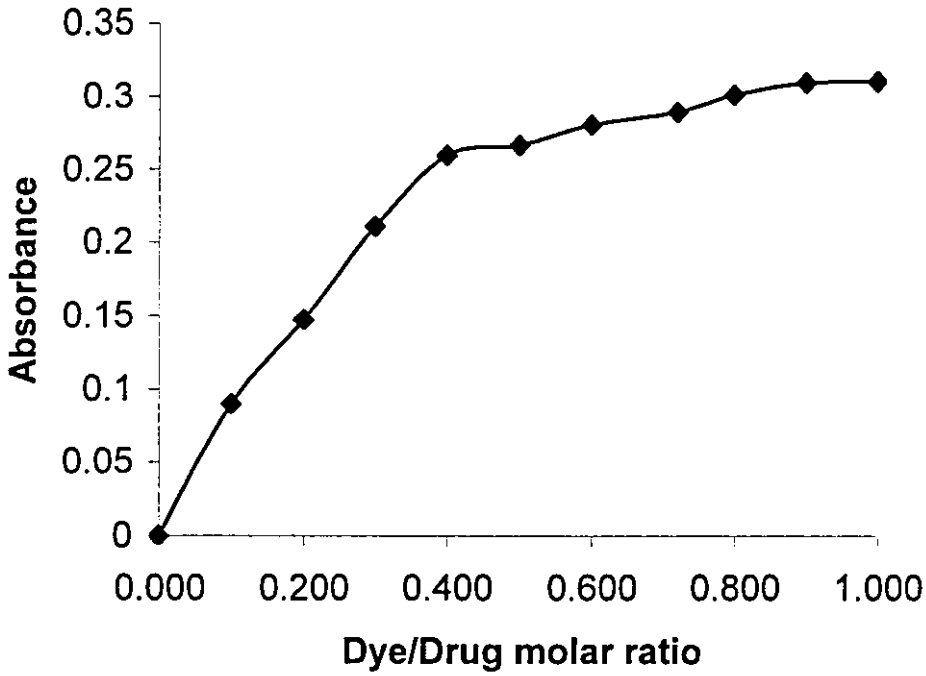


Figure 8 : Molar ratio method for compound **II** – BTB complex, λ_{max} = 418 nm, pH = 4.0, , [compound **II**] in aqueous phase = 1.0×10^{-3}M.

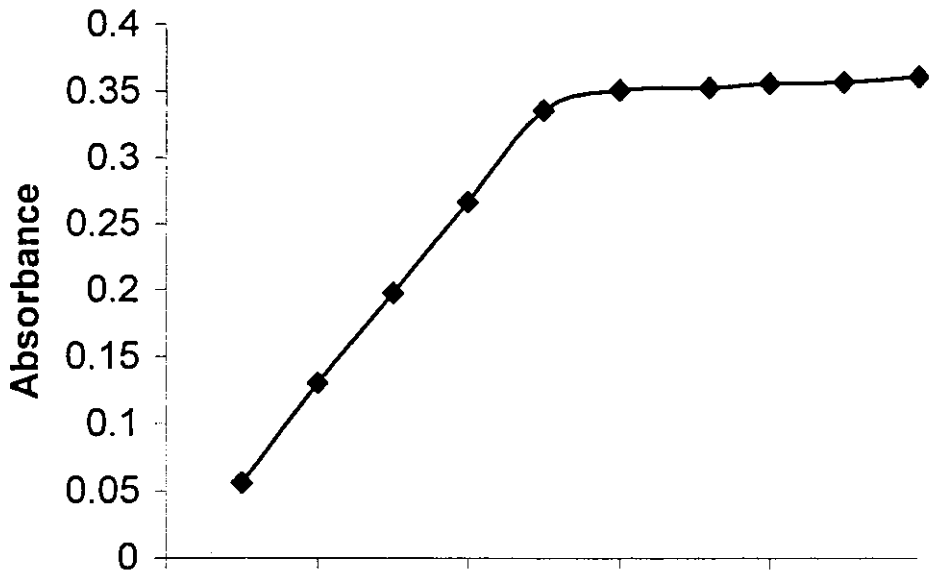


Figure 9 : Molar ratio method for compound **III** – BTB complex, λ_{max} = 418 nm, pH = 4.0, , [compound **III**] in aqueous phase = 1.0×10^{-3}M.

3.11 Applicability of Beer's Law

A series of standards of ion-pair complexes of the three compounds were prepared and the absorbance increase gradually with increasing concentration of investigated compounds at the optimum conditions. The absorbance was measured against a blank prepared similarly without the drug, following the recommended procedure. A linear relationship was obtained by measuring the absorbance as a function of the concentration. The calibration curve was recorded over the concentration range 0.84 – 5.10, 1.12 – 5.58 and 0.76 – 6.82 μg/ml for compounds **I, II** and **III,** respectively as shown in Figures 10, 11 and 12.

The molar absorptivity (ε) was calculated from the linear portion of the curve and found to be 8.0×10^3 L mol^{-1} cm^{-1} for compounds **I** and **II**, and 1.2×10^4 L mol^{-1} cm^{-1} for the complex of compound **III**. The spectral data for the reaction and each compound as well as characteristics of calibration curve is listed in table 8.

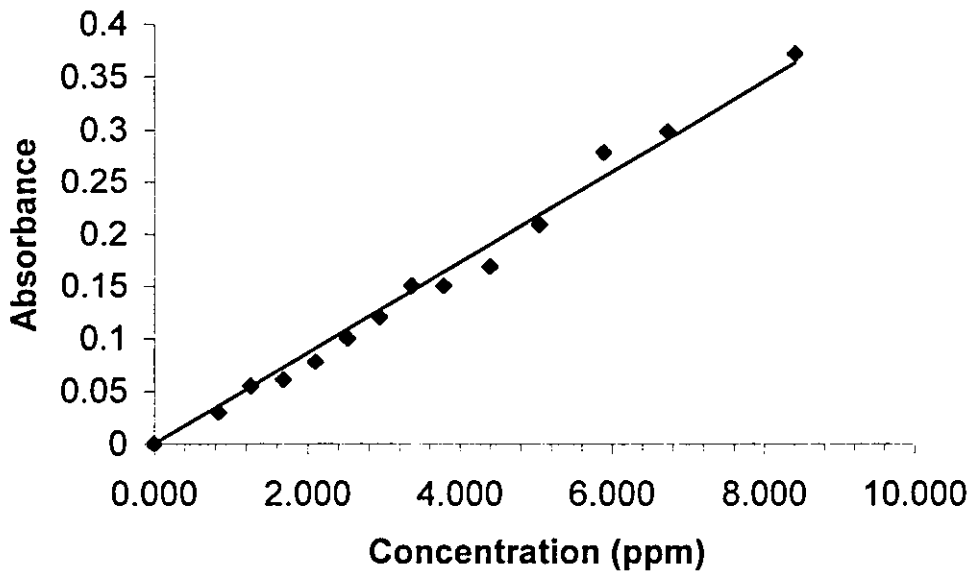


Figure 10 : Calibration graph for compound **I** – BTB complex, λ_{max} = 414 nm, pH = 5.0, [BTB] in aqueous phase = 1.0×10^{-3} M. Each point represents the average of 5 measurements.

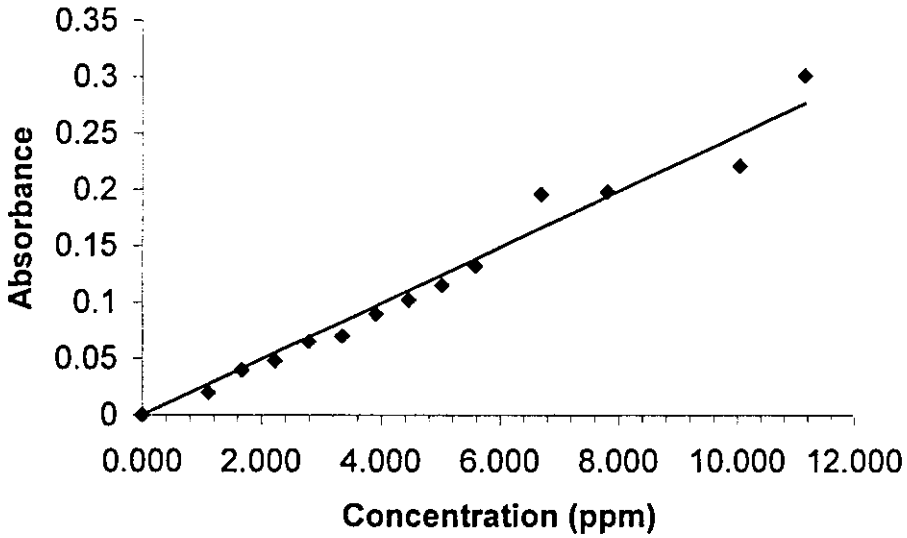


Figure 11 : Calibration graph for compound **II** – BTB complex, λ_{max} = 418 nm, pH = 4.0, [BTB] in aqueous phase= 1.0×10^{-3}M. Each point represents the average of 5 measurements.

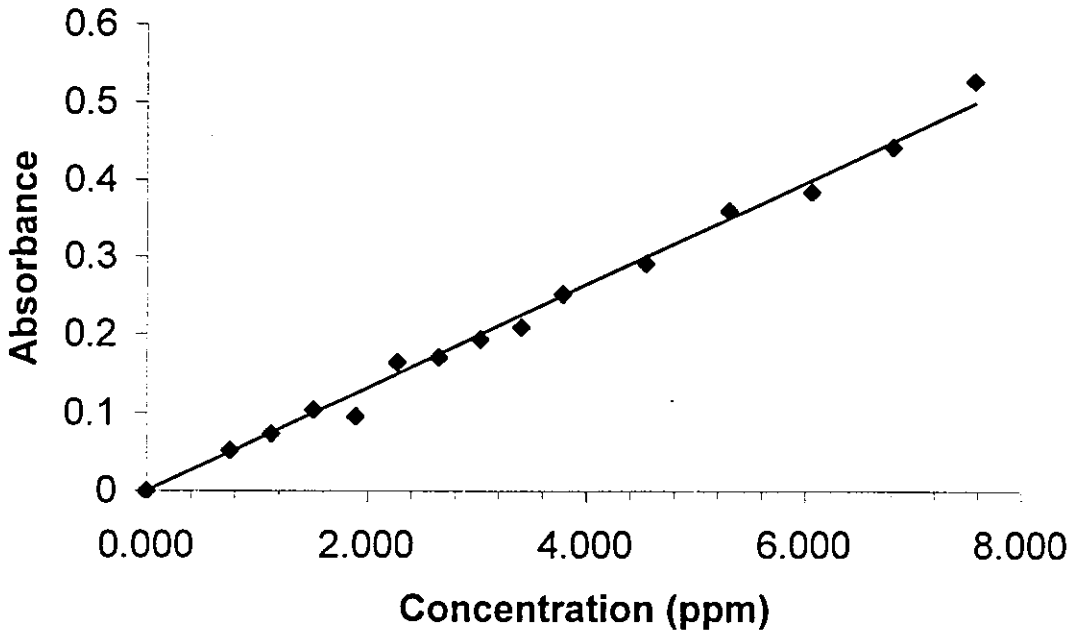


Figure 12 : Calibration graph for compound **III** – BTB complex, λ_{max} = 418 nm, pH = 4.0, [BTB] in aqueous phase = 1.0×10^{-3}M. Each point represents the average of 5 measurements.

Table (6) : Analytical characteristics for Ion-Pair formation methods

Parameter	Compound **I**	Compound **II**	Compound **III**
λ Max (nm)	414	418	418
Recommended pH	5.0	4.0	4.0
Shaking Time (s)	30	30	150
Concentration of BTB (M) in the aqueous phase	1×10^{-3}	1×10^{-3}	1×10^{-3}
Amount of Buffer (ml)	1.0	1.0	1.0
Solvent used	Chloroform	Dichloromethane	Dichloromethane
Range of linearity (ppm)	0.84 – 5.05	1.12 – 5.58	0.76 – 6.82
Molar absorptivity (ε) L mol^{-1} cm^{-1}	8.0×10^3	8.0×10^3	1.2×10^4
Detection limit (ppm)	0.84	1.12	0.76

Table 7, Statistical data for artificial synthetic solutions of I, II, III.

Sample	Taken (ppm)	Found (ppm)	Recovery %	rsd %
Compound I	2.50	2.30	95.0	7.10
	4.80	4.67	97.2	3.66
	6.00	6.12	102.0	2.70
Compound II	1.20	1.25	104.2	2.12
	3.40	3.70	110.0	4.30
	6.70	6.80	101.0	1.60
Compound III	0.60	0.58	96.6	1.15
	2.40	2.30	95.8	9.80
	6.20	6.00	96.7	8.20

Conclusion

A simple and sensitive spectrophotometric method was developed for the extractional spectrophotometric determination of new substituted tricyclic pyridopyrimidines compounds **(I)** (7-chloro-2,3-trimethylene-pyrido [1.2-a] pyrimidine-4-one), **(II)** (7-bromo-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one) and **(III)** (7-methyl-2,3-tetramethylene-pyrido [1.2-a] pyrimidine-4-one). The method was based on the formation of ion-pair complexes between compounds **I, II** and **III** with bromothymol blue (BTB). The absorbance of the produced ion-pair complexes were measured at 414, 418, and 418 nm for I-BTB, II-BTB and III-BTB respectively.

Other dyes can be tested for quantitative determination of these drugs. Polarographic analysis methods for quantitative determination of the studied compounds haven't been done, so further work for polagraphics determination can be investigated.

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بسم الله الرحمن الرحيم

ملخـــص

تكمن أهمية مركبات "البيريدوبايربميدين" pyridopyrimidine في علاج كثير مـــن انـــواع السرطان وكذلك في علاج انواع كثيرة من البكتيريا، والمركبات التي قمنا بدراستها لها فعالية كبيرة فـــي علاج البكتيريا ومن الاحتمال ان تستخدم في علاج السرطان كباقي مركباتpyridopyrimidine وقد تم تحليل هذه المركبات I, II, III باستخدام جهاز الامتصاص الطيفي (Spectrophotometer).

تعتمد هذه الطريقة على تكوين معقد ايوني مزدوج Ion- pair complex له لون اصفر مـــا بين المركبات I, II, III من جهة والبرموثايمول الازرق BTB من جهة أخرى. حيث تم اســـتخلاص المعقد الأيوني من الوسط المائي باستخدام الكلوروفورم للمركب I وثنائي كلوروميثان للمركبيـن II,III وتم قياس مقدار الامتصاص عند أطوال الموجات 414، 418، 418 نانوميتر. للمركبـــات I, II, III على التوالي. وطريقة التحليل المتبعة هنا مفيدة من الناحية الكمية (quantitative) بقراءة امتصـــاص تراكيز مختلفة من المركبات الدوائية الثلاثة.

لقد تمت دراسة مختلف العوامل التي تؤثر على تكوين الأيون المعقد مثل درجـــة الحموضـــة، نوع المذيب وكميته ...الخ. ولقد تم تطبيق قوانين الامتصاص الطيفي على النتائج مثـــل قـــانون بـــير (Beer's Law) حيث كانت هناك علاقة خطية مستقيمة محصورة ما بيـــن 0.84 – 5.05 ، 1.12 – 5.58 ، 0.75 – 6.82 مايكروغرام / ملم للمركبات I, II, III على التوالي.