Determination of Ibuprpfen in Aqueaus Solutions and Pharmacetical Preparations by UV-VIS Spectrophotometric

Hadi H. Jasim and Nehad K. Abed
Department of Chemistry, College of Science, University of Al- Mustansiriya, Baghdad-Iraq.

Abstract

A method has been developed for the determination of the ibuprofen drug in aqueous solution and pharmaceutical preparation using UV-Vis spectrophotometry. The opitimum experimental condition were based on the formation of complex compound and studied, the best temperature (303 k°), reaction time (13 min), solvent extraction (3 ml) and extraction time (5 min). Mole ratio and Job –method was used to found the ratio between the ligand (drug) and the metal ion (Co), the complex output ratio of (1:1). Detection of limit =0.223 µg/ml, Re% =96.8, r =0.9561, linearity ($1x10^{-3}$ – $2x10^{-2}$ M) and sandell sensitivity S =0.1008.

Keyword: Ibuprofen, Non-steroidal anti-inflammatory (NSAID), COX (Cyclooxygenase enzyme).

Introduction

Ibuprofen is a weakly acidic, non-steroidal anti-inflammatory drug (NSAID), It is active antipyretic, analgesic which is used in mild to fever, solubility in aqueous media is poor (2.5 mg/ml)[1-3]. To improve the solubility, several approaches such as solid dispersion,[4] prodrug and inclusion complex, It was derived from propionic acid by the research arm of boots group during 1960 s.[5] It is chemically (RS)-2-(4-(2-METHYL PROPYL) PHENYL ISOPROPIONIC ACID (Fig.(1)).[6,7]

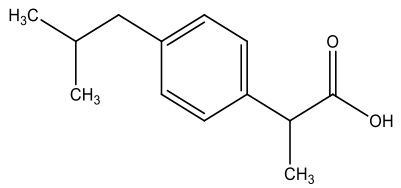

Fig.(1) Chemical structure of Ibuprofen.

It is known that most of (NSAIDs) inhibit the enzyme COX (Cyclooxygenase enzyme) and production of prostaglandins. traditional NSAIDs, differ in their relative inhibitory potency against to iso-forms of COX:COX-1 and COX-2.[8-9] The masking of the ibuprofen –free carboxylic group seems to be principally the basis of this reduced topical irritant action.[10] Ibuprofen has been modified into various heterocyclic amide derivatives having improved analgesic activity and lower effects, as aminoprofen, an amide derivative of ibuprofen has been used for its topical anti-inflammatory activity.[11] Literature review revels that the simultaneous spectrophotometric estimation of ibuprofen in tablet dosage form which has been reported.[12] They also review the estimation of ibuprofen in individual dosage form by HPLC method. [13-14] for ibuprofen stability indicating method was reported.[15] the anthelmintic and fungistatic agent thiabendazole, which is used for the treatment of several parasitic diseases, forms a Co^{+2} complex with metal : drug ratio of 1:2 [16]

Experimental

Apparatus:

A UV-visible spectrophotometer model varian –cary 100 con with 1 cm matched Quartize cells was used for all absorbance measurements. The pH values of solutions were measured using HANA pH meter. FTIR-8400 S FOURIER TRANSFORM INFRARED SPECTROPHOTOMETER SHIMADZU used to determine the functional groups of drug and complex.

Reagents

All reagents and chemical used were of analytical grade. Double distilled water was used to prepare all solutions. cobalt chloride $CoCl_2.6H_2O$(M.wt=237.9 g/mol) stock solution ($2x10^{-1}$M)was prepared. mixture of solvents (benzene and cyclohexane (2:3)) used for extraction the complex.Ibuprofen was generously supplied by the drug industries and medical Appliances profinal by Gulfar UEA and APIFEN tablet (400 mg) form API-CO by aganta pharma /India.

From stock solution of ibuprofen (100 µg/ml) was prepared by dissolving 10 mg of pure ibuprofen in 100 ml and dissolved in weak acidic water (pH=8.5). The working standard solutions were then prepared by suitable dilutions of the stock solution with water

Procedures:

Calibration Curve

Eight standard solution were prepared from stock solution (0.2 M complex) by mixing equal volume (10 ml) of each sample of drug with different concentration of cobalt ion as follows (0.01,0.02,0.03,0.05,0.07,0.08,0.09,0.10 M), then configure complex when the optimum conditions complex for the process complexity Each solution was extracted by 4 ml of organic phase mixture (benzene and cyclohexane) after shaking for 5 min at room temperature. Then it had been measured at wave length (603 nm). The analytical curve was obtained by plotting absorbance against Ibuprofen concentration and the corresponding lineare regression equation was used to convert absorbance into Co concentration for all analyzed tablets samples. Under the optimum experimental conditions described, linearity, detection limit, molar absorptivity, and sandell's sensitivity were show in Table (1), and results of statistically evaluated shows in Table (2).

Table (1)

Results of Recovery percentage, linearity, Detection of Limit and Sandell's Sensitivity.

DRUGE	*Linearity rang (M)*	*Dol µg/ml*	*Molar absorpitivit Ɛ ($Lmol^{-1}$ cm^{-1})*	*Sandell's sensitivity S(µg /cm^2)*	*Rec %*	*Ere%*	*RSD%*
Ibuprofen	$1x10^{-3}$-$10x1^{-3}$	0.223	$0.374 x10^4$	0.1008	96.8%	3.2 -	0.1802

Table (2)

Results values of recreation equation, correlation coefficients, T-test and confidence Limit of Ibu-Co (ll) complex.

Regnession equation y=BX+A	*Correlation cofficent R*	*T-test calculated*	*T-test tablet %95 c.l*	*Conf-limit for the slope b± sbt*	*Conf. Limit for the interapt a±sat*
Y=4.1734X+0.1868	0.9561	16.81	2.36	60±0.251	0.132 ±

Determination of Ibuprofen in Pharmaceuticals Preparation

The proposed method was applied for the assay of Ibu in tablets by using direct calibration and standard additions procedures Fig.(2) under optimum conditions. The Ibu was determined by measuring the absorbance of complex after extracted by mixture (benzene and cyclohexane (2:3)) and compared with the calibration curve. The results for the determination of Ibuprofen by standard method are summarized in Table (3) after addition 1 ml of standard solution $1x10^{-3}$ M Ibuprofen for each solution.

Table (3)
Shows the absorbance of calibration curve and standard addition.

NO.	Calibration curve conc.(M)	Absorbance	Standard addition conc.(M)	Absorbance
1	$1x10^{-2}$	0.2210	$1x10^{-2}$	0.2792
2	$2x10^{-2}$	0.2721	$2x10^{-2}$	0.3422
3	$3x10^{-2}$	0.3112	$3x10^{-2}$	0.3876
4	$5x10^{-2}$	0.3928	$5x10^{-2}$	0.4661
5	$7x10^{-2}$	0.4750	$7x10^{-2}$	0.5371
6	$8x10^{-2}$	0.5251	$8x10^{-2}$	0.5810
7	$9x10^{-2}$	0.5621	$9x10^{-2}$	0.6491
8	$1x10^{-1}$	0.6512	$1x10^{-1}$	0.6812

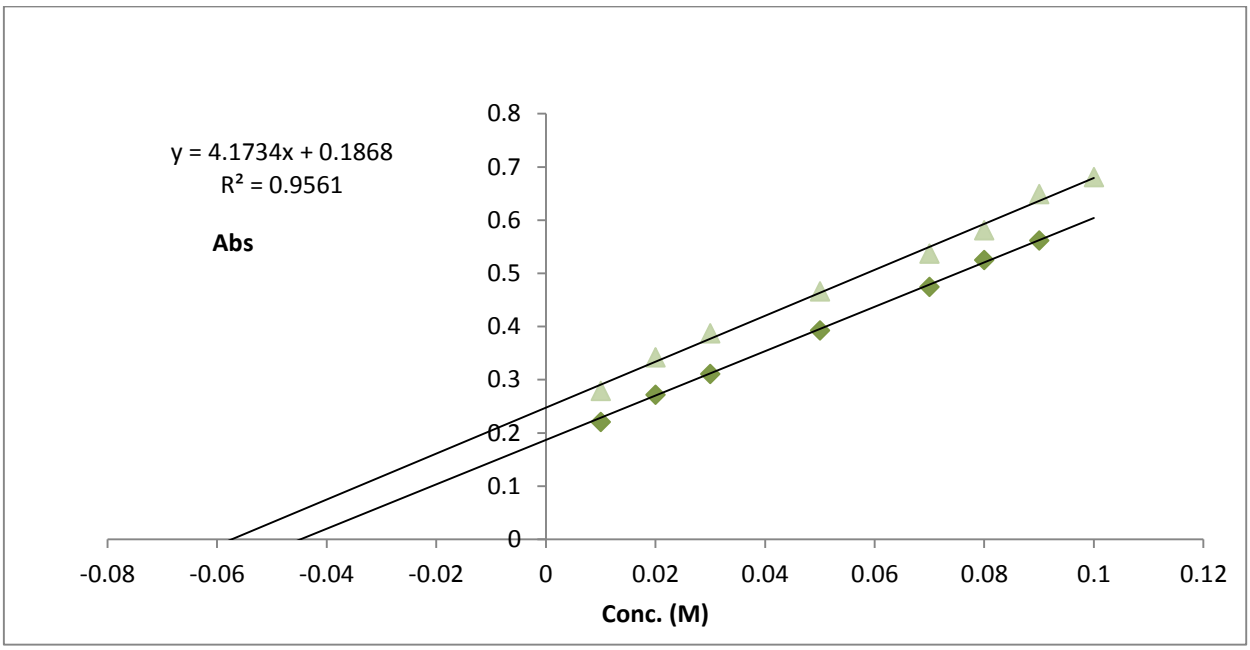

Fig. (2) Calibration curve and standard addition of Ibu-Co(II) complex.

Preparation of Drug APIFEN Tablets:

10 tablets of APIFEN were crushed in a clean agate mortar, to from powdered. A quantity equivalent to one tablet was taken and dissolved in water (pH=8.5) with one drope NH_4OH solution, the solution was transferred into 100 ml volumetric flask and diluted to the mark with water.

Mole Ratio Method

An aliquot (1 ml) of solution ($2x10^{-2}$M) of cobalt solution was added to a series of (25 ml) volumetric flask containing (0.3, 0.5, 1, 2, 3, 4 and 5) ml of ($2x10^{-2}$ M) of ibuprofen Then it seized the optimum conditions for the process complexity. The complex formed in each flask was extracted by mixture of organic solvent (2:3) benzene: cyclohexane, respectively, the absorbance of the complex extract was measured at ʎ max (603 nm). The absorbance versus the volume ratio of Ibu/Co(ll) was plotted from which the stoichiometry of ion-association complex was determined. Molar ratio method was employed to elucidate the composition of Ibu-Co (ll) complex formed at optimal condition. Fig. (3) revealed that a (1:1) Ibu-Co (ll) are formed at max 603 nm.

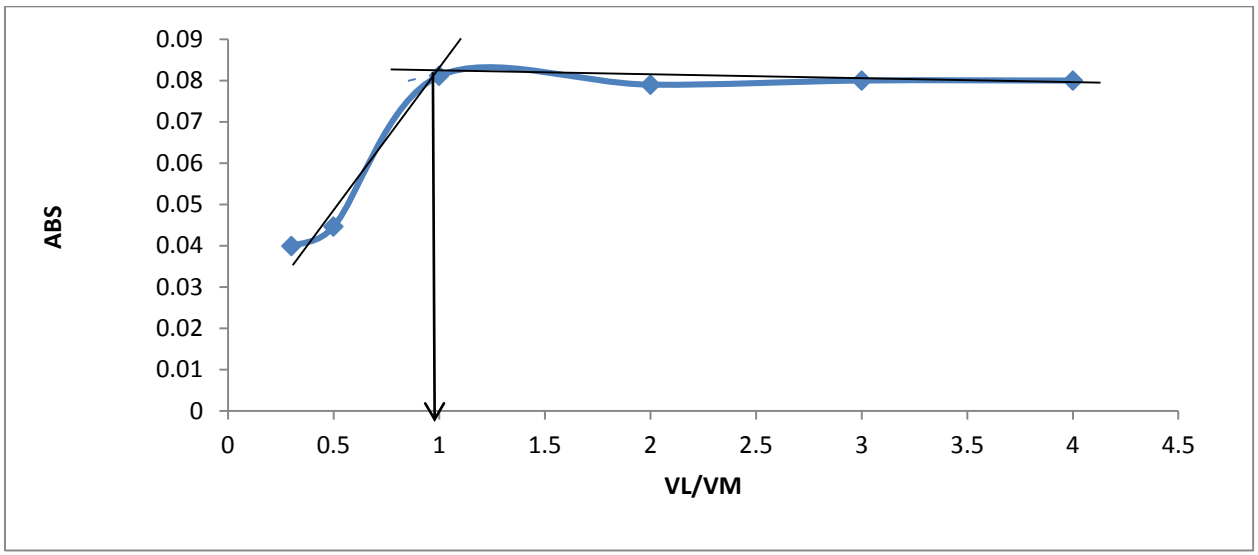

Fig.(3) Mole Ratio Method of the Complexation between IBU and Co (II) salt.

Job Method

In this procedure, both Ibuprofen and cobalt ion with the same concentration ($2x10^{-2}$M) was used to prepare (10 ml) of different ratio of mixtures Ibu-Co (ll) shown in Table (4):

Table (4)
The volumes used for Co(ll) and Ibu with the same concentration $2x10^{-2}$ M.

Co (ll) ml Conc. ($2x10^{-2}$ M)	1	2	3	4	5	6	7	8	9
Ibu(ml) Conc.$2x10^{-2}$ M	9	8	7	6	5	4	3	2	1

Then seized the optimum conditions for the process complexity. The complex formed in each flask was extracted with mixture solvent (benzene and cyclohexane) and the absorbance of complex extracted was measured at ʎ max = 603 nm. The absorbance versus the volume ratio Ibo/Co was plotted Fig.(4) from which the stoichiometry of ion-association complex was determined.

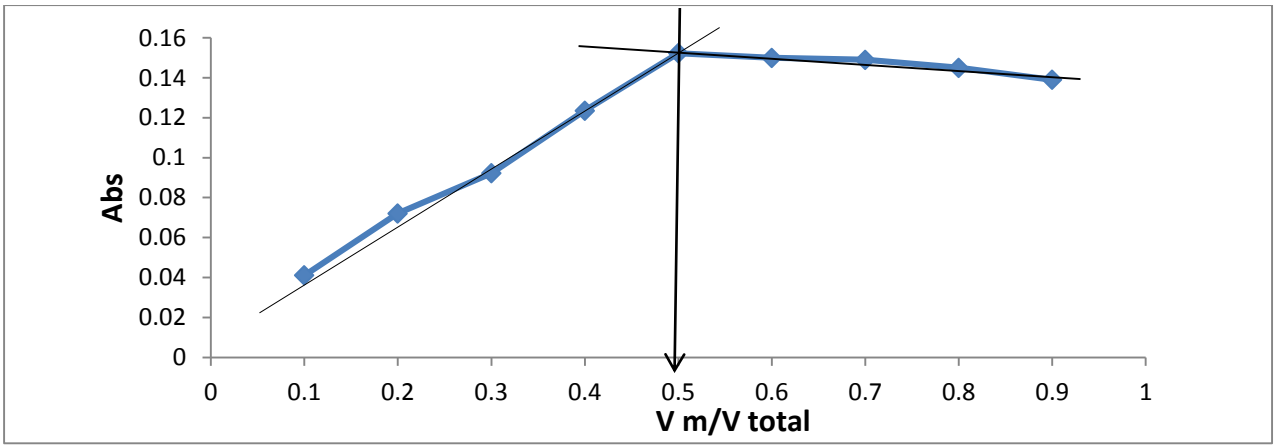

Fig. (4) Determination the mole ratio between Co(ll) and Ibu by Job-method.

Results and Discussion

Absorption spectra:

Uv-vis spectra of the pure ibuprofen drug, pure cobalt salt and the complex Ibu-Co (ll) were scanned using UV-VIS spectrophotometer for recoding the spectra to verify of the formation of complex. It was shown Fig.(5) that the pure drug gave two absorption maxima 218 and 264 nm. Fig.(6) shown the pure $CoCl_2.6H_2O$(ll). Distinctive absorption maximum at 509 nm, while the Ibo-Co complex gave an absorption maximum at (603) nm Fig.(7), indicating the formation of complex between the drug and organic solvent.

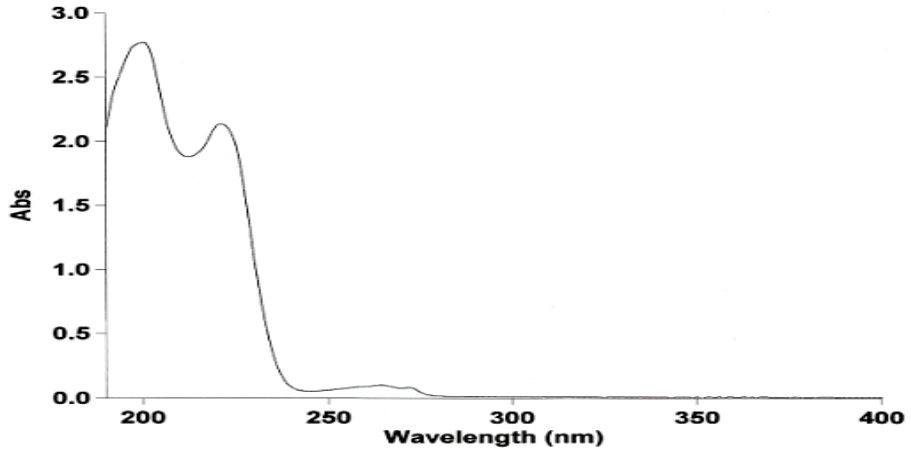

Fig.(5) Spectram uv-vis of the pure Ibuprofen standard solution.

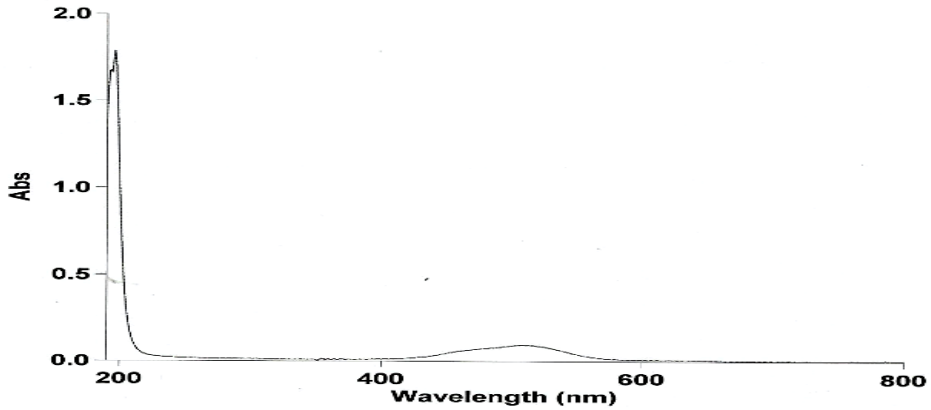

Fig.(6) Spectrum of Co(II) solution ($2x10^{-2}$ M).

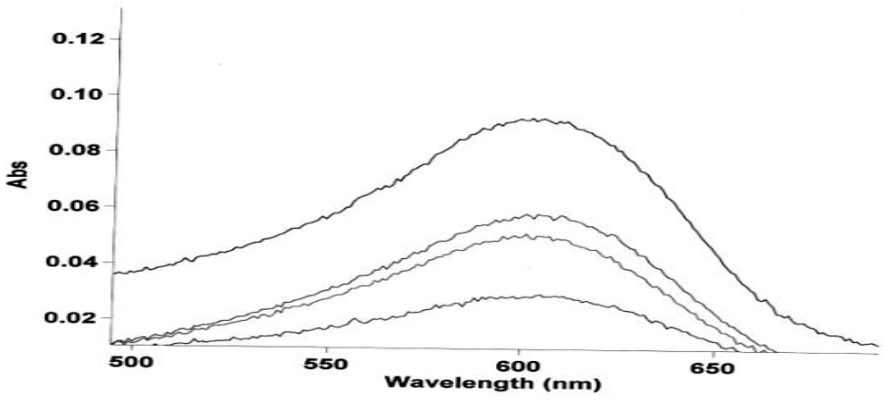

Fig.(7) Spectrum of complex IBU-Co) (ll) with different concentration.

OPTIMIZATION CONDETAION

Effect of pH value:

The effect of pH on formation of (Ibu-Co(II)) complex, mixed (5 ml) of Ibu. That concentration 100 µg/ml with (5 ml) of $CoCl_2.6H_2O$ that concentration of 100 µg/ml with different values (6.5, 7.5, 8.5, 9.5, 10.5, 11) of pH solution in each volumetric flask (10)ml. For the optimum conditions complex for the process complexity. The method mentioned in experimental work is depicted in Fig.(8). It was shown the absorbance increase with increasing pH until reached a maximum at (pH=8.5) after that absorbance decreased due to dissociation of the complex at higher than pH =8.5. Thus pH=(8.5) was selected as optimum value for complete formation of ion-association complex**.**

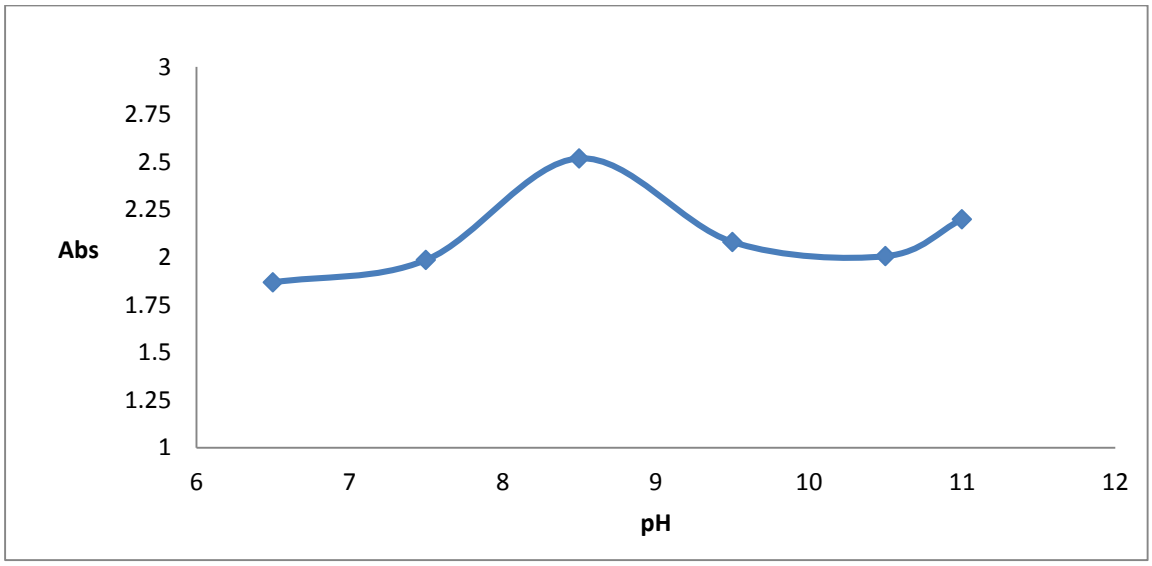

Fig. (8) pH effect of the formation of the IBU-Co(II) complex.

Effect of Co(ll) Concentration:

The effect of concentration was studied by measuring the absorbance of the mixture solutions containing a fixed concentration of Ibuprofen (5 ml) of 100 µg/ml with different volumes of 100 µg/ml $CoCl_2.6H_2O$ (0.5, 1, 2, 3, 5, 6) ml at optimum pH. It was found that the absorbance of (Ibu-Co) complex increases linearity with the concentration of $CoCl_2.6H_2O$ increases and then slightly decreases after (2ml) of Co (II) solution Fig.(9). Consequently, the optimum concentration of Co of (2 ml) was selected for complete complex formation.

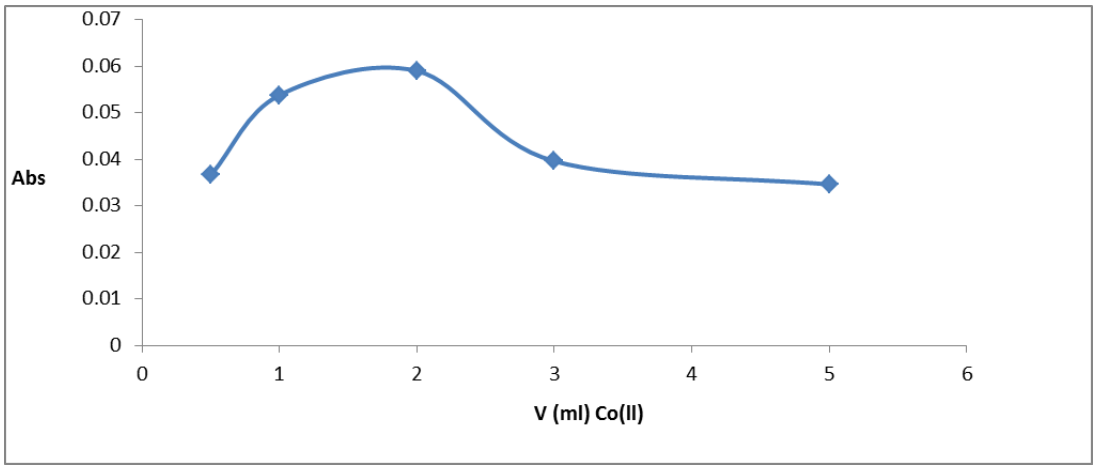

Fig.(9) Concentration effect of Co(II) for the complexion method.

Effect of Reaction time:

A 5 ml of 100 µg/ml Ibuprofen mixed with 5 ML of 100 µg/ml Co(ll) was mixed, were fixed other conditions before extraction. Shake the mixture with different time (5, 7, 10, 13, 15, 20) mint and measured the absorbance of complex after extraction for each time used. Fig.(10) show the absorbance increase with time shaking until (13 min), after that the absorbance decreases when the reaction time increase.

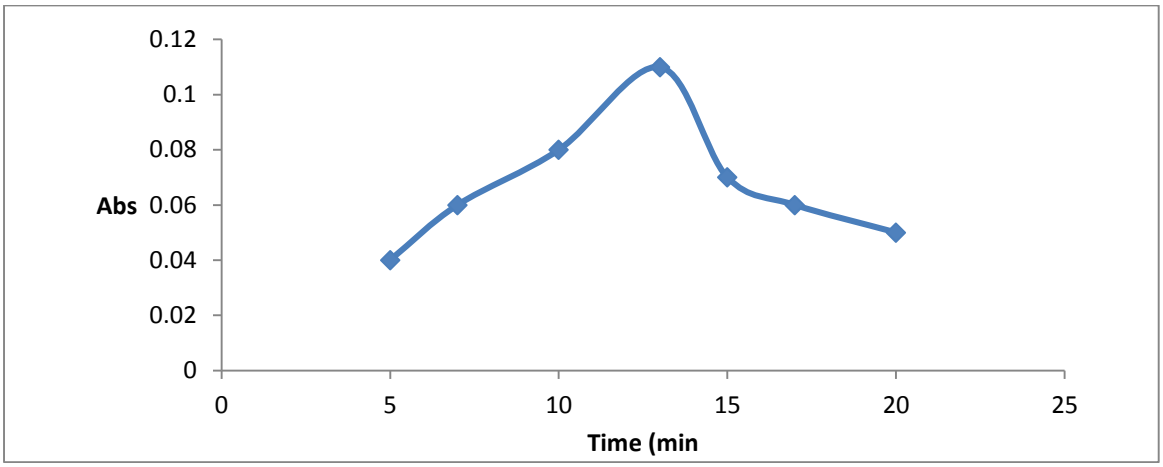

Fig. (10) Effect of reaction time on the formation of Ibu/Co complex.

Effect of Extraction time:

After the complex formed extracted by (4ml) of organic solvent (2:3) mixture (benzene and cyclohexane). Fixed all the conditions and shaking the mixture with of different (2,3,4,5,6,7) min to to choice the sutabil shaking time for the complex extraction and measure the absorbance after each shaking, use UV-VIS spectroscopy.

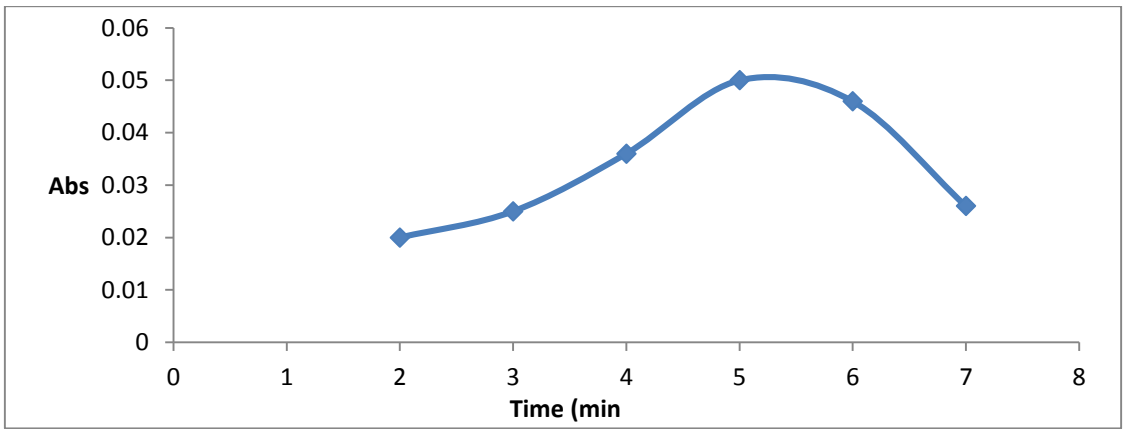

Fig. (11) Effect of extraction time on the formation of IBU-Co(II) complex.

IR Spectra

Infrared spectra of pure Ibuprofen and complex are shown in Table (5), all vibration peaks, we can show that in Table (5).

Table (5)
Show the shift of some wave number of peaks.

	ύ (O-H)	*ύ(C-H) aromatic*	*ύ (C-H) alphatic*	*ύ(C=O)*	*ύ (Co-O)*
Ibuprofen	3208	3010	2956, 2897	1712	
Complex	3090	3045	2953, 2928	1691	524

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الخلاصة

في هذه الدراسة تم حساب تركيز عقار الايبوبروفين في المحاليل المائية والمستحضرات الصيدلانية باستخدام تقنية uv-vis. كما درست الظروف المثلى لعملية التعقيد فكانت درجة الحرارة المثالية لتكوين المعقد (303) كلفن، اما فترة التفاعل فكانت (13) دقيقة وحجم مذيب الاستخلاص (3) مل وفترة الاستخلاص (5) دقيقة وباستخدام طريقتي النسب المولية وطريقة جوب تبين ان معقد الناتج بنسبة (1:1) مابين ايون الكوبلت واللجنة وكانت قيمة معامل الامتصاص المولاري $\varepsilon=0.374x10^{4}$ لتر. مول.$^{-1}$ سم$^{-1}$, اما حدود الكشف في هذه الطريقة DOL= 0.223 µg/ml ونسبة الاسترجاع Rec%=96.8 وحساسية ساندل S=0.1008 ومعامل الارتباط r= 0.9561 وظهر من منحني المعايرة ان التراكيز المطاوعة لقانون لامبرت بير تراوحت ما بين($1x10^{-3}$-$1x10^{-2}$ M).