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Spectrophotometric Determination of bisoprolol fumarate By Using 1, 2 Naphthaquinolinc-4-Sulphonate Sodium Reagent

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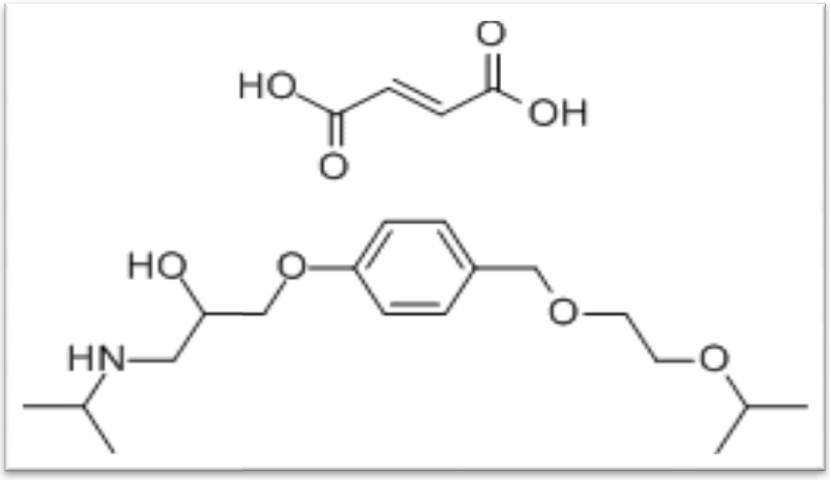
Abstract— In this study, simple and sensitive spectrophotometric method for the determination of Bisoprolol fumarate (BIF) in pharmaceutical formulations was reported. The proposed method was based on the reaction between (BIF) and 1, 2-naphthoquine-4-sulphonate (NQS) at alkaline medium (pH 10) to form deep red product. Beer's law was obeyed in the range of(4-40µg.mL^{-1})of Bisoprolol tartrate at maximum wavelength of 516 nm. Under optimized reaction conditions, linear regression equation of the calibration curve was y = 0.0229x +0.1585 (µg.mL^{-1}) with a linear correlation coefficient of 0.9988. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.2620µg.mL^{-1}and 0.8733µg.mL^{-1}, respectively. The method was successfully applied to the determination of (BIF) in pharmaceutical formulations.

Keywords: Spectrophotometric, Bisoprolol fumarate (BIF), pharmaceutical formulation; 1-2-naphthoquine-4- sulfonate (NQS)

Introduction

Bisoprolol is a synthetic, beta1-selective (cardioselective) adrenoceptorblocking agent without significant membrane stabilizing activity or intrinsic sympathomimetic activity in its therapeutic dosage range. The chemical name of bisoprolol fumarate is 1-(propan-2-ylamino)-3-[4-(2- propan-2-yloxyethoxymethyl) phenoxy]propan-2-ol Figure (1) [1].

There are few spectrophotometric methods for the assay of beta blockers and fewer for bisoprolol [2, 3]. It should be noted that the actual spectrophotometric methods used for bisoprolol determination are UV-based and few HPLC methods for the assay of beta blockers and fewer for bisoprolol [4, 5] and volumetric method [6].



Figure(1) Chemical structure of bisoprolol fumarate

Bisoprolol is currently used for prevention of cardiovascular events following a heart attack in patients with risk factors for disease progression,[7] in the management of congestive heart failure with reduced ejection fraction,[8] and as a second-line agent for hypertension[9].

Bisoprolol may be beneficial in the treatment of high blood pressure, but it is not recommended as a first-line anti-hypertensive agent without an accompanying comorbid condition, for example, congestive heart failure.[10,11].

1,2-Naphthoquinone-4-sulfonic acid sodium salt)(NQS): Synonyms: beta-Naphthoquinone-4-sulfonate sodium salt; Sodium 3,4- dihydro-3,4-dioxo-1-naphthalenesulfonate; Sodium beta-naphthoquinone-4-sulfonate; Sodium 1,2-naphthoquinone-4-sulfonate Fig .(2).

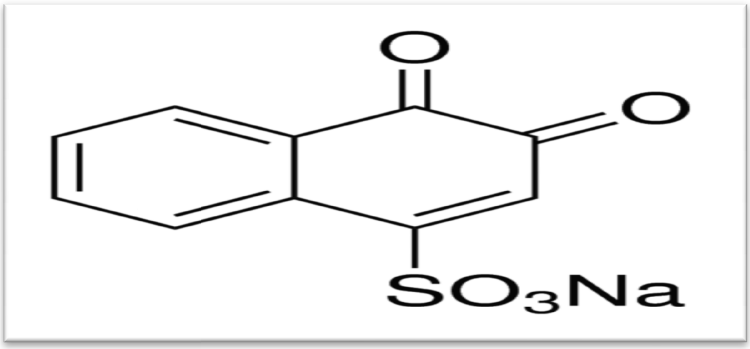


Figure (2). Chemical structure (1,2-Naphthoquinone-4-sulfonic acid sodium salt) (Folin's reagent) (NQS)

1, 2-naphthoquinone-4-sulfonic sulfonate (NQS) has been used as a chromogenic reagent for the spectrophotometric determination of many pharmaceutical amines.[12,13] .It is a popular

spectrophotometric reagent due to its efficient reactivity with both primary and secondary amines, and high reaction rate [14]. NQS proved to be a useful and sensitive analytical derivatizing agent for spectrophotometric analysis of pharmaceuticals bearing a primary or secondary amino group[15].Many researchers have intensively used NQS as a chromogenic reagent to determine amines and the results obtained showed that the reaction products have the general structure shown in fig. (3)[16,17].

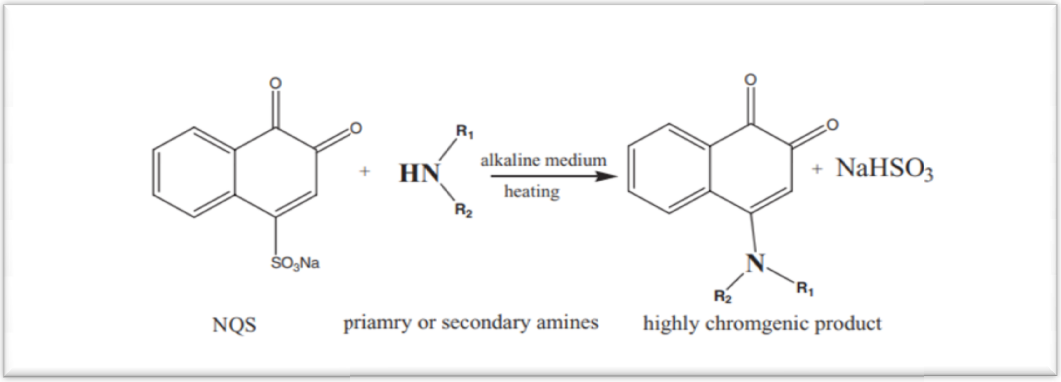


Figure (3): Reaction scheme of amines with NQS

Experimental

Apparatus

Absorbance was carried out by using 6100 PC UV- visible spectrophotometer, Shimadzu, Japan (Double beam), with quartz cells of 1 cm optical path length, pH meter was used for pH measurements, analytical balance and water bath.

Material and reagent

Bisoprolol fumarate wereobtainedfromDevelopmentCompany,(agentof Hyber chem), used as received, thepurity of which was 98%. The preparation of the solution of BIF involved dissolving (0.02)g Bisoprolol in the deionized waterin 100mL volumetric flask. A solution of 0.4% (w/v) NQS was prepared by dissolving (0.4)g in deionized water, transferred into a 100 mL volumetric flask and diluted to the mark with Deionized water and mixed well. The solutionwasfreshlypreparedandprotectedfromlight.during use; buffer solution of pH 10 was prepared from$NaOH/NaHCO_3$.

Preparation of standard and sample solution

The standard stock solution of (200µg.mL^{-1}) was prepared from (0.02)g Bisoprolol dissolved in50 deionized water , then transferred into 100 mL volumetric flask, diluted to the mark with the same solvent and mixed well. This stock solution was further diluted to obtain working solutions in the range of (4-40)µg.mL^{-1}.

Solution of Pharmaceutical Preparations of Bisoprolol fumarate

Ten tablets were weighed and finely powdered from each type of tablets separately . An accurately weighed portion of the powder equivalent to (0.02)g of Bisoprolol fumarate which depends on the type of tablets that be used, it was dissolved in 10 mL of deionized water. After that it was filtered to separate then dissolved components, and transfer to a 100mL calibrated flask and to diluted to the mark with distilled water. Later, the suitable amount of each record solution was taken and treated in the same conditions that were used in the based way of working to find a concentration depending on a calibration curve .

Procedure

1 mL of 200μg.mL^{-1}Bisoprolol was transferred into 10 mL volumetric flask; 1 mL of 0.4 % (w/v)NQS was added and added 1 ml from buffer solution of pH 10 (NaOH / $NaHCO_3$). The reaction was completed to volume bydeionized water, and the resulting solution was measured at 516 nm against reagent blank treated similarly.

Job's method

The Job's method of continuous variation and mole ratio [18] were employed to evaluate the stoichiometric ratio of formation reaction. Master equimolar (4×10^{-3} mol) aqueous solution of Bisoprolol and NQS were prepared. Series of 10 mL portions of the master solution of Bisoprolol and NQS were made comprising different complementary proportions (0.1:0.9,…0.9:0.1, inclusive) of reagent and BIF under optimal condition at wavelength of 516 nm and the ratio of drug to reagent at 1:1.

Results and Discussion

Absorption spectra

The absorption spectrum of Bisoprolol (BIF) was recorded against water. It was found that BIS exhibits a maximum absorption peak (λ_{max}) at 271 nm. The reaction between BIF and NQS was performed, and the absorption spectrum of the product was recorded against the reagent blank Figure (6).It was found that the product was colored exhibiting (λ_{max}) at 516nm, and the (λ_{max}) of NQS was 342 nm.The (λmax) of BIF- NQS derivative was red-shifted, eliminating any potential interference. Therefore, the measurements were carried out at 516 nm .

The UV-visible spectrum ofBIF, Figure (5), showed a band at wavelength (271) due to the electron transition (n→ π*). As for the spectrum resulting from the interaction of the drug with the NQS reagent, Figure (6), it is located at the wavelength (516 nm), which is a beam that goes back to the electronic transition (n→ π*). We note from the results that the beam (n→ π*) has a red shift in the resulting spectrum.

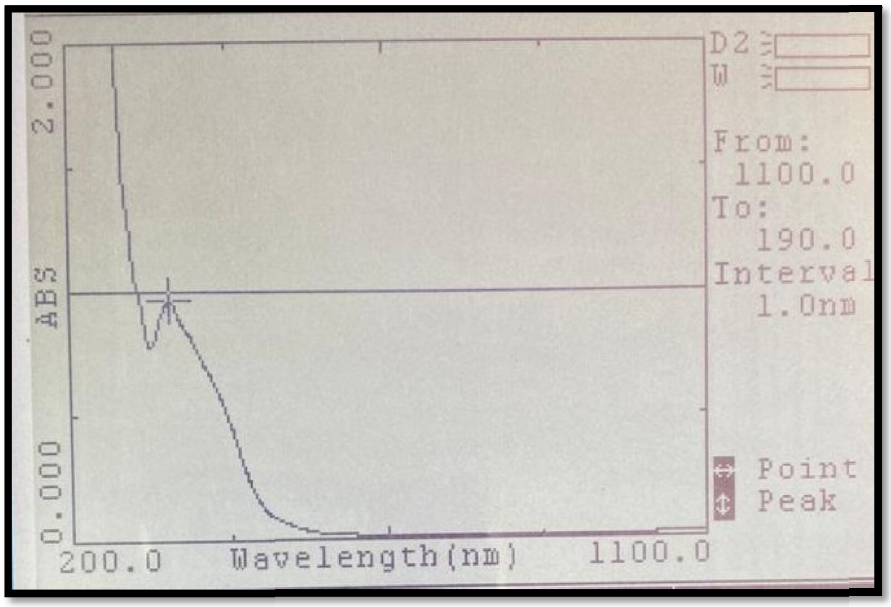


Figure (4):UV-Visible Spectrophotometer for reagent1, 2 Naphthoquinone-4-sulfonic acid sodium salt (NQS)

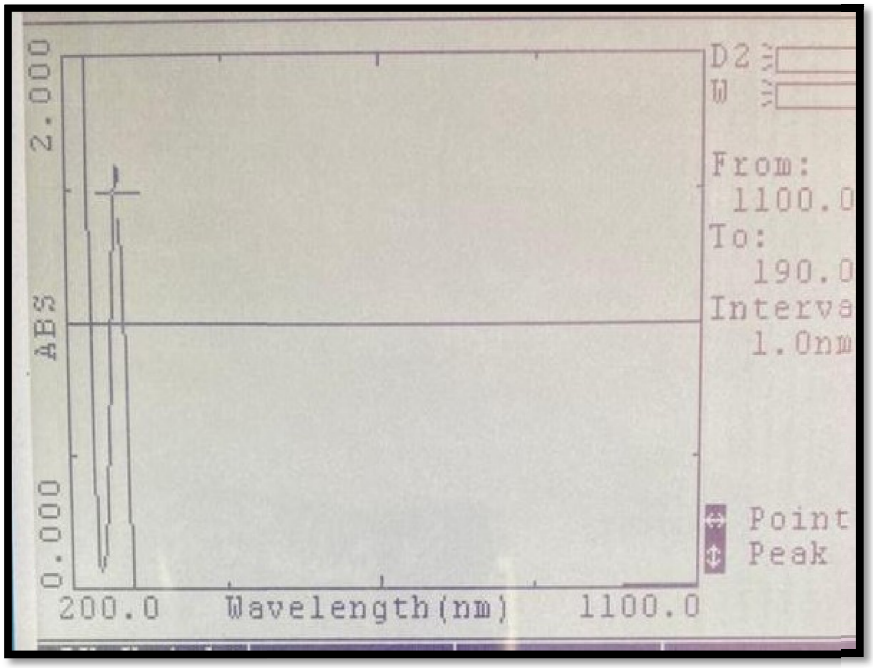


Figure (5) : The UV-visible spectrum of pure BIF

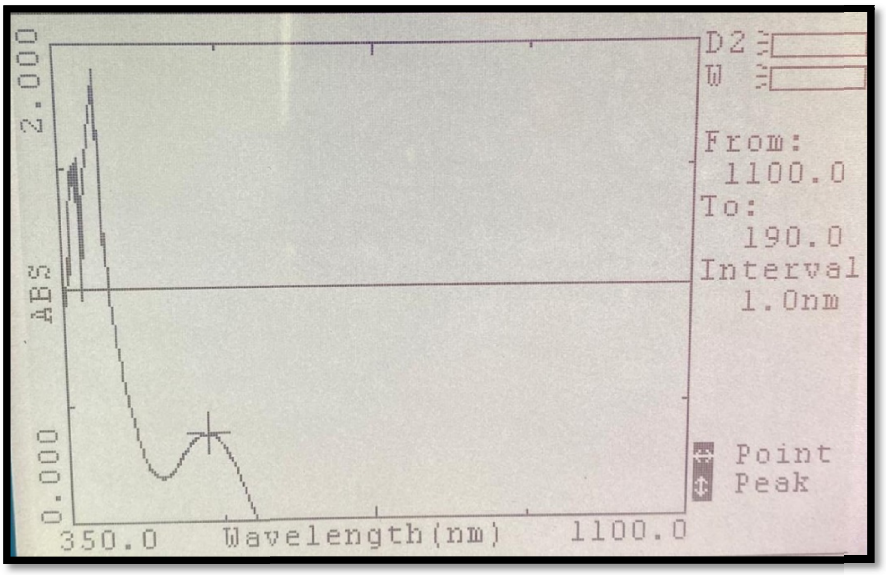


Figure (6): UV-visible spectrum of the reaction product of BIF with the NQS reagent

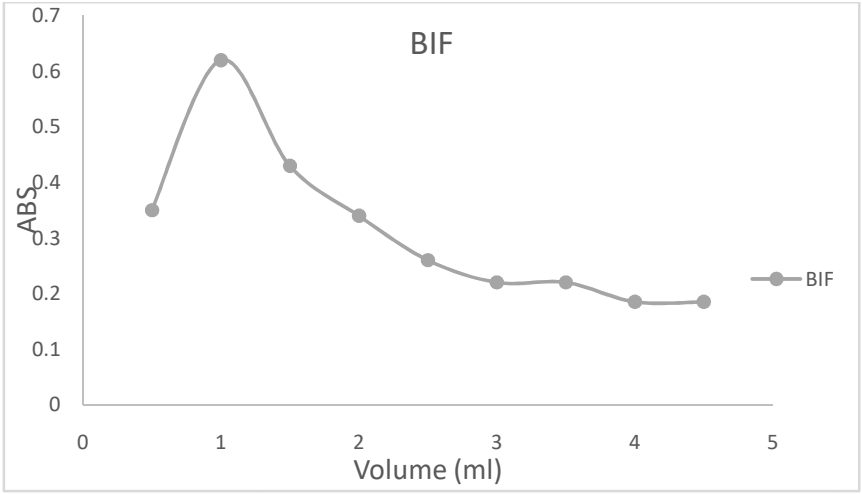


Figure (7): Effect of Volume Drugs

Effect of (NQS) Concentration

The studying of (NQS) concentrations revealed that the reaction was dependent on (NQS) reagent. The highest absorption intensity was attained at (NQS) concentration of 0.4 (w/v)%,(0.015M) the higher concentration of (NQS) (1.0 w/v%) had no effect on the absorption values in the Drug(BIF) as shown in Figure (8).

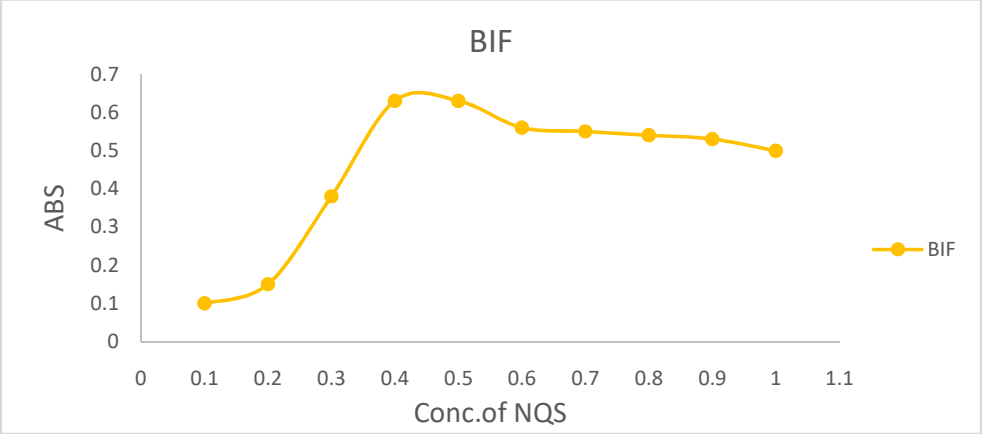


Figure (8): Effect of NQS concentration on the reaction of BIF with NQS Concentration (W/V)%.

Effect of Reagent Volume

The effect of the volume of reagent on the intensity ofabsorptionoftheresultingdyewasstudiedbytaking different volumes of reagent with a concentration of 0.4% (w/v) NQS for BIF. The highest absorption intensity was detected at 1 mL (Figuer.9).

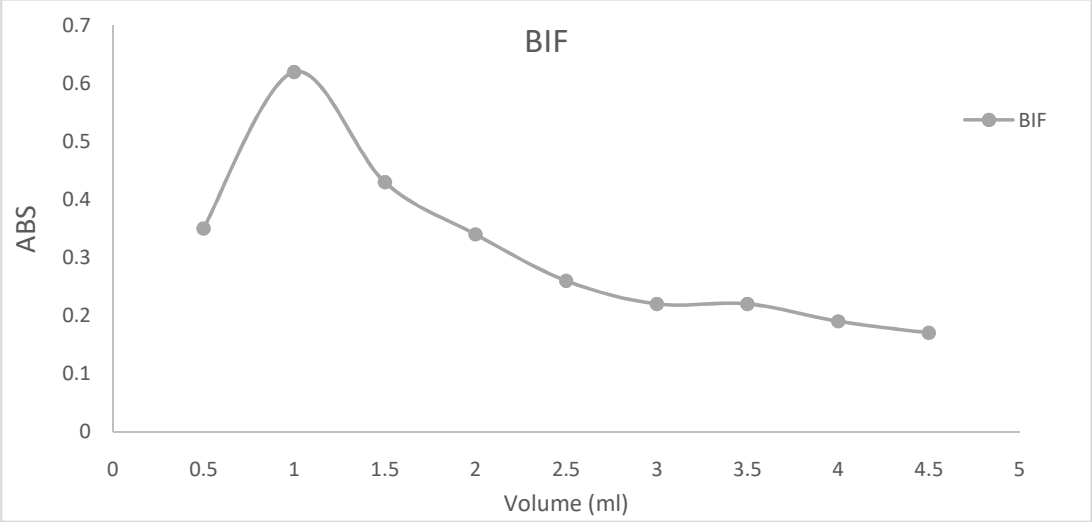
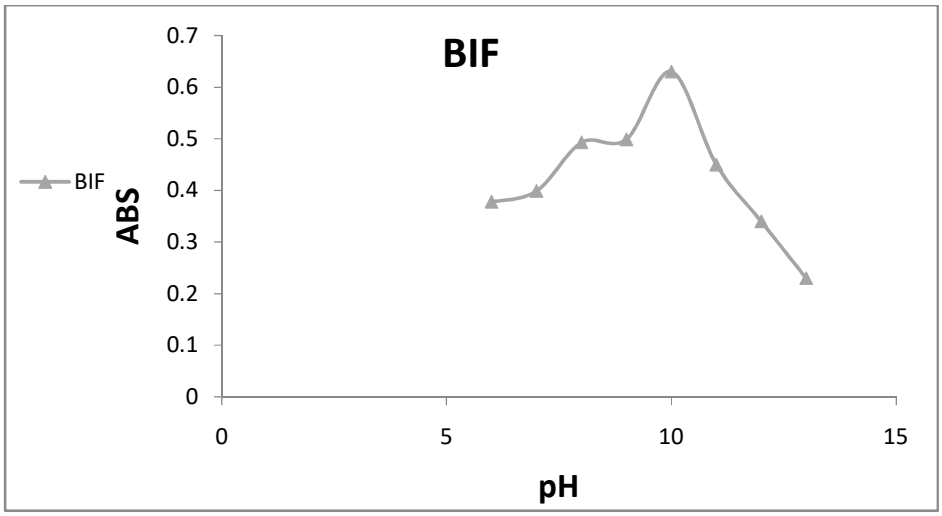


Figure (9): Effect of Volume (NQS).

Effect of pH of the buffer solution

After the installation of condition of the best in the past experiences were study effect of pH on the reaction Drugs BIF with(NQS) was examined by a varying pH form (6.0 - 13.0). As shown in Figure (10), the absorbance of the product is low at pH 9.0, indicating that the Drug has a difficulty to react with (NQS) in pH 9.0 .This was possibly due to the existence of the

amino group of Drugs in the form of salt, thus it loses its nucleophilic substitution capability. The maximum readings were attained at, the value of the of drugBIF was equal 10.



Figure(10) : Effect of pH on the reaction of BIF and with NQS.

Effect of amount of the buffer

The effect of the amount of buffer solutions of Drugs (BIF) on the absorbance of the reaction product was also studied. figure (11) shows that the absorbance of the reaction product enhances rapidly with the rise of the amount of buffer solutions until to (1mL) to ensure the highest absorbance.

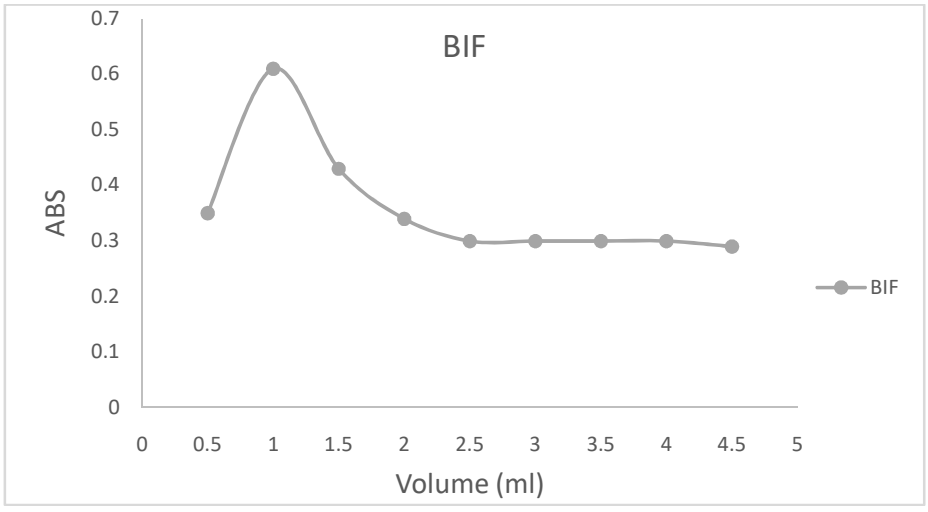


Figure (11) :Effect of Volume (pH).

Effect of Reaction Time

For the purpose of studying the effect of time in the stability of the mixture consisting of the (NQS) and Drug, the absorbance of the reaction product was determined at a different time as in figure (12).The absorbance of the reaction product was measured after standing for different time

under the other optimal condition . The best reaction times of the mixture are detected depending on the high absorbance from Drugs (BIF) are 15 min.

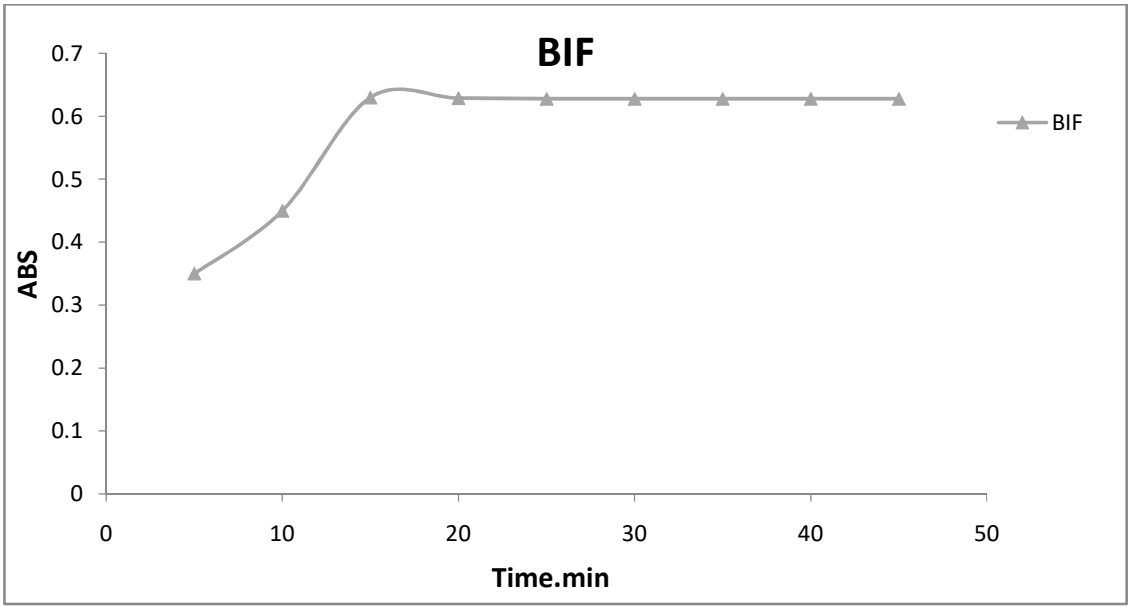


Figure (12): Effect of Time in minutes.

Effect of temperature

The effect of temperature on the stability of NQS and Drug reaction was detected. Fig. (13) reveals the best temperature for reaction was 25 °C when BIF gave the highest absorption.

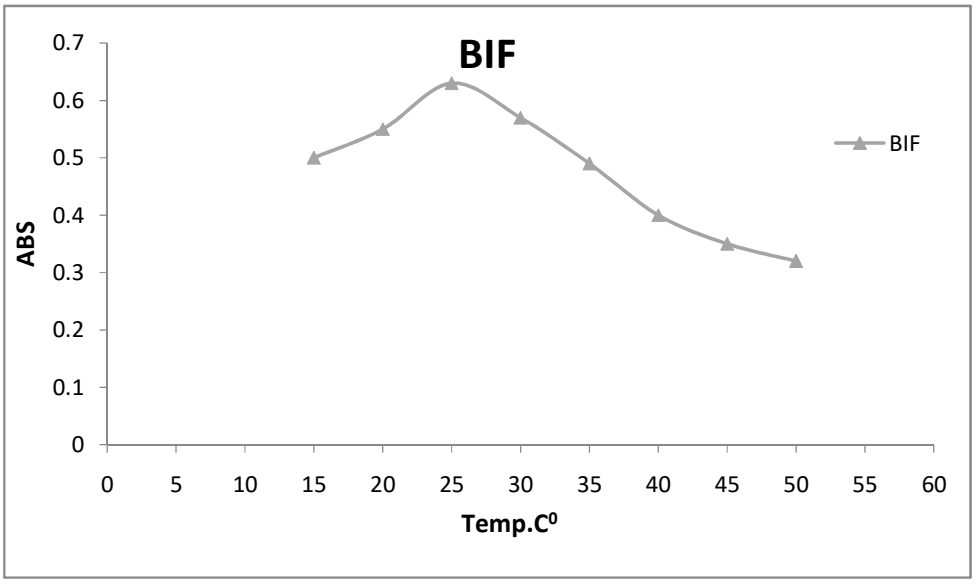


Figure (13) : Effect of Temperature (C°).

Calibration Curve Drug (BIF)

Figure (14) shows the standard calibration curve for the estimation of the Drug (BIF). It turns out that it obeys the Beer's Law between the range of (4-40)µg.mL^{-1} under the best conditions at the maximum wavelength of (516) nm and the correlation coefficient (R^2=0.9988). As for the value of was (Ɛ) molar absorptivity, it was equal to (1011×10^5)L.mol^{-1}.cm^{-1}. The sandell's sensitivity was calculated by calculating the coefficient of specific absorption (a) of the following relationship and was equal to (0.6301)**.**The value of molar high absorptive and the sandell's sensitivity make this analytical method preferred for Drug (BIF) determination at low concentrations.

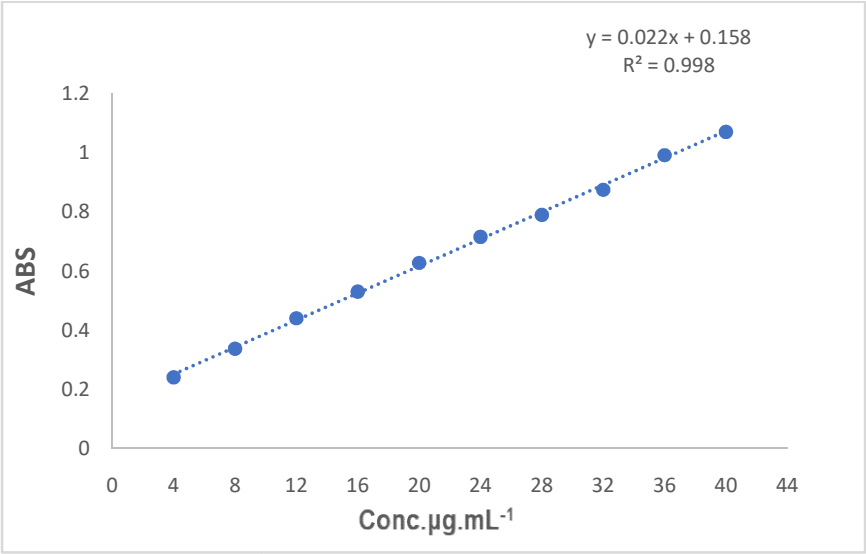


Figure (14) : Calibration Curve Drug (BIF).

Table (1) :Analytic parameter for (BIF) determination.

parameter Value	BIF
Beer's law limit (µg.mL^{-1})	(4-40)
Molar absorptivity (L.mol^{-1}.cm^{-1})	0.1011X10^5
Sandell's sensitivity(µg.cm^{-2})	0.6301
Detection limit (µg.mL^{-1})	0.2620
Quantitation limit (µg.mL^{-1})	0.8733
Determination coefficient(R^2)	0.9988

b)	**0.0229**
Intercept(a)	**0.1585**

Estimation the Composition of the Product

Drug (BIF)

In the present work, the stoichiometric ratio of Drug (BIF) and (NQS) was investigated applying the continuous variation (Job's methods) and the mole ratio methods to evaluate the formation of the reaction between the reagent and Drug (BIF) under the optimal condition at a wavelength (516)nm ,as seen in figure (15). It was found that theDrug forms a product with (NQS) in the ratio (1:1).

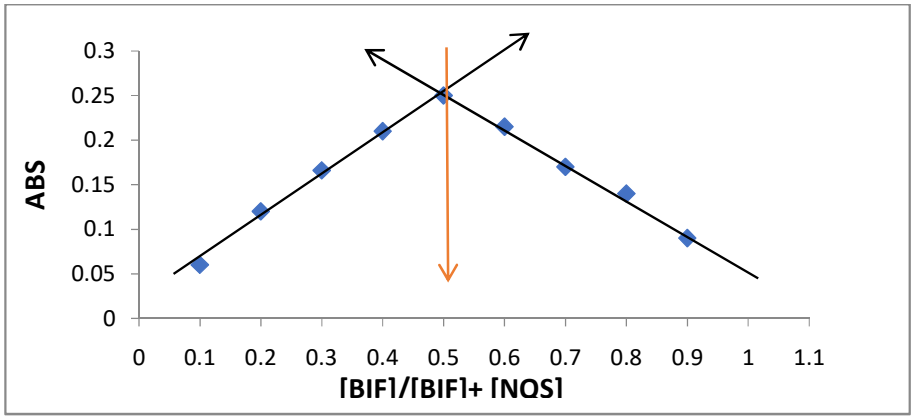


Figure (15) the continuous variation (Job's method) Drug (BIF).

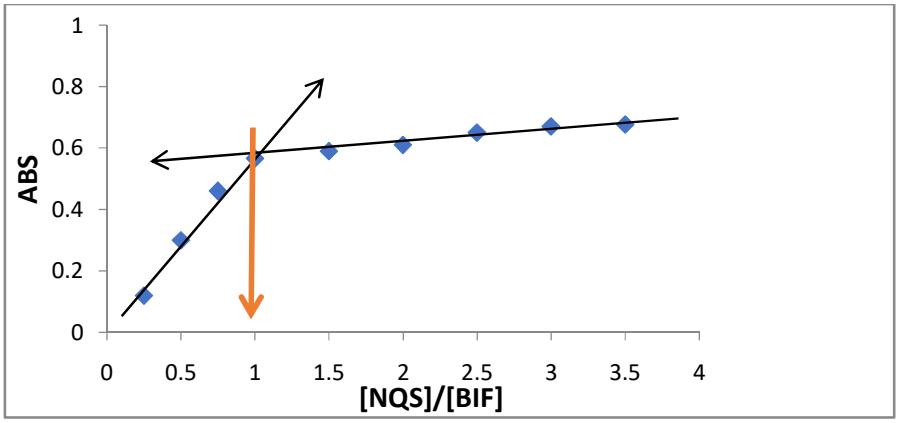
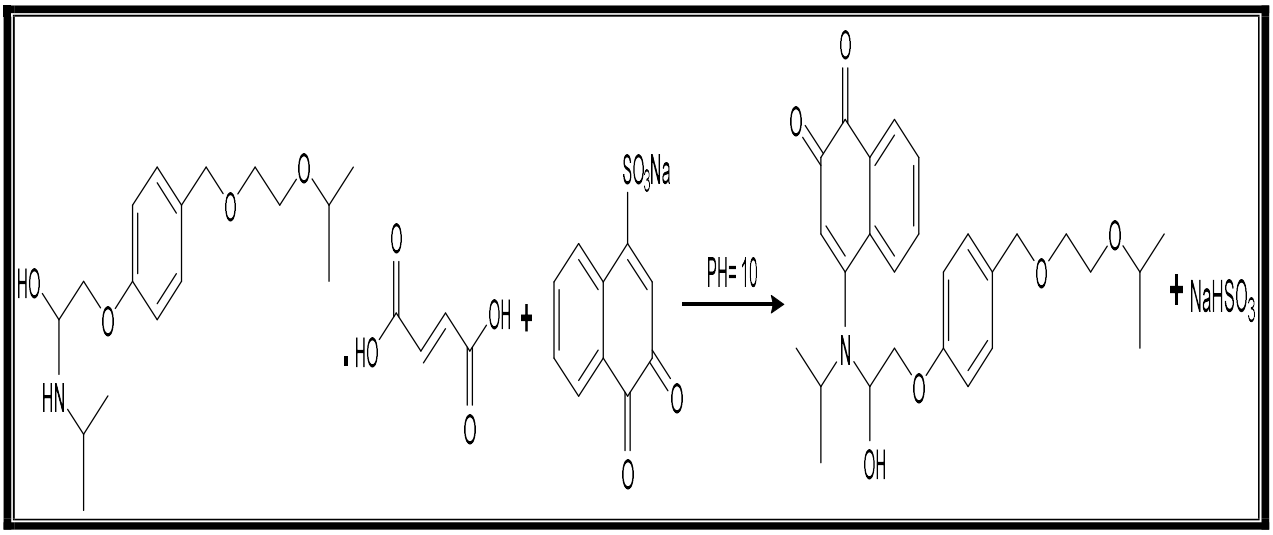


Figure (16) mole ratio Drug (BIF)



Reaction suggest Bisoprolol fumarate(BIF)

Table (2): Relative errors and recovery as parameters expressing accuracy of methods to determine Drugs.

Values	Drug (BIF)
wavelength(nm)	516
Conc.	20 µg.mL^{-1}
X	0.629
R.S.D %	0.317%
Error %	2.8%
%Recovery	102.81

Application of the proposed method to analyse BIF drug formulations

The proposed method indicated the analytic purpose of determining BIF in tablets . The results are listed in Table (3) to determine Drug in pharmacological formula by spectrophotometric methods.

Table(3):analytical applications (BIF).

Preparations containing (BIF)	Concentration \ (ppm)			
	Present	Found	Error %	Recovery %
Bisolek 10 mg	12	11.90	-0.84	99.16
	20	19.99	-0.05	99.95
	36	36.01	+0.02	100.02

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