Spectrophotometric Determination of Propranolol Hydrochloride and Application to Pharmaceutical Preparations

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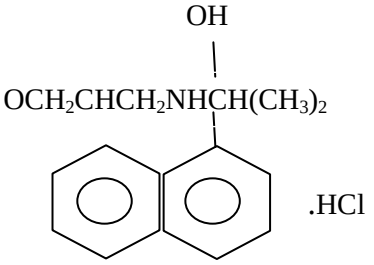
Abstract

A spectroscopic method has been used in this study for determining the drug compound (Propranolol Hydrochloride) as a pure substance and in pharmaceutical preparations using UV-Vis. spectroscopy. The procedure included reduction of Fe (III) ions to Fe (II) ions which reacted with potassium, hexa ferriccyanide, to form a bluish-green precipitate soluble in acidic solution. The maximum absorption has been measured at wavelength (726)nm. The reaction conditions have been studied including sequence additions, concentration and volume of reactants, acidity, temperature and time of reaction. The optimum conditions of reaction have been fixed and two methods have been used for determining Propranolol hydrochloride (PPH), the first, is the direct standard calibration curve, and the second is standard additions curve. Both methods showed linearity range between (0.25-7.0)µg.ml^{-1}, detection limit (0.084)µg.ml^{-1}, correlation coefficient (r) = 0.9998 and the absorption coefficient molarities for the complex formed (Ɛ) = 2.9 $\times 10^4$ L.mol^{-1}.cm^{-1}, and sandel sensitivity = (0.0007)µg.cm^2, recovery percentage value (%Rec.) = 99.932, the relative standard deviation (%RSD) = 0.5, which means that there are matching between both two methods in determination clearly.

Introduction

Chemically, 2 – Propanol - 1 - [(1 – methylethyl) amino] - 3 - (1-naphthalenyloxy)-,hydrochloride[1]. Propranolol hydrochloride (PPH) is a nonselective, beta-adrenergic receptor-blocking agent for oral administration, available as an extended release product[2]. Propranolol Hydrochloride (PPH) as a white, crystalline powder, solid with little or no odour, it is freely soluble in methanol, dissolves in water to the extent of one part in twenty at 20°C and has a similar solubility in 95% ethanol, but is only slightly soluble in chloroform. Its structural formula is:[3]



($C_{16}H_{21}NO_2$.HCl), M.W. = 295.80

Propranolol hydrochloride is a nonselective beta adrenergic receptor blocking agent possessing no other autonomic nervous system activity. It specifically competes with beta-adrenergic receptor stimulating agents for available receptor sites[2,4]. The most important effect of (PPH) is to reduce the influence of excessive sympathetic nervous stimulation on the heart[1,3,5], and has been widely used in the treatment of hypertension, angina pectoris, pheochromocytoma and cardiac arrhythmias, because of its relatively short plasma half-life, patients are routinely asked to take (PPH) in divided daily doses, once every 6 to 8h[6], as well as it used in the treatment or prevention of many disorders including acute myocardial in farction, hypertensive emergencies, hyperthyroidism, migraine, menopause, and anxiety[7]. It is reported to be of value in cardiovascular disorders, many of which are associated with central nervous system[8]. Various methods suggested for the determination of (PPH) include: UV-Vis. Spectrophotometric[9], Cerimetric [10], Voltammetric[11], high-performance liquid chromatography (HPLC), reversed phase RP-HPLC, liquid chromatography, thin layer chromatography, fluorimetry, phosphorimetric, luminescence techniques involve an expensive experimental setup and are not always easily available GC-MS, spectrophotometric methods based on a charge-transfer complexation reaction[12-14].

The aim of the work is to determine of propranolol hydrochloride and application to pharmaceutical preparations.

Experimental part

Instruments and Apparatus Used: UV-Vis. spectrophotometer: JASCO V – 530, (Japan), pH meter of the type: Orion Research Microprocessor Analyzer 90, (Germany), Electronic balance of the type: Thermo Orion, (Switzer land).

Reagents and Chemicals Used

Used chemicals and reagents of analytical with a high degree of purity and origins of the well known international companies:

Table (1): Chemicals and analytical reagents used

Chemical Name	M.W	Assay	Formula	Company
Potassium ferric cyanide hexagonal	329.0	%99	$K_3Fe(CN)_6$	Hopkins & Williams
Ferric Nitrate	242.0	%98.5	$Fe(NO_3)_3.9H_2O$	BDH
Sodium hydroxide	40.0	%98.7	NaOH	BDH
Hydrochloric acid	36.5	Anal R	HCl	Fluka
Propranolol hydrochloride	295.80	%99.6	$C_{16}H_{21}NO_2.HCl$	SDI-Iraq
Sulfuric acid	98.0	Anal R	H_2SO_4	Fluka

Procedure

(1ml) of (PPH) solution with concentration (100)µg.ml^{-1} has been mixed by transferring to volumetric flask (25ml), (1ml) of (1×10^{-3})M of standard solution of ferric nitrate and (1ml) of (1×10^{-2})M of a solution of potassium, hexa ferriccyanide have been added to the above solution, (30minutes) later the color of solution changed to the bluish-green instead of yellow, the pre-color while, the blank solution color did not change. The colored solution showed a maximum absorption (726)nm after the dilution with distilled water.

Results and Discussion

- The spectrum of PPH (100 µg.ml^{-1}) in the wavelength ranges of (190-800 nm), is shown on figure (1).
- The spectrum of reagent (potassium, hexa ferriccyanide), and the spectrum of ferric nitrate solution, are shown on figure (2) and (3) respectively.
- Figure (4), shows the absorption spectrum of the complex, and found to absorbs at (726)nm. The position and shape of the peak of the complex allow the possibility of investment of this interaction to estimate the PPH without overlapping with the peaks of (PPH), and previous solutions.

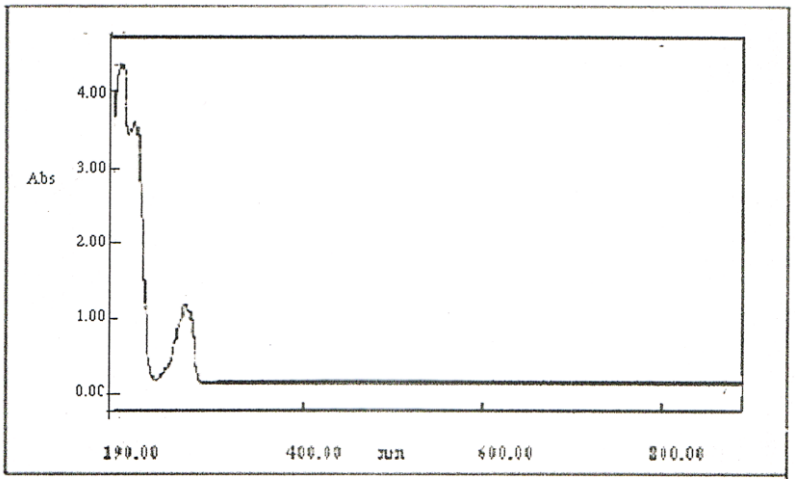


Figure (1): Absorption spectrum of (PPH) solution

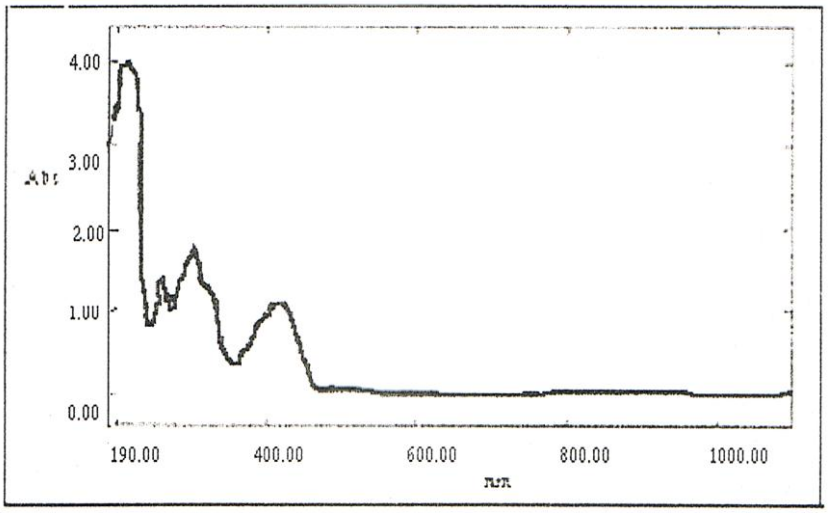


Figure (2): Absorption spectrum of reagent Potassium, hexa ferriccyanide

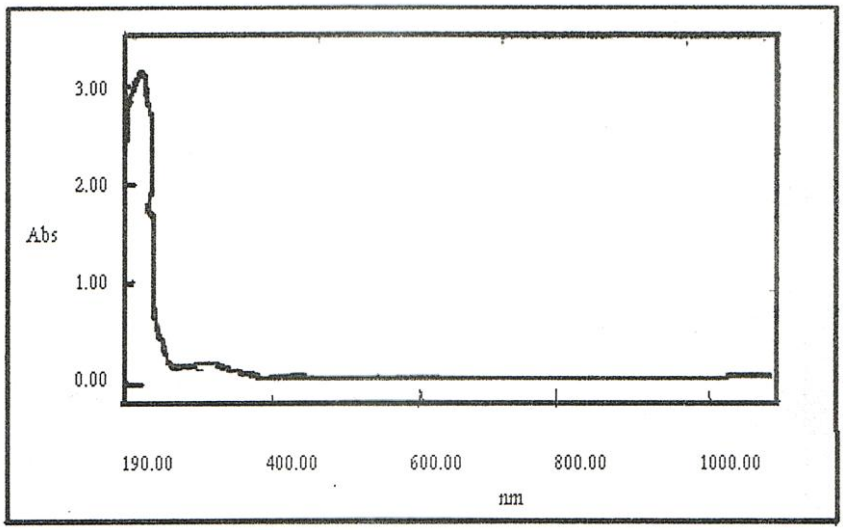


Figure (3): Absorption spectrum of ferric nitrate solution

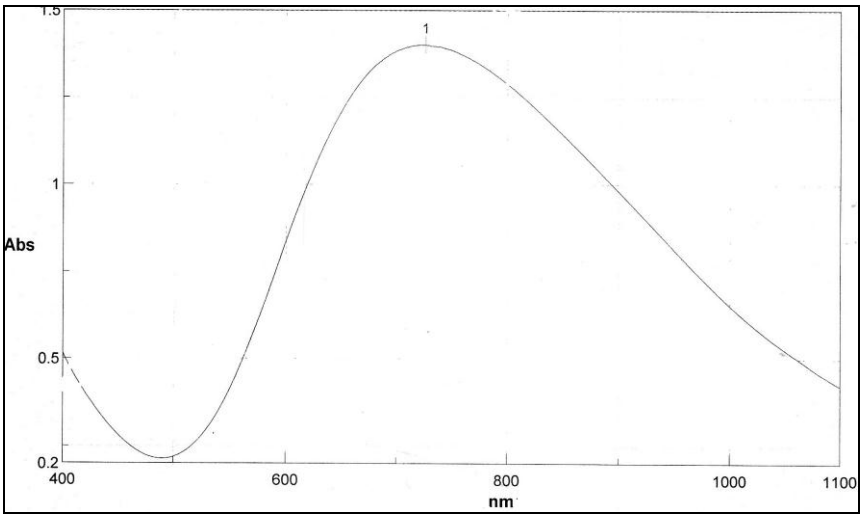


Figure (4): Absorption spectrum of the complex

Mechanism of the reaction

The procedure depends on oxidative reaction for Propranolol hydrochloride with Fe (III) followed by coordination with ferric (III) cyanide potassium to form the colored product, The steps of reaction can be illustrated by the following equations:

PPH (reductant) + Fe^{+3} ⟶ Fe^{+2} + PPH (oxidant)

Fe^{+2} + $K_3[Fe^{III}(CN)_6]$ ⟶ $KFe^{II}[Fe^{III}(CN)_6].XH_2O$

Potassiumferro ferriccyanide

Study the optimum conditions for determination of (PPH)

- The optimum conditions for the complex formation was investigated. The order of addition was found to be: (compound drug + ferric nitrate + potassium, hexa ferriccyanide).
- The effect of pH in the range (3-7) and the volume of sulfuric acid solution was (2-10ml) concentration of (3M).
- The optimum reaction time was (40minuts), and temperature (25^0C).

Determination of the drug compound (PPH)

By applying the optimum conditions of a series of solutions (0.25-7.0)µg.ml^{-1} of (PPH) were prepared and was measured absorbance at a wavelength at maximum absorption of the complex in this method. Figure (5) shows the calibration curve with a linear of (0.25-7.0)µg.ml^{-1} and r = 0.9998.

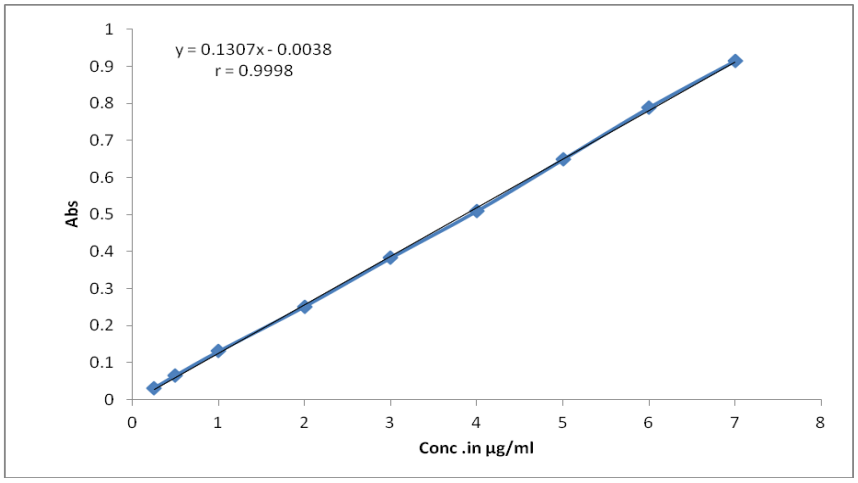


Figure (5): Calibration curve of (PPH) complex

The concentration of (PPH) in (Inderal: U.K and Becardin: SDI-Iraq) was determined by direct method (calibration curve in fig. 5) and by (standard addition methods in fig. 6). The results are shown on table (2).

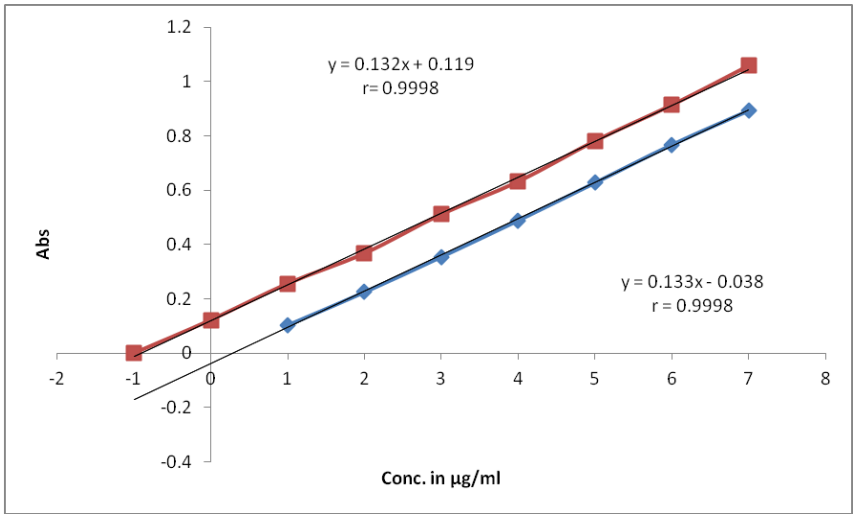


Figure (6): Curve of the standard addition method of determination of PPH

{By taking the square root of the coefficient of determination (R^2) from the linear equation, to extract the correlation coefficient(r)}

Table (2): Results of determination of (PPH)

Pharmaceutical Solution	**manufacturer**	**Present (mg/ml)**	**Found (direct calb.) (mg/ml)**	**Found (St.add) (mg/ml)**	**%RSD**
Inderal	U.K	10	9.62	9.61	0.472
Becardin	SDI-Iraq	12	10.92	10.93	0.480

From the results obtained, the (PPH) drug can be determined by both methods direct and standard addition methods. The following is a comparison of the results obtained using this method with the literature methods:

Table (3): Comparison of the results for the method used with the results of other methods

Source of method	pH	Time (min.)	λmax. (nm)	%RSD	D.L	%Rec.	(r)	Linear range µg/ml
The method used	3-7	40	726	0.5	0.084 µg/ml	99.932	0.9998	0.25-7.0
[7]	3.52	2.33	229	0.675	0.3 µg/ml	100.03	0.9992	2-24
[15]	2.3	10	214	0.27	0.4 µg/ml	100.01	0.9981	4-30
[16]	-	-	242	1.44	0.63 µg/ml	99.65	0.9980	2.5-30
[17]	4.0	20.5	290	0.97	7.22 ng/ml	98.11	0.9995	10-50

Conclusions

The present method showed the possibility of determination of (PPH) drug (one of the amines) in the measurement when the availability of appropriate technical. The results obtained showed the success of this method in according to the analytical results and statistical data obtained. It also showed that the method is of high precision its pharmaceutical preparations (Inderal and Becardin).

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التقدير الطيفي للمركب الدوائي بروبرانولول هيدروكلورايد وتطبيقاته على المستحضرات الصيدلانية

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الملخص

استخدمت في هذه الدراسة طريقة طيفية لتقدير المركب الدوائي (بروبرانولول هيدروكلورايد Propranolol Hydrochloride) بصورته النقية وفي المستحضرات الصيدلانية باستعمال مطيافية الاشعة المرئية – فوق البنفسجية. تضمنت الطريقة اختزال هيدروكلوريد البروبرانولول لأيونات الحديد (III) إلى ايونات الحديد (II) التي بدورها تتفاعل مع سداسي سيانيد الحديديك البوتاسيوم، اذ يتكون راسب اخضر مزرق ذائب في المحلول الحامضي، حيث اظهر اقصى امتصاص عند طول موجي (726) نانوميتر، درست ظروف التفاعل من حيث تسلسل الاضافات وتركيز وحجم المواد المتفاعلة والحامضية ودرجة الحرارة وزمن التفاعل، وثبتت الظروف المثلى للتفاعل. اتبع اسلوبان لتقدير هيدروكلوريد البروبرانولول، هما اسلوب منحنى المعايرة القياسي المباشر واسلوب منحنى اضافات القياس، وقد اظهر كل من الاسلوبان مدى خطية بين (0.25–7.0) مايكروغرام.مل$^{-1}$، وحد كشف (0.084) مايكروغرام.مل$^{-1}$، ومعامل الارتباط (r)=0.9998، وبلغ معامل الامتصاص المولاري(ε) للمعقد المتكون 2.9×10^4 لتر.مول$^{-1}$.سم$^{-1}$، وحساسية ساندل (0.0007) مايكروغرام.سم^{2}، وقيمة معدل الاسترجاعية المئوية (.Rec%) = 99.932، وبلغ الانحراف القياسي النسبي المئوي (RSD%) = 0.5، وهذا يعني أن هناك تطابق واضح بين نتائج الاسلوبين المستعملين في التقدير.