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Novel analytical method for the determination of Atenolol in pharmaceutical preparations

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ABSTRACT

An accurate and sensitive novel method was designated chemically for the determination of atenolol in pharmaceutical drugs. The complex formation between copper(II) and atenolol was studied both in aqueous and methanolic media. Complex formation depends on reaction conditions at different metal-to-ligand molar ratios. The mononuclear violet complex cation $Cu(Atenolol)_4^{+2}$ contains two ligands in an anionic bidentate form (through the hydroxyl oxygen and amino nitrogen) and two in a neutral form bound monodentately with an distorted octahedral geometry. The new analytical method based on measuring absorbance in UV-visible at λmax 350nm. Optimum pH and divalent copper ion concentration were estimated. Linearity (40-250), detection limits $07*10^{-7}$M. were determined. The complex is identified with UV-visible and IR spectra. The molar ratio also investigated and found 1:4(Cu:Atn).

Keywords: Atenolol, copper, determination, and metal complex.

INTRODUCTION

Atenolol is a member of a class of drugs known as beta-blockers (beta adrenergic antagonists) [1]. Atenolol designated chemically as (RS)-4-(2-hydroxy-3-isopropylaminopropoxy) phenylacetamide, is commercially available as a racemic mixture, atenolol and metoprolol (internal standard). The S (–) form is the active isomer with no significant pharmacological activity reported for the R (+)-isomer [2-3].Atenolol (Atn) is a β_1-selective (cardio selective) β-

adrenergic receptor-blocking agent without membrane-stabilizing or intrinsic sympathomimetic (partial agonist) activities. This preferential effect is not absolute however, and, at higher doses, Atn inhibits β_2-adrenoreceptors, chiefly located in the bronchial and vascular musculature [4]. Like other antihypertensive drugs, Atn lowers the systolic and diastolic blood pressure by 15% to 20% in a single drug treatment. In long-term treatment, it has the ability to reduce cardiovascular mortality [5]. Atn is also used to treat myocardial infarction (heart attack) and arrhythmias (rhythm disorders), angina (chest pains), and disorders arising from decreased circulation and vascular constriction, including migraine. Atn may be used alone or concomitantly with other antihypertensive agent s including thiazide-type diuretics, hydralazine, prazosin, and α-methyldopa [6]. The most serious adverse effects are heart failure, heart block, and bronchospasm. Reactions tend to be more severe after intravenous injection as opposed to oral administration [7].

EXPERIMENTAL SECTION

Standard Solutions:
Stock solution of Atenolol (1000ppm) was prepared in distilled water. Stock solution of Copper (1000ppm) from $CuCl_2.H_2O$ was prepared in distilled water.

Optimum conditions for the complex
1: Concentration of metal ion: Optimum concentration of the metal ion determined by the additions of 0.2- 0.4 mL of 1000ppm solution of metal ion to 4mL of 1000ppm Atenolol then extracting the complex after each addition and measuring the absorbance at λmax =350nm (as shown in fig.1).

2: pH: Optimum pH for the complex were determined by changing the pHs, of the reaction solution (1-8) by the addition of 0.1N HCl to the solution of metal ion and the drug. The complex is extracted after each addition and measuring the absorbance at λmax =350nm (as shown in fig.2).

3: Effect of Temperature: Optimum temperature degree for the complex were determined by changing the temperature of solution (50 C^o to 70C^o) and extracting the complex and measuring the absorbance at λmax =350nm (as shown in fig.3).

4: Molar ratio of metal to Atenolol(M:L): (By using the Mole-Ratio method), the addition of 1mL (0.002M) standard metal solution to the same concentration of atenolol solutions (3.5, 4, 4.5, 5) mL. then extracting the complex and measuring the absorbance at λ_{max} =350nm, (as shown in fig.4).

Preparation of Standard Curve: The complex was standardized by the reaction of (0.1-1mL) 1000ppm Atenolol standard solution with 1000ppm (0.5mL) Cuppric chloride standard solution and extracting the complex and measuring the absorbance at λmax =350nm (as shown in fig.5).

Extraction Procedure: Crash the Atenolol tablets then dissolve in methanol. The filtrate dried and recrystalized from methanol. The complex was synthesized by the reaction of Atenolol solution with copper ion solution, then extraction of complex by methanol and measure the absorbance at λmax, 350nm.

RESULTS AND DISCUSSION

The Copper ion reacts hardly with the ligand in molar ratio 1:4 and 1:1. The molar ratio 1:4 (our target) produce the violet crystal of the complex $CuAt_4$ in methanolic medium, and the molar ratio 1:1 produce the green crystal of the complex Cu_2At_2 in aqueous medium. The violet crystal of the complex $CuAt_4$ is soluble in pH 2.5 and denaturated at pH over 6. The chemical structure of the ligand (Atenolol) has more than one coordination center because there is hydroxyl, carbonyl, and amino groups. When we compare the IR spectrum of ligand with that of complex we found:

1: The hydroxy band become broader in the complex than of the ligand that mean there is a bonding between hydroxyl Group (the oxygen of hydroxy group) and the metal, another evidence for that is the band at 470cm^{-1} for the coordination of metal with oxygen of hydroxy group, and there is another band at 430cm^{-1} for the coordination of metal with amino group.

2: Changing of carbonyl band from 1700cm^{-1} (in the ligand) to 1660cm^{-1} (in the complex) and that may refer to the stability of the carbonyl group.

3: Changing of hydroxyl band from 3400cm^{-1} (in the ligand) to 3200cm^{-1}(in the complex) and changing of amino band from 3500cm^{-1} (for the ligand) to 3400cm^{-1}(for the complex) and that may be refer to the stability of the hydroxyl and amino groups, or that mean these groups are flat with metal.

Table 1: The IR spectrum (cm^{-1}) of the ligand and the complex

Com.	N-H	O-H	C=O	C-$H_{Aro.}$	C-$H_{Ali.}$	Cu-O	Cu-N	C-O-C
Ligand (Atn)	3500	3400	1700	3100	2950	-	-	1200, 1050
Complex	3400	3200_{Broad}	1660	-	-	470	430	1300, 1100

Atenolol react with Cu(II) in methanolic medium in molar ratio M:L_4 at the pH 2 to give violet crystal of the complex $(CuAtn_4)^{2+}$. The complex dissolved at the pH 2.5 and decomposed at pH 6.

Table 2: The wave length and ABS of the legand and the complex

Compound	Wave length(nm)	Abs
Ligand (Atn)	400, 295, 266	0.665, 2.211, 1.397
Complex, $Cu(Atn)_4$	630, 405, 285, 247	0.093, 0.350, 1.811, 2.117

Optimum conditions for the complex

1: Concentration of metal ion: Optimum concentration of the metal ion determined as it found form Figure1 (Concentration vs absorbance). The best concentration were given from the highest absorbance,

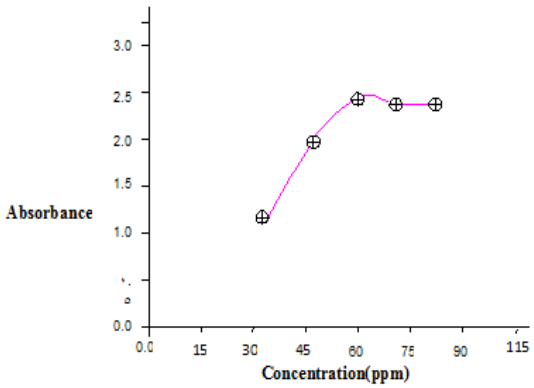


Figure 1: Concentration vs absorbance

2: pH: Optimum pH of the complex formation determined as it found from Figure 2 (Concentration vs pH) The best pH (pH= 2.0) were given from the highest absorbance

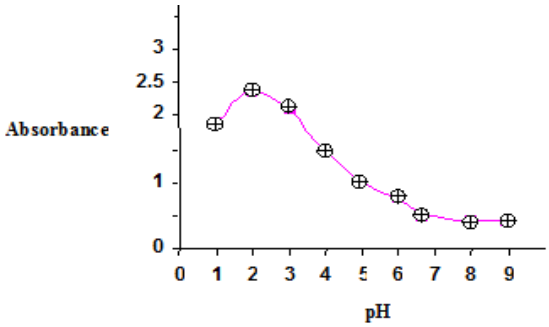


Figure 2: Absorbance vs p

3: **Temperature** : Optimum Temperature (C^o) of the complex formation determined as it found from Figure 3 (Temperature vs Absorbance). The best temperature (t= 85C^0) were given from the highest absorbance

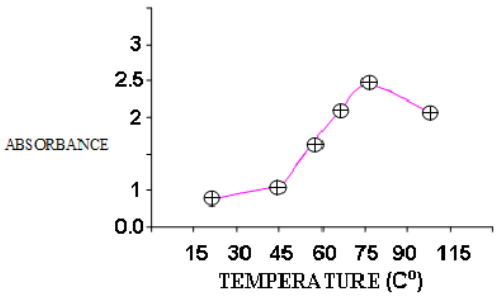


Figure 3: Temperature vs Absorbance

4: Molar ratio of metal to Atenolol (M:L): The Mole-Ratio of metal ion to the atenolol (in the complex) is found from Figure 4 (Volume vs Absorbance) at λmax =350nm

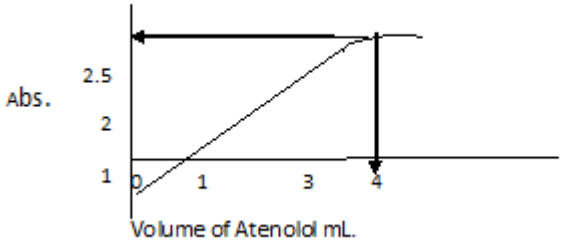


Figure 4: Molar ratio of metal to Atenolol at (0.002M), show that M:L equal to 1:4

Standard Curve For our complex: Fig.5 represents the concentration of Atn. vs absorbance under Beer Law, Showing the linearity(40-250µg).

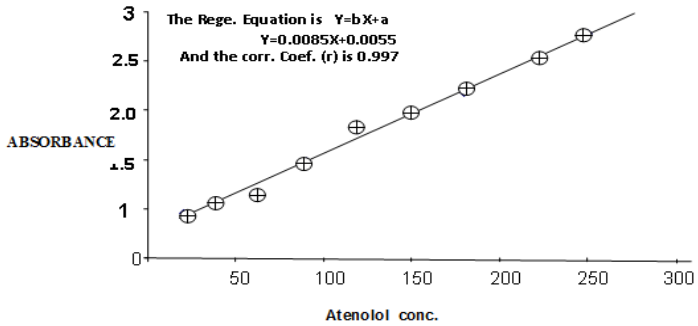


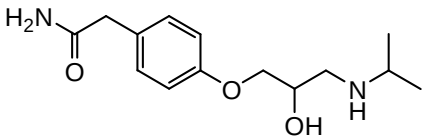
Figure 5: Standard curve or determination of Atenolol in pharmaceutical preparations at λ_{max} =350nm.

Table 3: The λ_{max}, Linearity, Detection limit and Sensitivity of the complex

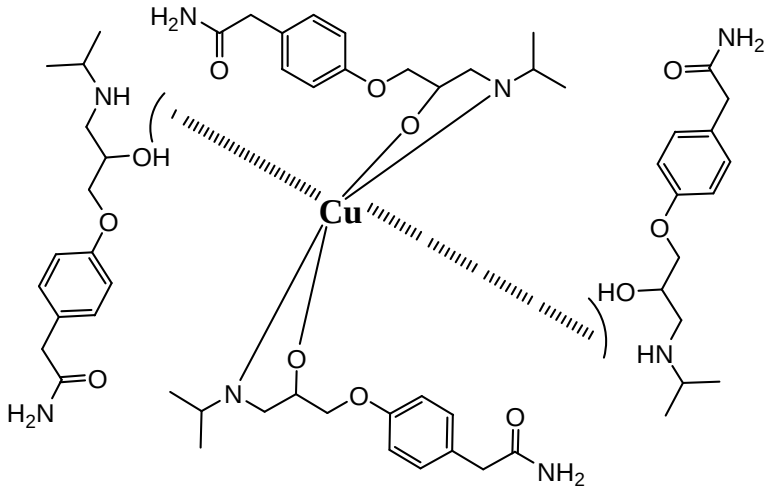
λ_{max} (nm)	Linearity µg/ml	Detection limit	Sensitivity
350	40-250	$07*10^{-7}$M	0.143

Table 4: The results of atenolol determination in pharmaceutical

Pharmaceutical	Stated	Found	Recovery %
Atenolol SDI (IRAQ)	100mg	96mg	96%



Scheme 1: The structure of atenolol



Scheme 2: The structure of atenolol complex **($CuAt_4$)**

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