Spectrophotometric Determination of Capoten In Pure Form and Commercial Tablets

تقدير الكابوتين طيفيا في صورته النقية والاقراص التجارية

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Abstract:

A simple and accurate spectrophotometric method for the determination of capoten is applied. The procedure is based on the chelate formation with nickel(II) in acidic buffer medium. The complex has a maximum absorption at 617 nm. The optimum conditions for the complex formation were ascertained and the method was developed for the determination of capoten in the concentration range of (20–60) mg/L. The empirical formula of the formed complex was determined, by applying different spectrophotometric methods, at optimum pH of (3-5) and an ionic strength of μ equal to 0.5 M. The stoichiometric ratio was found to be 2:1 of Capoten-Nickel (II) complex as calculated by continuous variations and the mole ratio methods. The continuous variations method was applied for the determination of the conditional stability constant of the formed red complex and was found to be 3.27×10^7. The proposed method was found to be suitable for the determination of capoten in pure form and in its commercial tablets.

الخلاصة :

تم تطبيق طريقة طيفية بسيطة ودقيقة لتقدير الكابوتين . ان الطريقة المقترحة تعتمد على تكوين مركب كيليتي مع أيون النيكل الثنائي بوجود محلول منظم حامضي. تكون امتصاصية المعقد العظمى عند (617 nm) تم تطبيق الظروف المثلى للتحقق من تكوين المعقد وتطبيق الطريقة لتقدير الكابوتين عند تركيز ما بين (20-60) mg/L . تم تحديد الصيغة التجريبية للمعقد بواسطة تطبيق الطرق الطيفية عند دالة حامضية ما بين (3-5) وقوة ايونية مساوية الى 0.5 مولاري . ووجد ان النسبة هي 2:1 للمعقد الكابوتين – النيكل الثنائي وتم حسابها باستخدام طريقتي المتغيرات المستمرة و النسب المولية. تم تطبيق طريقة المتغيرات المستمرة لحساب ثابت استقرارية المعقد الاحمر المتكون وجد بانه مساوي الى 3.27×10^7 . تم تطبيق الطريقة المقترحة لتقدير الكابوتين بصورته النقية واقراصه التجارية .

Keywords: Spectrophotometric, Capoten, Capoten-Nickel(II) complex and Commercial tablets.

Introduction:

The first drug planned to be used for arterial hypertension treatment was capoten, 1-[(2S)-3-mercapto-2-methylpropionyl] pyrrolidine-2-carboxylic acid (Fig. 1), which belongs to the class of angiotensin-converting enzyme (ACE) inhibitors. This drug interacts with ACE due to its similarity with a dipeptide and the sulphydryl group also plays an important role, linking covalently to the zinc atom in the enzyme active site. This drug is widely used mainly for arterial hypertension treatment, but also in diabetic nephropathy and congestive cardiac insufficiency [1-3].

Several methods for the determination of capoten which includes gas chromatography [4], high performance liquid chromatography [5], potentiometry [6], chemiluminescence [7], capillary electrophoresis [8], flow injection analysis [9], polarography [10], radioimmunoassay (RIA) [11], titrimetry [12], and atomic absorption spectrophotometry [13] and amperometry [14].

Many spectrophotometric methods involve the use of reagents that react with this compound to form species that absorb in the visible region. One of the sensitive methods uses Folin-Ciocalteu reagent [15], which is reduced to a blue species and measured at 760 nm. The same procedure has been automated by adapting to flow-injection device using online solid phase extraction, but the sensitivity has been far less than the manual procedure [16]. Emmanuel and Haluankar [17] have proposed a method, which involves the treatment of capoten with citric acid and boiling for 30 min at 98 °C followed by addition of acetic anhydride and measurement at 570 nm. Methods [18] using phenylfurone or dichlorophenol indophenol also involves heating for 60 min besides lacking sensitivity. The drug has also been estimated in tablets by three procedures [19] involving iron (III).

The methods reported by Ashry and Ibrahim [20] either lack sensitivity (using N-bromophthalimide-promethazine) or involves boiling for 30 min (using molybdophosphoric acid), and hence unsuitable for routine analysis. A few indirect spectrophotometric methods involving the use of bromate-celestine blue [21], 2,2′-diphenyl-1-picryl hydrazyl [22], chromium(VI)-metol-primary arylamine [23], iron (III)-1,10-phenanthroline [24] and metavanadate-H_2O_2 [25] combinations are also found in literature, but suffer from one or the other disadvantage.

This paper describes sensitive and simple spectrophotometric method for the determination of capoten in pure form and in its commercial tablets by using $Ni(NO_3)_2.6H_2O$.

EXPERIMENTAL

1- Apparatus
A UV-Visible Shimadzu spectrophotometer model UV-1650 PC with 1 cm quartz cell was used throughout this research work. Water bath model Memment and pH-meter model Ionlop-720.

2- Materials and reagents
Analytical reagent grade of acetic acid, ammonium chloride, ammonium hydroxide, hydrochloric acid, potassium nitrate, sodium acetate, sodium hydroxide and double-distilled water were used. A standard solution of 5×10^{-3} M of $Ni(NO_3)_2.6H_2O$ was prepared by dissolving 0.1454 gm of $Ni(NO_3)_2.6H_2O$ in a minimum amount of distilled water in a 100 ml volumetric flask and the volume was made up to the mark with distilled water. pH range 1–10, was prepared by acidic buffer which mixing different volumes of 0.1 M acetic acid with 0.1 M sodium acetate solutions; and basic buffer which mixing different volumes of 0.1 M ammonium hydroxide with 0.1 M NH_4Cl solutions. The pH of the solutions was adjusted by HCl or NaOH. A stock solution of 200 mg/L of capoten was prepared by dissolving 0.0200 gm of capoten in a minimum amount of distilled water in a (100 ml) volumetric flask and the volume was made up to the mark with distilled water. The ionic strength (μ) of the final solutions used for the spectrophotometric measurements was kept constant at (0.5 M) by the addition of 2.5 M potassium nitrate solution.

3- General procedure and construction of calibration graph
To a set of 10 ml volumetric flasks, different volumes of capoten standard solution (1–3 ml, in 0.2 ml increment) (20-60) mg/L were quantitatively transferred. To each flask, 1 ml buffer solution followed by 3 ml of $Ni(NO_3)_2.6H_2O$ solution and 2 ml potassium nitrate (2.5 M) solution was added and the solution was diluted to volume with water and mixed, and absorbance was measured after 5 min at 617 nm against a reagent blank which was carried out under the same condition without drug.

4- Composition of the Capoten-Nickel(II) complex
The composition of the complex was established by two different methods: Job's method of continuous variation method [26] and molar ratio method [27]. The absorbance was measured after 5 min at 617 nm against a reagent blank.

Job's method of continuous variation method was performed by mixed different proportions of solutions of capoten and $Ni(NO_3)_2.6H_2O$. The final volume in each series was maintained constant. The absorbance of each mixture was recorded and plotted against the volume of the variable component.

Molar ratio method was employed by preparing a series of mixtures by adding a constant volume of capoten solution with varying amount of $Ni(NO_3)_2.6H_2O$ keeping the final volume constant and adjusting the pH. The absorbance was then measured as in the Job's method and plotted against the molar ratio of $Ni(NO_3)_2.6H_2O$ in the mixture.

5- Procedure for the Assay of Capoten in Commercial Tablets
Three tablets (Acetin, Angiopril and captopril) containing the capoten were powdered. An accurate quantity of powder equivalent to 20 mg of capoten was weighed, followed by addition of 1 ml buffer solution followed by 3 ml of $Ni(NO_3)_2.6H_2O$ solution and 2 ml potassium nitrate (2.5 M), the application of the proposed general procedure.

RESULTS AND DISCUSSION

Transition elements were found to form stable complexes with many ligands containing heteroatoms. There is preference for amines, halogens, CN^-, tertiary phosphrines and sulfides. Nickel(II), as one of the transition elements was found to form complexes of square shape with the general formula of ML_2X_2, where L is a neutral ligand and X a uninegative ion [28]. Nickel(II) was found to form stable complexes with many drugs; for example: Acetylsalicylic acid [29], fluoxetine [30], vitamin C [31] and ephedrine [32]. Theoretically and from what was mentioned above, capoten could form chelate, through its nitrogen and oxygen atoms, with Nickel(II). Addition of $Ni(NO_3)_2.6H_2O$ to capoten produced red complex that is soluble in acetate buffer and showed a maximum absorbance at 617 nm (Fig. 2), which was therefore used for the analytical determination. Capoten which gave an absorption peak at 326 nm, it was colorless solution (Fig. 3). While $Ni(NO_3)_2.6H_2O$ gave an absorption peak at 520 nm (Fig. 4). At the wavelength of the maximum absorbance of the complex, all measurements were performed against a reagent blank. Because of $n \rightarrow \Box^*$ transition for capoten molecule and valence electrons in the nickel ion's d-orbital [33], occur red shift for the Capoten-Nickel(II) complex at 617 nm.

1- Effect of pH
The influence pH was studies over the rang (1-10) on the absorbance of complex at 617 nm. The results were evaluated as shown in (Fig. 5). The shape of the absorption spectrum, the position of the absorption maximum and the apparent molar absorptivity of Capoten-Nickel(II) complex do vary with pH, where the maximum absorbance obtained in the rang of pH (3-5), but at natural and basic media the Capoten-Nickel(II) complex was precipitate.

2- Effect of Reaction Time
The stability of the absorbance with the time was studied from 1-60 min. (Fig. 6) shows the relation ship between absorbance and the time, where the maximum absorbance was reached at the 5 min after the addition of $Ni(NO_3)_2.6H_2O$ to capoten, the absorbance after this optimal time was, almost stable.

3- Effect of volume of $Ni(NO_3)_2.6H_2O$
The volume of $Ni(NO_3)_2.6H_2O$ has a great effect on the formation of Capoten-Nickel(II) complex. (Fig. 7) shows that 3 ml of $5x10^{-3}$ M of $Ni(NO_3)_2.6H_2O$ solution was sufficient to give a maximum absorbance. Increasing the volume of $Ni(NO_3)_2.6H_2O$ produced the same effect.

4- Effect of temperature
The effect of temperature was studied in the range of (5-60°C) on the produce of complex of capoten with $Ni(NO_3)_2.6H_2O$ as shown in (Fig. 8). The maximum absorbance was obtained when the temperature was varied between (20 – 40) °C. The temperature over 40 °C, the absorbance of complex begin low because of disintegration of capoten-Nickel(II).

5- Composition of the complex
The reaction stoichiometry between capoten and $Ni(NO_3)_2.6H_2O$ has been determined spectrophotometrically by applying Job's method of continuous variation method and molar ratio method. For Job's method, the plot reached a maximum value at a molar concentration of the complex formed of 0.66 which indicated the formation of a 2:1 (capoten-Nickel(II)) complex (Scheme 1 and Fig. 9). The plot obtained by the mole ratio method also confirm the formation of (capoten-Nickel(II)) complex in a mole ratio of 2:1, where a break point at 0.5 was obtained (Fig. 10).
By Job's method and from Fig. 8, the conditional stability constant (K) was calculated and found to be $3.27x10^7$. The values of log K equal to 7.514, indicating very good agreement and high stability of the complex.

6- Calibration graph and statistical analysis
By using the above spectrophotometric procedure, a linear regression equation was obtained. The regression plot showed a linear dependence of the absorbance over the Beer's law range given in

Table 1. The molar absorptivity, slope, intercept and correlation coefficient obtained by the linear least square treatment of the results were listed in Table 1. The good linearity of the calibration graph and the negligible scatter of the experimental points were clearly evident from the values of the correlation coefficient and variance. The accuracy and precision of the method was checked by analyzing five replicate samples within the Beer's law range containing the same amount of drug. The RSD values are 0.625%. The lower RSD values indicate the good precision and reproducibility of the method. The calibration curve is linear over the concentration range of (20-60) mg/L as shown in (Fig. 11).

7- Application to the analysis of commercial tablets
The proposed method has been applied for the analysis of capoten in its commercial tablets. The recovery of the drug was tested. The recovery was almost quantitative (Table 2). The proposed method was reproducible, simple and easily applied in the quality control laboratories.
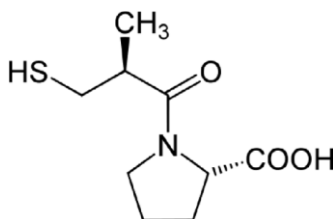
Fig. 1: Molecular structure of capoten.
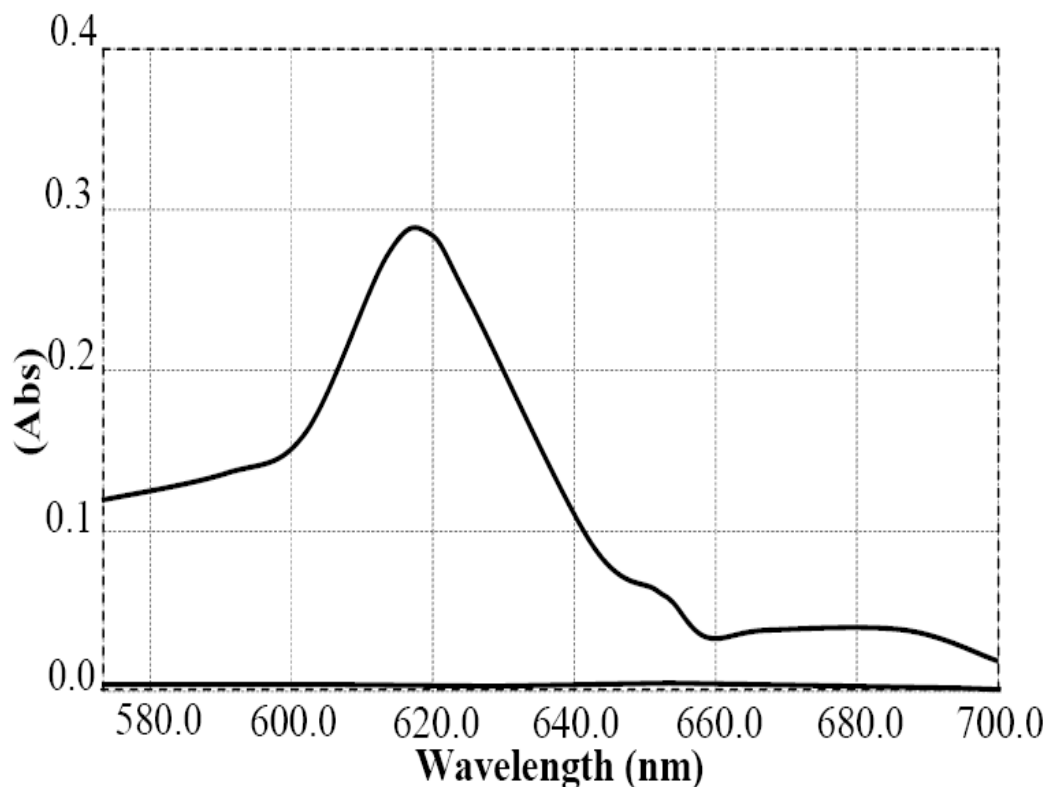
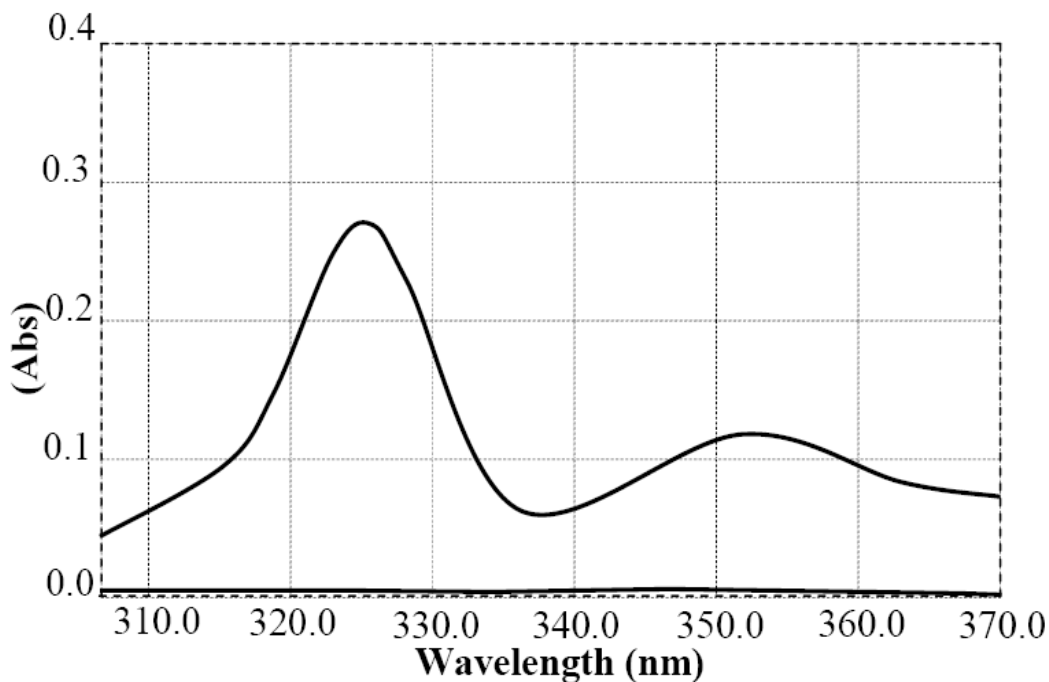Fig. 2: Absorption spectrum of Capoten-Nickel(II) complex.
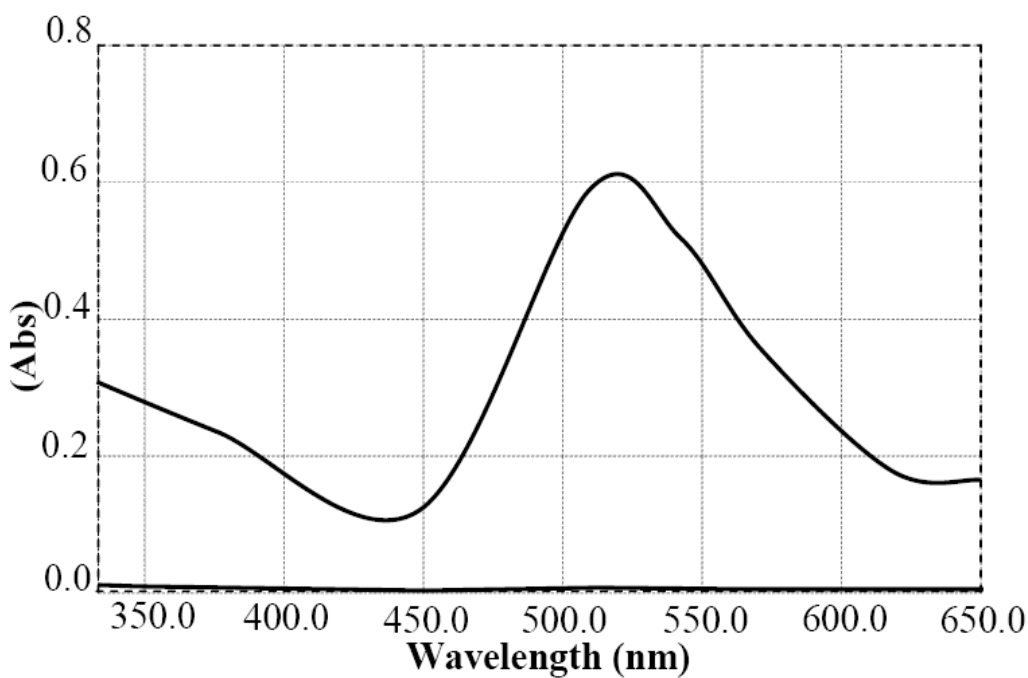
Fig. 3: Absorption spectrum of Capoten.

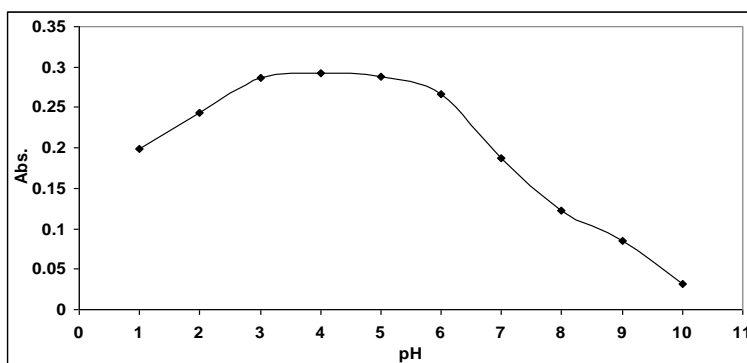
Fig. 4: Absorption spectrum of $Ni(NO_3)_2.6H_2O$.

Fig. 5: Effect of pH on the absorbance of Capoten-Nickel(II) complex.
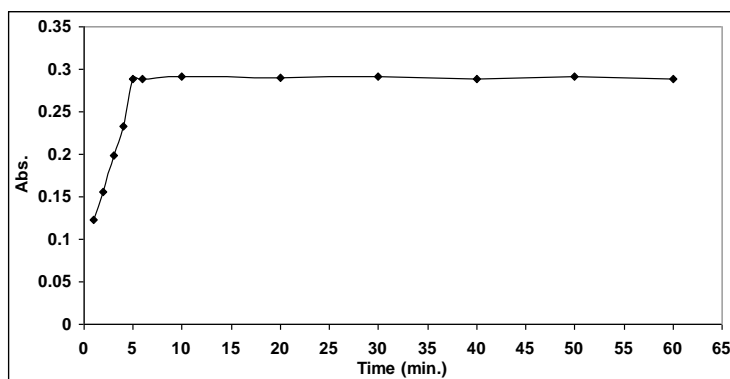
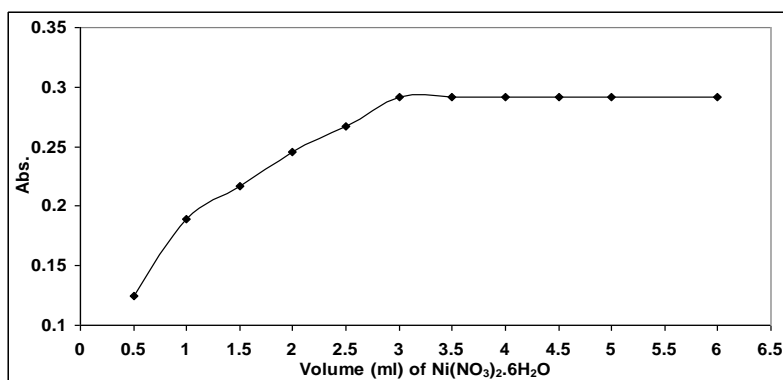Fig. 6: Effect of time on the absorbance of Capoten-Nickel(II) complex.

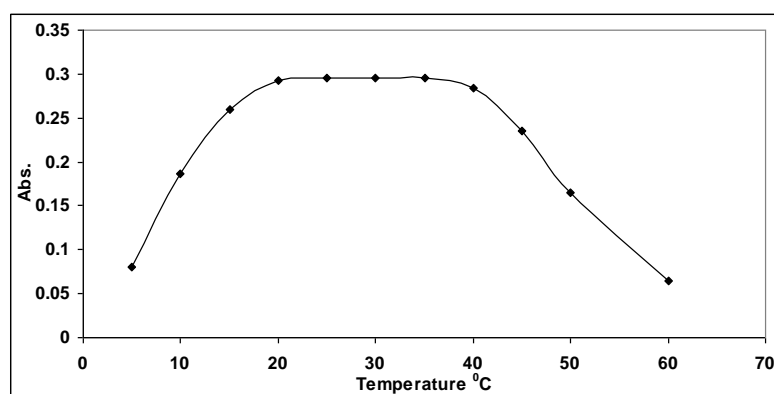Fig. 7: Effect of volume of $Ni(NO_3)_2.6H_2O$ on the absorbance.

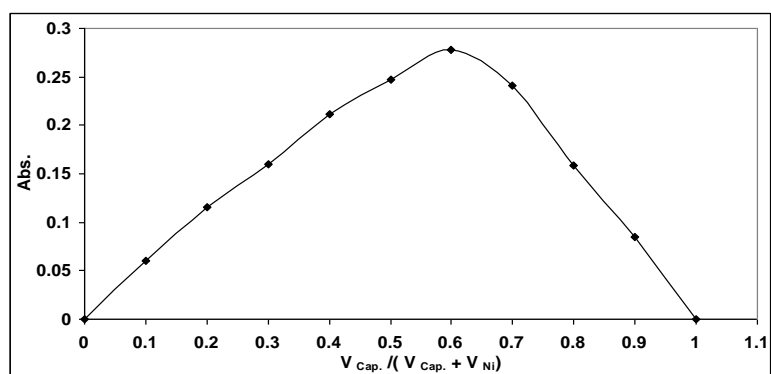Fig. 8: Effect of temperature on the absorbance of Capoten-Nickel(II) complex.

Fig. 9: Job's method of continuous variation plot for
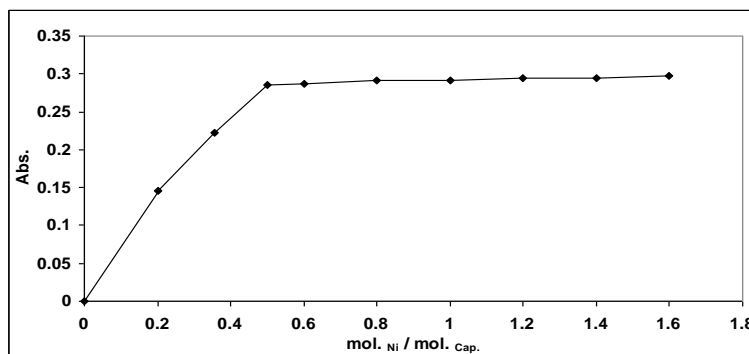Capoten-Nickel(II) complex ratio.

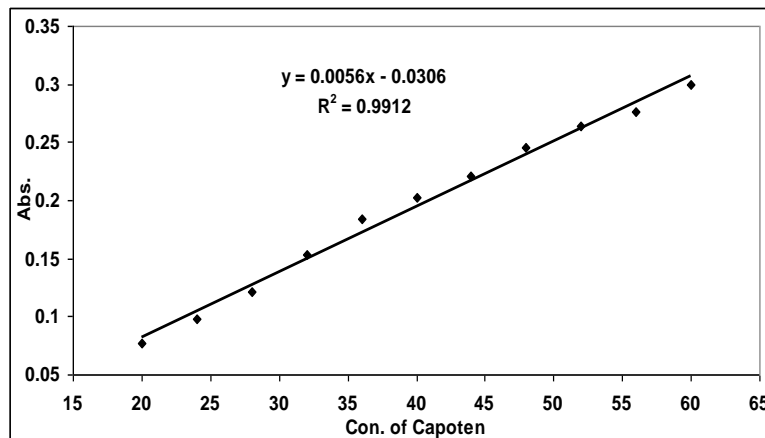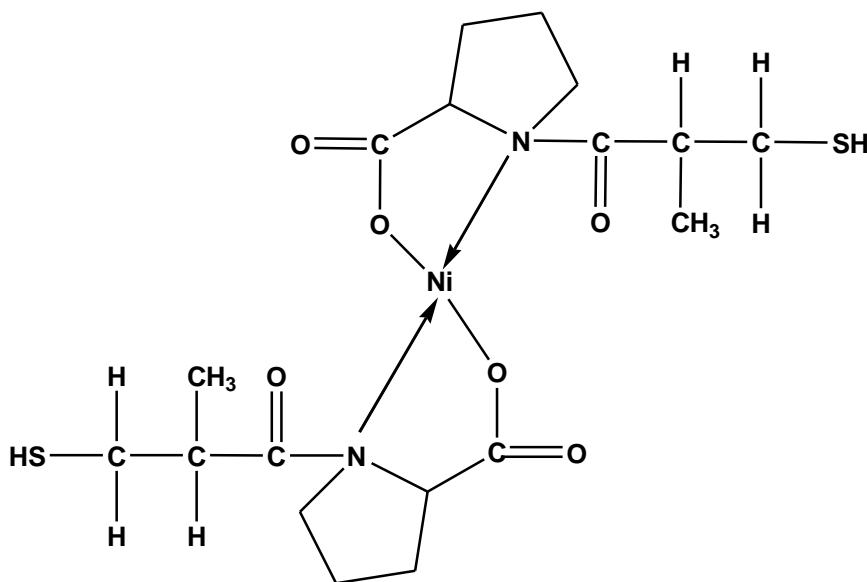Fig. 10: molar ratio plot for Capoten-Nickel(II) complex ratio.

Fig. 11: Calibration curve of Capoten-Nickel(II) complex.

Scheme 1: The structure of Capoten-Nickel(II) complex.

Table 1: Optical Characteristics and Statistical Data for the Regression Equation of the Proposed Method

Parameters	Values
λ_{max}	617 nm.
Color	Red
Beer's law limit (mg/L)	20-60
Molar absorptivity (l mol^{-1} cm^{-1})	1.096×10^3
Sandell's sensitivity (mg/L per 0.001 A)	1.98×10^{-1}
pH	3-5
Stability of color (min.)	5
Temperature (°C)	20-40
Regression equation (Y$^{\#}$)	
Slope (a)	5.6341
Intercept (b)	0.0306
Correlation coefficient (r)	0.9956
*RSD%	0.625

 # Y= aX+b, where X is the concentration of the analyte (mg/L) and Y is absorbance unit.

* Calculated from five determinations.

Table 2: Determination of Capoten in Commercial Tablets by the Proposed Method

Commercial Tablets	Found %	$^{\&}$Recovery %	RSD%
Acetin	97.03	99.80	0.52
Angiopril	99.74	100.30	0.65
Captopril	96.54	99.60	0.66

& A verage of 5 independent analyses.

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