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QUANTITATIVE ESTIMATION OF CAPTOPRIL IN PHARMACEUTICALS: A SPECTROPHOTOMETRIC APPROACH WITH O-CHLORANIL

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Abstract

A novel, easy, quick, and precise spectrophotometric method for the estimation of captopril in pure form and in pharmaceutical preparations is proposed by a charge transfer (CT) complex formation reaction with o-Chloranil as the electron acceptor (π-acceptor). The reaction product exhibited a distinct orange color, which was measured at a maximum absorption wavelength of 466 nm against the blank solution. The method demonstrated excellent adherence to Beer-Lambert's law over the concentration range of 4–64 µg/mL, with a high molar absorptivity of 1390.656 $L.mol^{-1}.cm^{-1}$ and Sandall's sensitivity 0.640µg/cm2. The lower detection limits were found to be 0.3024 µg/mL and 1.471 µg/mL, respectively. the method has been successfully applied to pharmaceutical preparations for captopril present in tablets containing known

Keywords: Charge Transfer Complex; Captopril, o-chloranil, Spectrophotometric.

INTRODUCTION

Captopril (CPL), is an orally active inhibitor its angiotensin I-converting enzyme inhibitor [1] It is been widely it is frequently used to treat hypertension and congestive heart failure [2], and cardiovascular diseases [3,4]. CAP is mainly removed in the urine after being metabolized in the liver[5], The crystalline powder of captopril is off-white in color and has a little mercaptan smell, The chemical name 1-(3-mercapto-2-D-methy1-1 -oxopropyl)-L-proline (S,S), has a molecular weight 217.29g/ mole, Molecular formula C9H15NOS3, and the chemical structure of the drug captopril is shown in Fig 1[6].It is considered an active agent in many pharmaceutical preparations as an ACE inhibitor [7]. Captopril is considered the drug is the preferred for the treatment of antihypertensive due to its efficacy and low toxicity [8]. Several instrumental techniques have been documented for the quantification of captopril in biological fluids and pharmacological formulations, UV–Vis absorption spectrophotometry[9], capillary zone electrophoresis [10], electro-chemical detection (ECD)[11], mass spectrometry [12], fluorimetry gas chromatography(13), liquid chromatography with electrochemical metho The purpose of the present study is to develop and validate a sensitive, easy, and specific spectrophotometric method for accurately determining the concentration of captopril (CPL) in pharmaceutical formulations.ds, fluorescence, chemiluminescence, potentiometry, flow injection analysis, high performance liquid chromatography, amperometry, and gas chromatography [13].The purpose of the present study is to develop and validate a sensitive, easy, and specific

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spectrophotometric method for accurately determining the concentration of captopril (CPL) in pharmaceutical formulations.

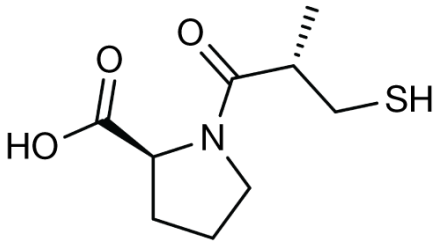

Figure 1 The chemical structure of Captopril

Materials and Methods

Instrumentation.

In this study, spectrophotometric measurements were conducted using a state-of-the-art UV-visible double beam spectrophotometer, specifically the SHIMADZU UV-Visible-1800 from Japan. The measurements were performed in 1cm quartz cells to ensure accurate and consistent results. Additionally, pH values were determined using the reliable model 3310 pH meter from JENWAY Company, and the analytical balance used was from Sartorius in Germany. These advanced instruments were carefully selected to guarantee precise and reliable data collection throughout the experimental process.

Reagents and chemicals

All the chemicals utilized in this method were of exceptionally high purity. Standard Captopril for Drug Production - Samarra Drug of Iraq SDI was supplied by the General Company. Additionally, Captopril tablets (25 mg / tablet) were procured from reputable pharmaceutical and commercial sources. To ensure the accuracy of the solutions, double distilled water with specific conductivity was used in their preparation, adhering to rigorous quality standards.

Standard Captopril solution (1000 µg.mL^{-1})

A small amount of distilled water was used to dissolve 0. 1g of the material in order to carefully prepare the solution. The volume was then cautiously increased to the appropriate level in a 100 mL volumetric flask using the same solvent.

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6,5,4,3, -tetra chloro-ortho-benzokynen (o- Chloranil) Solution (0.005M)

The solution was prepared by dissolving 0.123g of ortho Chloranil powder in a suitable amount of methanol., the volume was precisely adjusted to the mark in a 100 mL volumetric flask.

Pharmaceutical Solutions (Tablets).

Rilcapton (Tablets 25mg) Pharmaceutical Industries- Samarra SDI, the weight of each tablet was measured using 10 different weight scales. Following homogenization, they were finely powdered.

After precisely weighing 0.5955 g of the powder, which is about 1.488 g of captopril, it was dissolved in 30 mL of water after 10 minutes of ultrasonication in an ultrasonic bath. After filtering the mix, the mixture was then diluted with water in a 100 mL flask (1000µg/mL) and evaluated using the same method as for captopril in its pure form.

Approximate Potassium Hydroxide Solution (0.1M)

A solution was prepared by dissolving as little as 0.561g of the substance in distilled water. Care was taken to disperse the material completely. The same solution was then accurately adjusted to the mark in a 100 mL flask.

Surface active substances solution (0.1%)

Its preparation involves dissolving 0.100g of each surfactant compound (SDS, CTAB, Triton X-100) in a suitable solution. Care was taken to ensure complete dispersion of the mixtures. The volume was then adjusted accurately to 100 mL in the volumetric flask, ensuring accurate and consistent preparation of the solution This well-prepared solution is now ready for further testing and analysis.

The method's general principle

The method revolves around the interesting interaction between Captopril and o-chloranil as π-acceptors. This interaction occurs in an alkaline medium, and the results reveal an absorbance at 466 nm compared to a blank solution This analytical technique allows us to investigate and quantify the formation of these complexes, providing insight valuable for further research and applications in this chemical system

RESULTS AND DISCUSSION

Various parameters were studied and the reaction conditions were optimized to fully analyze the spectrophotometric properties. Subsequent experiments used a 25 mL volumetric flask, containing 1 mL of 0.005M O-chloranil, 1 mL of 100 µg/mL Captopril (CPL), and 0.5 mL of 0.1 M Potassium hydroxide, respectively All spectrophotometric readings were ensured that the measurement accuracy Taken at the maximum absorption wavelength of 466 nm, was compared with the blank solution.

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Effect of bases solution

At 0.1M concentration, the alkaline solution was generated. The Captopril solution was added to a constant volume of 1 mL of each of these chemicals, and the absorbance was measured at 466 nm. The findings were result and shown in Table 1. We were able to study the impact of Captopril's absorption behavior due to this methodical process that also provided the data.

Table 1. Effect of base types

Type of base	Absorbance
NaOH	0.21
Na_2CO_3	0.15
KOH	0.34

Table 1 shows the effect of different bases on the absorbance of Captopril complex at 466 nm. The results show that Potassium hydroxide exhibited the strongest color, with an absorbance of 0.34. In comparison, sodium carbonate and sodium hydroxide showed low absorbance values of 0.15 and 0.21, respectively.

Based on the data in the table, we can conclude that Potassium hydroxide is the most suitable base for color intensification of Captopril, and thus it is the one recommended for subsequent studies. The high absorption value of Potassium hydroxide indicates a strong interaction between Captopril and this specific base, which may be important for further research and the use of Captopril in analytical and clinical studies

Effect of potassium Hydroxide volume

The effect of different concentrations of potassium hydroxide on the absorption of Captopril was investigated. Volumes varying from 0.2 to 2 mL were added to volumetric flasks containing 1 mL of Captopril solution (100µg/mL) and 1 mL of reagent solution (5×10^{-3}M) and the final volume was adjusted with distilled water went to 25 mL.

Table 2 displays the results obtained from these experiments, illustrating the effect of potassium Hydroxide volume on the absorbance values:

Table 2. Effect of potassium Hydroxide volume

Vol. of KOH (mL)	Absorbance
0.2	0.11
0.4	0.15
0.6	0.21
0.9	0.28
1	0.34
1.2	0.39

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1.4	0.24
1.6	0.20
1.8	0.19
2	0.17

Upon analyzing the data, it was observed that the absorbance of Captopril reached its highest value when 0.39mL potassium of Hydroxide 1×10^{-1}M with a pH of 9.5 was utilized.

Effect of ortho- Chloranil reagent amount

The influence of varying amounts of ortho-Chloranil reagent on the absorbance of the Captopril solution was investigated. Different volumes, ranging from 0.2 to 2 mL, of a 5×10^{-3}M reagent solution was added to volumetric flasks containing 25 mL of Captopril solution 100µg/mL. Subsequently1.2 mL of 1×10^{-1}M potassium Hydroxide was added, and the volume was adjusted to 25 mL using distilled water.

Table 3 presents the results obtained from these experiments, illustrating the effect of the ortho-Chloranil reagent's volume on the absorbance values:

Table 3. Effect of the amount ortho-Chloranil reagent.

Vol. of Chloranil (mL)	**Absorbance**
0.2	0. 13
0.4	0.16
0.6	0. 24
0.8	0. 43
1	0.39
1.2	0.33
1.4	0.28
1.6	0. 24
1.8	0.21
2	0.19

Upon analyzing the data, it was observed that the absorbance of Captopril reached its highest value when 1mL of the ortho-Chloranil reagent (5×10^{-3}M) was utilized. Therefore, this specific volume of the reagent was considered optimal and was adopted for subsequent experiments.

Effect of Surface-active substances.

The effect of various metabolites on the intensity of absorption of the Captopril-ortho-chloranyl complex was investigated. Three metabolites were studied: sodium dodecyl sulfate (SDS), Triton X-100, and cetyl trimethyl ammonium bromide (CTAB). The experiments were conducted and it was found that these surfactants decreased the water absorption rate, making them unsuitable for further use, as shown in

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Table 4.

Table 4. Effect of Surface-active substances

Surfactant 0.1% (1mL)	**Absorbance at 466 nm**
Without Surfactant	0.39
SDS	0.117
Triton x-100	0.113
CTAB	Turbid

As can be seen from the table, the solution without any surfactant showed the highest absorbance value of 0.39. However, the addition of SDS slightly decreased the absorbance to 0.117. and 0.113 of Triton X-100, the addition CTAB resulted in a turbid solution.

They were not considered suitable for subsequent tests due to the observed decrease in leaching or impurities due to reactivity The lack of chemical surfactants gave reliable results was most robust for the Captopril-ortho-chloranil complex, ensuring accurate data collection and interpretation in other experimental studies

Temperature Effect.

The effect of temperature (15°C to 50°C) on charge transfer complex reaction was investigated under optimized conditions. The results show that the absorption rate varied with temperature, and the maximum absorption was observed at 30°C, as shown in Table 5

Table 5. Effect of Temperature

Temperature (C°)	**Absorbance**
15	0.13
20	0.19
25	0.39
30	0.42
35	0.32
40	0.109
45	0.107
50	0.097

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Data analysis showed that the reaction of the charge transfer complex exhibited the most significant adsorption at 30°C. Consequently, this temperature was considered optimal and was selected for subsequent experiments. The absorbance values showed a distinct temperature-dependent behavior. At higher temperatures, the tensile strength increased up to 30 °C, after which it started to decrease. This finding is very useful in understanding the kinetics and thermodynamics involved in the formation of charge transfer complexes.

Effect of Order of addition.

Comprehensive experiments were carried out to evaluate the effect of different modification schemes on the absorption of the orange material. The findings of the three specific methods are detailed and presented in Table 6.

Table 6. Effect of Order of Addition.

Order of Addition	Absorbance
Reag. + KOH + Drug	0.12
Drug + Reag. + KOH	0.42
Drug + KOH + Reag.	0.09

After a careful analysis of the data, it is clear that the absorption of the orange material is significantly influenced by the additive structure Absorption level shows variations depending on the reagent, sodium hydroxide, and drug added on.

1. When the reagent was added first, followed by KOH and then the drug, the absorbance was recorded as 0.09.

2. Conversely, when the drug was added first, followed by the reagent and then KOH, the absorbance was significantly higher at 0.42.

3. Finally, when the drug was added first, followed by KOH and then the reagent, the absorbance was relatively lower at 0.05.

The experimental results reveal the important role of additive structure in orange product formation and consequently the main absorption of the second combined system (Drug + Reag. + KOH) exhibited the highest absorption, making it preferred settings for subsequent tests Reasonable setting of this setting is needed.

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Effect of reaction time.

The aim of the experiment was to investigate the effect of time on the stability of the pigment complex formed under optimal experimental conditions, after mixing of the reactants At least pigments absorption is stable for 60 min, as shown in Table 7.

Table 7. Effect of Tim

Time (min)	Absorbance
1	0. 40
5	0.42
10	0.42
15	0.42
20	0.42
25	0.40
30	0.41
35	0.40
40	0.40
45	0.40
50	0.39
55	0.39
60	0.39

.

This result indicates that the color complexity formed after mixing reaction components under optimal experimental conditions is stable for approximately 50 min This information is valuable for experimental design, and ensures further research and the use of complex colors in a complex environment for reliable and consistent effects.

Final absorption spectrum.

Absorption spectrum of the synthesized color material, resulting from the coupling of 4 µg/mL (Captopril) and ortho-Chloranil reagent (5×10^{-3}M) in 1×10^{-1} M KOH in the starting solution (pH 9.5) at 30°C, recorded, the maximum absorbance (λ max) was observed at 466.0 nm. This is illustrated in Figure 2.

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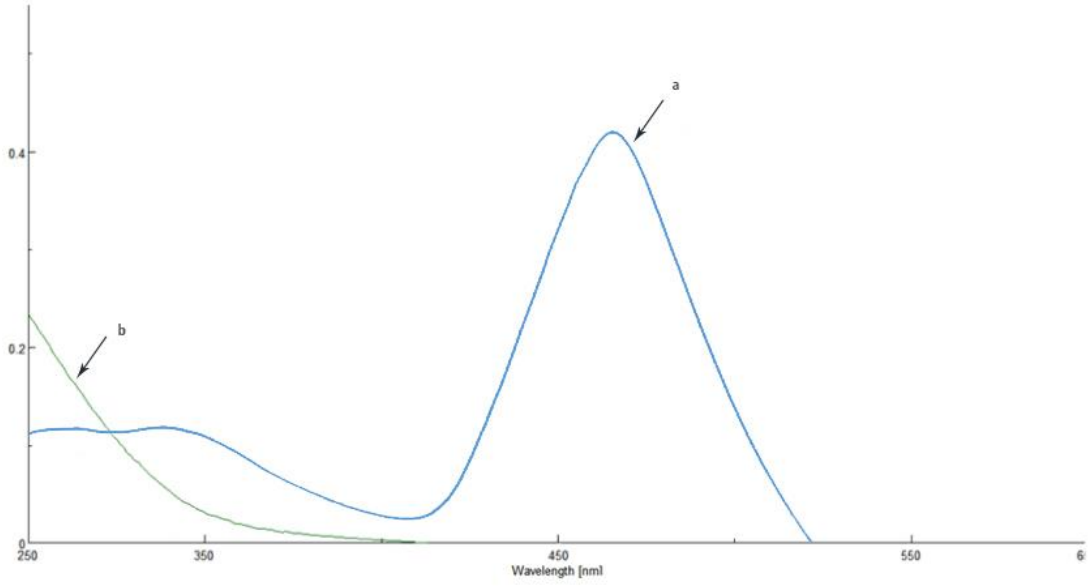

Figure 2. Absorption spectrum of a: 4µg/mL Captopril with ortho –Chloranil complexes and b: reagent blank.

Based on the obtained results, the optimum conditions for the formation of the CPL - ortho –Chloranil complexes were summarized in Table 8.

Table 8. The optimal conditions

Condition of Experimentation	
max λ	466 nm
Amount of 0.1 M potassium Hydroxide	1.4 mL
Amount of 5×10^{-3} M ortho chloranil reagent	01mL
Temperature	30 C°
Solvent	Water
pH	9.5

Calibration curve

1mL of 0.005M o-chloranil solution and 1.2 mL of 1×10^{-1} M potassium hydroxide was added one at a time to create a combination in a 25 mL volumetric flask. Next, various volumes of 100 µg/mL captopril

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solution were added, ranging from 1 mL to 18 mL. After the reaction, their absorbance was measured compared to the blank solution at a wavelength of 465 nm. The obtained results presented in Figure 5 show compliance with Beer's law in the concentration range of 4–64 µg/mL for the captopril compound, The molar absorption coefficient of the solution was determined to be 0.10649×104 $L.mol^{-1}.cm^{-1}$. Furthermore, the calculated Sandel's sensitivity, a measure of the sensitivity of the method, was found to be 0.0311 $\mu g.cm^{-2}$. A high correlation of 0.997 indicates a strong correlation between the experimental data, confirming the reliability and accuracy of the analytical method. These data contribute to the robustness and accuracy of the spectrophotometric determination of captopril concentration.

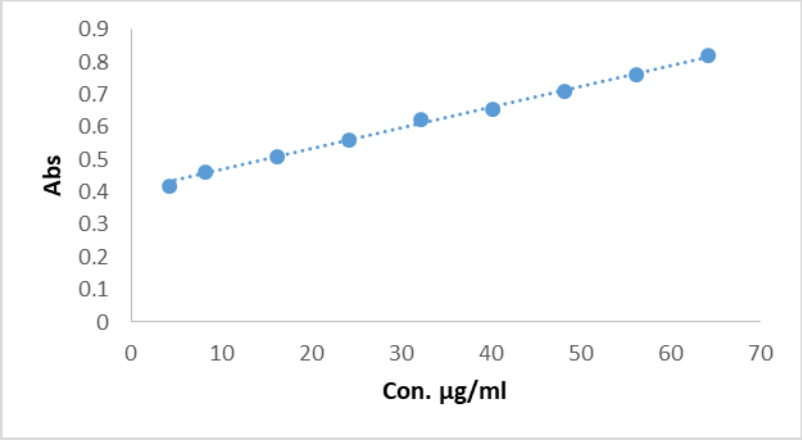

Figure 3. Calibration curve for the determination of Captopril

Accuracy and precision.

The accuracy and precision of the method were evaluated using three different concentrations, each at a concentration of 100 µg/mL, as shown by the recovery percentage (Rec%) and relative standard deviation (RSD%). The recovery rate was found to be 99.93%, with a relative standard deviation range from 0.0772% to 0.0928%, by averaging six observations for each concentration. The findings shown in Table 9 support the method's dependability with their high accuracy and great agreement.

Table 9. Precision and accuracy

Conc. Taken µg/ mL of Captopril	Conc. Found µg/ mL of Captopril	Rec%	Average of Rec%	RSD%
16	16.11	100.68		0.0928
32	31.871	99.59	100.05	0.0681
48	47.951	99.89		0.0772

Con. Concentration; Rec%: Recovery; RSD%: Relative Standard Division.

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Table 10. Optical Characteristic and validation data Spectrophotometric method.

Parameters data	Data
λ max nm	466
slope	0.0064
Intercept	0.4042
Beers Law limit µg/mL	4 - 64
Color	Orange
Correlation Coefficient	0.9977
Sandells sensitivity µg/cm²	0.64
Molar absorptivity L/mol.cm	1390.656
Average of Rec%	100.345
LOD (µg/mL)	1.134
LOQ (µg/mL)	3.437

Stoichiometry of reaction.

The reaction's stoichiometry between ortho-chloranil and CPL The drug and reagent concentrations were equivalent at 5×10^{-3} M using the Job's approach and the molar ratio method. Job's method involved using a number of volumetric flasks.25 mL, the ratio is 1:1, as shown in Figure 4's data.

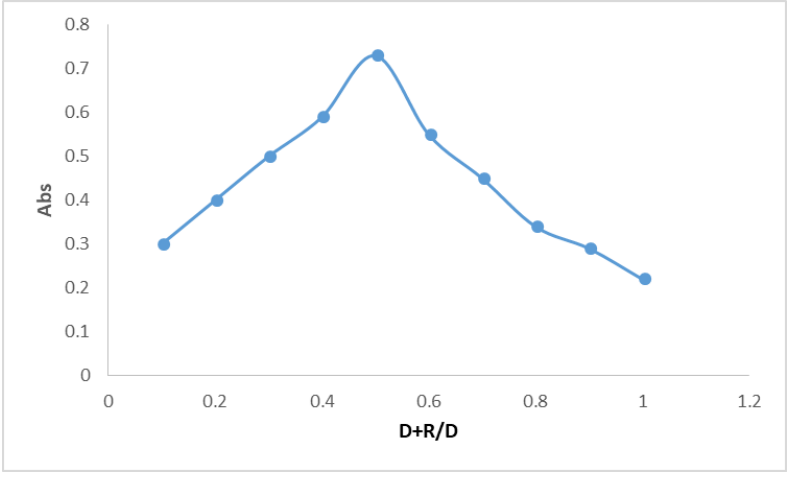

Figure 4. Job methods for captopril - o-Chloranil

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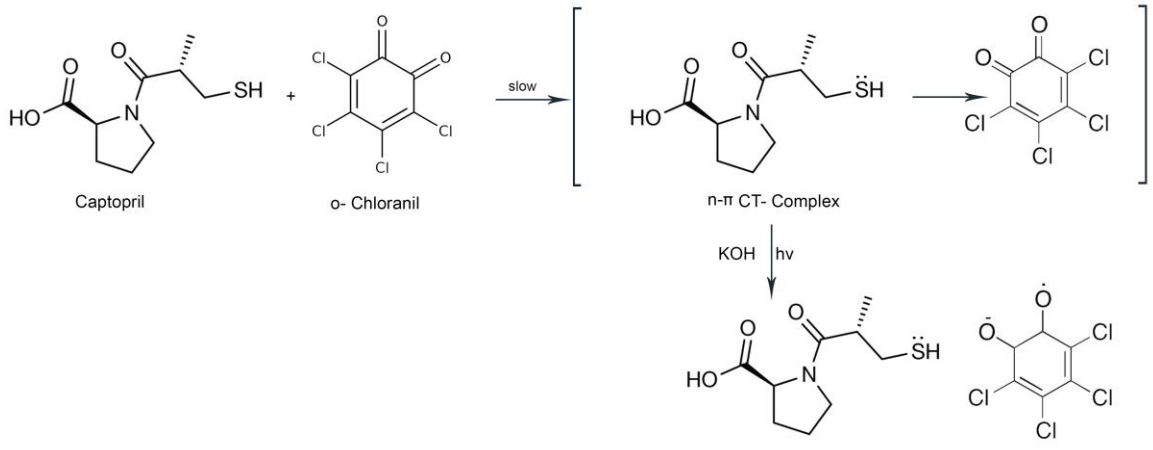
The Suggested chemical reaction.

o-Chloranil is a reagent known for its ability to accept π electrons and form strong interactions with atoms that possess a pair of non-bonding electrons, particularly nitrogen atoms [14]. The resulting complex between o-Chloranil and a nitrogen atom has a ratio of 2:1 (nitrogen: o-Chloranil), indicating the involvement of the nitrogen atoms in the complex formation. This complex exhibits a distinct peak resulting from charge transfer, which differs from the absorbance peaks of both the donor and acceptor molecules. This new peak signifies the formation of a n-π charge transfer (CT) complex. Upon exposure to visible or UV radiation, this complex undergoes further transformation, leading to the generation of a pair of free radical ions, namely D^+ and A^- [15].

The presence of hydroxide KOH facilitates the rapid formation of free radicals. The complex formation reaction involving charge transfer and the generation of free radicals can be expressed as follows:



This process involving o-Chloranil and the hydroxyl group in the formation of charge transfer complexes and subsequent free radical generation is of particular interest in various chemical reactions and analytical applications. It demonstrates the significance of o-Chloranil as a π-acceptor reagent and its role in studying and understanding complex formation mechanisms and free radical reactions.

Applications

This method was used on drug formulations that contained CPL at a dosage of 25 mg per tablet. Three different concentrations were taken (4, 12, 20) µg/mL the solution treated with the same steps as the calibration curve and measured at 466. nm, the result show in Table 11 which Indicate to success the suggested method in Assessment CPL in pharmaceutical preparation.

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Table 11. Direct method

Pharmaceutical preparation	Taken µg/mL	Found µg/mL	Average of Rec%	RSD%
Tablets (25 mg)	8	8.109		1.415
	16	16.103	**100.586**	0.913
	24	23.941		00.982

Conclusion

The proposed method developed was simple, selective and a wide range of determination 4-64 µg/mL without the need for heating or solvent extraction. and then complex formation orange color soluble in water and stable for a R^2 = 0.9977 period of time of at least 55 minutes maximum absorption at a wave-length of 466nm and effectively used to determine the amount in pharmaceutical preparation

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