

## Spectrophotometric Determination of Thiocctic Acid in its Dosage Forms through Complex Formation with Pd(II)

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A simple and sensitive spectrophotometric method has been developed for the determination of thiocctic acid in pharmaceutical preparations. The proposed method is based upon the formation of a complex with palladium(II) in acetate buffer of pH 4.8 with an absorption maximum at 318 nm. The absorbance obeyed Beer's law over the range of 2-20  $\mu\text{g mL}^{-1}$  with a minimum detection limit of 0.15  $\mu\text{g mL}^{-1}$  and molar absorptivity ( $\zeta$ ) of  $7 \times 10^3 \text{ L mol}^{-1} \cdot \text{cm}^{-1}$ . The different experimental parameters affecting the development and stability of the color were carefully studied and optimized. The proposed method was successfully applied to the analysis of commercial tablets and ampoules. The results obtained were in good agreement with those obtained using a reference spectrophotometric method. A proposal of the reaction pathway is presented.

**Keywords:** Thiocctic acid; Spectrophotometry; Chelation; Palladium chloride; Pharmaceutical preparations.

### INTRODUCTION

Thiocctic acid (TCA), 1,2-Dithiolane-3-pentanoic acid (Fig. 1), is frequently used in the treatment of liver dysfunction, diabetic neuropathy,<sup>1</sup> and in subacute necrotising encephalopathy. Moreover, it is a useful antidote in amanitin poisoning following ingestion of the mushroom *Amanita phalloides*.<sup>1</sup>

The literature survey reveals few analytical methods for the determination of thiocctic acid in pharmaceutical preparations and biological fluids; these methods include: spectrophotometry,<sup>2,3</sup> electrochemistry,<sup>4-9</sup> enzyme immunoassay,<sup>10</sup> GC-MS,<sup>11</sup> flow injection analysis,<sup>12</sup> and HPLC.<sup>13-17</sup> These methods are either insufficiently sensitive or tedious and require highly sophisticated instrumentation.<sup>11-17</sup>

The reported spectrophotometric methods<sup>2,3</sup> based on the use of sodium azide-iodine reagent,<sup>2</sup> or alkaline potas-

sium permanganate<sup>3</sup> are non-specific, as they use universal reagents for oxidation of several compounds. Moreover, formation of metal chelates renders the method more specific.

The molecular structure of TCA is characterized by the presence of a sulphur bridge (S-S) group which is susceptible to complexation with Pd(II) and initiated the present study. This reaction has been studied in an attempt to develop a simple and sensitive spectrophotometric method for determination of TCA in pharmaceutical preparations. The results obtained were promising.

### EXPERIMENTAL

#### Apparatus

The spectrophotometric measurements were established using a Shimadzu UV-Visible 1601 recording Spectrophotometer (P/N 206-67001). Recording range, 0-1.0; wavelength, 318 nm.

#### Materials and Reagents

All reagents and solvents were of Analytical Reagent

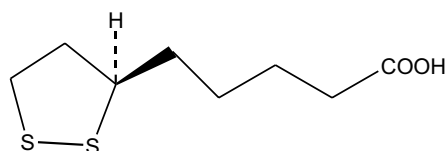


Fig. 1. Structural formula of thiocctic acid.

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grade.

Thioctic acid pure drug sample was kindly provided by Pharco. Pharmaceutical Co., Alexandria, Egypt. Its purity was 99.0%. Commercial tablets labeled to contain 300 mg of thioctic acid/tablet (Batch # 201016) and Thiotacid ampoules labeled to contain 300 mg of thioctic acid/10 mL (Batch # 006105) were obtained from commercial sources in the local market. Palladium(II) chloride (Sigma, Milwaukee, WI, USA)  $2 \times 10^{-3}$  M solution was prepared by dissolving 35.5 mg of palladium(II) chloride in 1 mL of hydrochloric acid, with the aid of heat, followed by the addition of 50 mL of boiled water then diluting to 100 mL with distilled water. This solution is stable for two weeks. Acetate buffers (pH 3.6-5.6)<sup>18</sup> were prepared by mixing 0.2 M acetic acid and 0.2 M sodium acetate; the pH has to be checked periodically. Methanol and hydrochloric acid (Merck, Darmstadt, Germany). Potassium chloride (BDH, UK) 2.5 M aqueous solution, freshly prepared.

#### Standard Solutions

A stock solution was prepared by dissolving 20.0 mg of thioctic acid in 100 mL of methanol and was further diluted with the same solvent as appropriate. The standard solutions were stable for seven days if kept in the refrigerator.

#### General Procedure

##### Construction of the Calibration Curve

Transfer aliquot volumes of TCA standard solution into a series of 10 mL volumetric flasks. Add 2 mL of acetate buffer (pH 4.8) followed by 0.8 mL of palladium(II) chloride solution and 2 mL of potassium chloride solution. Complete to the mark with water and mix well. Measure the absorbance of the resulting solution at 318 nm against a reagent blank simultaneously prepared. Base line correction was carried out to delete any absorbance reading of the blank. Plot the measured absorbance vs. the final concentration of the drug ( $\mu\text{g/mL}$ ) to get the calibration curve. Alternatively, derive the corresponding regression equation.

#### Applications

##### I- Procedure for the tablets

Weigh and pulverize twenty tablets. Transfer a weighed quantity of the powder equivalent to 20 mg of TCA into a small conical flask. Extract three successive times each with 30 mL of methanol. Filter the extract into a 100 mL volumetric flask. Wash the conical flask with a few mLs of

methanol. Pass the washings into the same volumetric flask and complete to the mark with the same solvent. Transfer aliquots covering the working concentration range cited in Table 1 into 10 mL volumetric flasks. Proceed as described under Construction of the Calibration Curve. Determine the nominal content of the tablets either from the calibration curve or using the corresponding regression equation.

##### ii- Procedure for the ampoules

Mix the contents of five ampoules. Transfer aliquots of the mixed solution equivalent to 20.0 mg into a 100 mL measuring flask, dilute and complete to volume with methanol. Transfer aliquots of this solution within the working concentration range into a series of 10 mL volumetric flasks. Proceed as described under Construction of the Calibration Curve. Determine the nominal content of the ampoule either from the calibration curve or using the corresponding regression equation.

## RESULTS AND DISCUSSION

TCA exhibits a low absorption band in the UV region with  $A_{1\text{cm}}^{1\%} = 15$  at 332 nm. As a consequence, poor sensitivity will be achieved by conventional UV spectrophotometric measurements, and this problem is more aggravated if it is needed to estimate the drug in biological fluids. However, the presence of the S-S group and the possibility of complex formation with  $\text{PdCl}_2$ , initiated the present study. The complex formed exhibits a maximum absorp-

Table 1. Effect of surfactants and sensitizers on the performance of the proposed method

| Surfactant / Sensitizer | Concentration ( $\mu\text{g mL}^{-1}$ ) | Absorbance | % Change |
|-------------------------|---|------------|----------|
| No surfactant           | 0                                       | 0.680      | -        |
| Cetrimide               | 2.5                                     | 0.515      | -24.3%   |
| Sodium lauryl sulfate   | 2.5                                     | 0.658      | -3.2%    |
| Gelatine                | 2.5                                     | 0.617      | -9.3%    |
| Cetrimide               | 7.5                                     | 0.548      | -19.4%   |
| Sodium lauryl sulfate   | 7.5                                     | 0.703      | +3.4%    |
| Gelatine                | 7.5                                     | 0.647      | -4.9%    |
| Cetrimide               | 15                                      | 0.565      | -16.9%   |
| Sodium lauryl sulfate   | 15                                      | 0.682      | +0.29%   |
| Gelatine                | 15                                      | 0.668      | -1.8%    |
| No sensitizer           | 0                                       | 0.680      | -        |
| Quinine                 | 5                                       | 0.765      | +12.5%   |
| Fluorescein             | 5                                       | 0.721      | +6.0%    |
| Rhodamine-B             | 5                                       | 0.705      | +3.7%    |

tion peak at 318 nm (Fig. 2). The complex was formed instantaneously and remained stable for more than 90 min.

Transition elements are reported to form stable complexes with many ligands containing heteroatoms. There is a preference for amines, halogens, CN<sup>-</sup>, tertiary phosphorines and sulfides. Palladium(II), as one of the transition elements, was reported to form complexes with many pharmaceutical compounds; viz, phenothiazines,<sup>19,20</sup> captopril,<sup>21</sup> N-acetyl-L-cysteine,<sup>22</sup> and timonacic.<sup>23</sup>

### Effect of Metal Type and Interference

Various metal salts were studied to select the most suitable one for the complex formation, viz: AlCl<sub>3</sub>, CuSO<sub>4</sub> and PdCl<sub>2</sub>, the latter was found to be the most suitable one since it gave the highest net absorbance readings. Other metal salts gave low absorbance values. Moreover, they

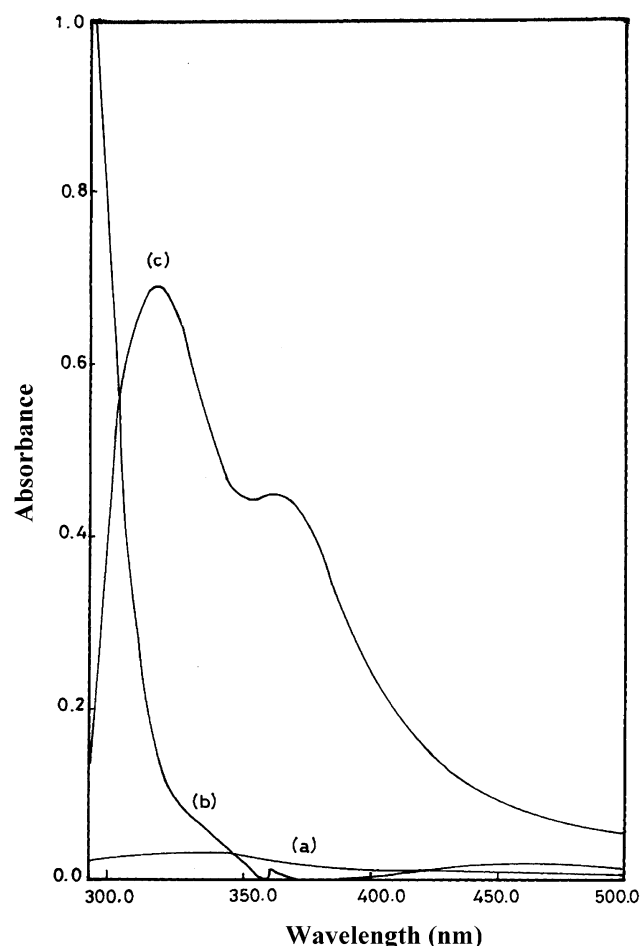


Fig. 2. Absorption spectra of (A) thioctic acid only ( $20 \mu\text{g mL}^{-1}$ ). (B) Palladium(II) ( $1.6 \times 10^{-4} \text{ M}$ ) only at pH 4.8. (C) The formed complex of thioctic acid ( $20 \mu\text{g mL}^{-1}$ ) with Pd(II) at pH 4.8.

positively interfered if they were present in the reaction medium with a percentage error of 29.4% and 32.3% for AlCl<sub>3</sub> and CuSO<sub>4</sub>, respectively.

### Optimization of the experimental parameters

The spectrophotometric properties of the colored product as well as the different experimental parameters affecting the color development and its stability were carefully studied and optimized. Such factors were changed individually while the others were kept constant. The factors include pH, type of buffer, concentration of buffer solution, different surfactants, different sensitizers, concentration of surfactant and palladium(II).

### Effect of pH

The study was conducted using  $16 \mu\text{g mL}^{-1}$  of thioctic acid and  $1.6 \times 10^{-4} \text{ M}$  Pd(II) (final concentration). Using different buffers such as phosphate, acetate or Britton Robinson Buffers gave almost the same results. However acetate buffer was used throughout the study because of the absence of possible interference produced by other buffers such as phosphate buffer. The influence of pH on the absorbance value of the formed complex was investigated over the pH range 3.6-5.6. Maximum absorbance was achieved at pH 4.8 (Fig. 3), using 2 mL of acetate buffer.

### Effect of Pd(II) concentration

The effect of Pd(II) concentrations on the absorbance of the complex was studied. Keeping all other variables constant, it was found that increasing the concentration of Pd(II) solution ( $1 \times 10^{-4} \text{ M}$ ) resulted in a corresponding increase in the absorbance of the complex up to  $1.2 \times 10^{-4} \text{ M}$ ;

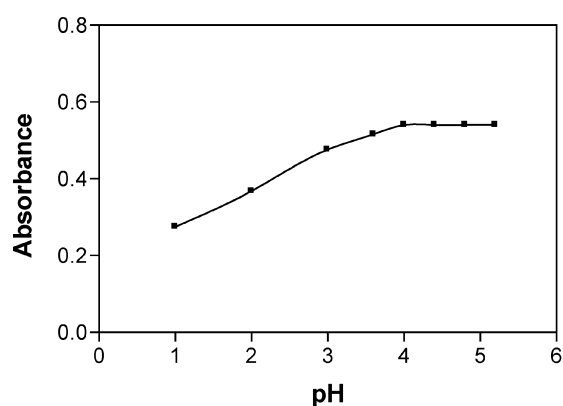


Fig. 3. Effect of pH on the absorbance of thioctic acid-Pd(II) complex. (TCA =  $16 \mu\text{g mL}^{-1}$ ) at  $1.6 \pm 0.4 \times 10^{-4} \text{ M}$  Pd(II) concentration.

it then remains constant up to  $2 \times 10^{-4}$  M; therefore,  $1.6 \pm 0.4 \times 10^{-4}$  M was used throughout the study (Fig. 4).

#### Effect of different surfactants

The effect of surfactants on the absorbance of the complex was investigated using different types, such as cetylpyridinium chloride (cationic), sodium lauryl sulphate (anionic) and gelatine (non ionic). Hopefully the surfactants may enhance the absorbance reading of the complex, but unfortunately, it was found that all the studied surfactants had no significant effect on the absorbance of the formed complex. Therefore, for a simple procedure there is no need to use surfactants. The results are abridged in Table 1.

#### Effect of different sensitizers

Similarly different sensitizers were studied, and thus quinine, fluorescein and rhodamine-B, at concentrations of  $5 \mu\text{g mL}^{-1}$  were tested. Addition of sensitizers to the reaction mixture was found to enhance the absorbance of the complex but with the lack of reproducibility. Therefore, the study was carried out without the addition of sensitizers. The results are shown in Table 1.

#### Analytical Performance

The absorbance-concentration plot was found to be linear over the range of  $2\text{--}20 \mu\text{g mL}^{-1}$ . Linear regression analysis of the data gave the following equation:

$$A = -1.056 \times 10^{-3} + 0.034 C \quad (r = 0.9999)$$

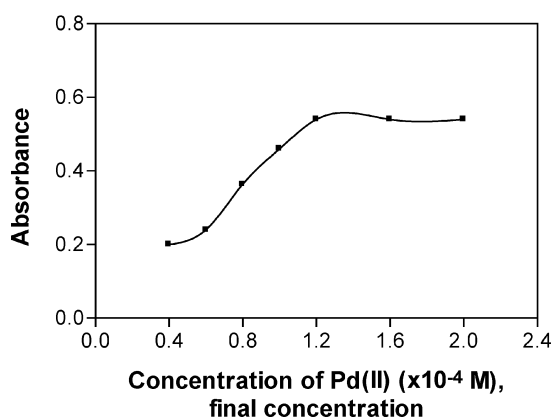


Fig. 4. Effect of concentration of Pd(II) ( $\times 10^{-4}$  M), final concentration on the absorbance value of thioctic acid-Pd(II) complex (TCA =  $16 \mu\text{g mL}^{-1}$ ) at pH  $4.8 \pm 0.4$ .

where A is the absorbance in 1-cm cell and C is the concentration of the drug in  $\mu\text{g mL}^{-1}$ .

The limit of quantification (LOQ) was determined by establishing the lowest concentration that can be measured according to ICH Q2B recommendations,<sup>24</sup> it and was found to be  $0.51 \mu\text{g mL}^{-1}$ .

LOQ was calculated according to the following equation:

$$\text{LOQ} = 10 \sigma/S$$

where  $\sigma$ : the standard deviation of the intercept of regression line.

S: Slope of the calibration curve.

The limit of detection (LOD) was determined by establishing the minimum level at which the analyte can be reliably detected and was found to be  $0.15 \mu\text{g mL}^{-1}$  ( $7 \times 10^{-7}$  M).

LOD was calculated according to the following equation:<sup>24</sup>

$$\text{LOD} = 3.3 \sigma/S$$

The proposed method was evaluated by studying the accuracy as percent relative error and precision as percent relative standard deviation (RSD%); the results are abridged in Table 2.

#### Validation of the Method

The method was tested for linearity, specificity, accuracy and precision. By using the above spectrophotometric procedure, a linear regression equation was obtained. The regression plot showed that there was a linear dependence of the absorbance value on the concentration of the drug over the range cited in Table 2. The validity of the proposed method was evaluated by statistical analysis of the regression data regarding the standard deviation of the residuals ( $S_{y/x}$ ), the standard deviation of the intercept ( $S_a$ ) and standard deviation of the slope ( $S_b$ ).<sup>25</sup> The results are given in Table 2. The small values of the figures point to the low scattering of the points around the calibration graph and high precision of the proposed method.

#### Accuracy

The accuracy of the proposed method was evaluated by analyzing standard solutions of TCA. The results ob-

Table 2. Performance data of the proposed method

| Parameter   | Value                   |
|---|-------------------------|
| - Concentration range ( $\mu\text{g mL}^{-1}$ )                           | 2-20                    |
| - Molar absorptivity ( $\zeta$ ) ( $\text{mol}^{-1}\cdot\text{cm}^{-1}$ ) | $7 \times 10^3$         |
| - LOD ( $\mu\text{g mL}^{-1}$ )   | 0.15                    |
| - LOQ ( $\mu\text{g mL}^{-1}$ )   | 0.51                    |
| - Correlation coefficient (r)   | 0.9999                  |
| - Slope (A. $\mu\text{g}^{-1}\cdot\text{mL}$ )                            | 0.034                   |
| - Intercept   | $-1.056 \times 10^{-3}$ |
| - $S_{y/x}$   | $2.75 \times 10^{-3}$   |
| - $S_a$   | $1.72 \times 10^{-3}$   |
| - $S_b$   | $1.76 \times 10^{-4}$   |
| - %Error  | 0.35                    |
| - RSD %   | 0.93                    |

N.B.:

-  $S_{y/x}$  = standard deviation of the residuals.-  $S_a$  = standard deviation of the intercept of regression line.-  $S_b$  = standard deviation of the slope of regression line.- % Error =  $\text{RSD}\% / \sqrt{n}$ .

tained by the proposed method were compared with those obtained by a reference method.<sup>3</sup> The latter involved oxidation of TCA with alkaline potassium permanganate and measuring the absorbance of the oxidation product at 610 nm.<sup>3</sup>

Statistical analysis<sup>25</sup> of the results obtained by the proposed and reference method using Student's t-test and variance ratio F-test, show no significant difference between the performance of the two methods regarding the accuracy and precision, respectively (Table 3).

## Precision

### a- Repeatability

The repeatability was evaluated through replicate analysis of TCA samples, pure drug or tablets or ampoules ( $12 \mu\text{g mL}^{-1}$ ). The percentage recoveries based on the average of four separate determinations were  $99.63 \pm 0.77$ ,  $99.37 \pm 0.33$  and  $100.83 \pm 0.83$ , for pure form, tablets and ampoules respectively, thus indicating the high precision of the method (Table 4).

### b- Intermediate precision

It was performed through replicate analysis of TCA samples, pure drug or tablets or ampoules ( $20 \mu\text{g mL}^{-1}$ ) on four successive days. The percentage recoveries based on the average of four separate determinations were  $99.41 \pm 0.50$ ,  $100.89 \pm 0.46$  and  $100.23 \pm 1.19$  for pure form, tablets and ampoules respectively. The results are shown in Table 4.

## Robustness of the Method

The robustness of the method adopted is demonstrated by the consistency of the absorbance values with the deliberately minor changes in the experimental parameters such as pH  $4.8 \pm 0.4$  produces a constant absorbance value of 0.54 at constant TCA concentration ( $16 \mu\text{g mL}^{-1}$ ); changing the concentration of Pd(II) solution ( $1 \times 10^{-4}$  M) resulted in a subsequence increase in the absorbance value of the complex up to  $1.2 \times 10^{-4}$  M, and it remained constant up to  $2 \times 10^{-4}$  M; therefore,  $1.6 \pm 0.4 \times 10^{-4}$  M was used throughout the study. This concentration produces a constant absorb-

Table 3. Application of the proposed and reference methods to the determination of thiocetic acid in pure form

| Parameter                 | $\mu\text{g}$ taken | $\mu\text{g}$ found | % recovery        | Reference method <sup>3</sup> |
|---------------------------|---------------------|---------------------|-------------------|-------------------------------|
|                           | 2.0                 | 2.03                | 101.50            | 100.43                        |
|                           | 4.0                 | 3.97                | 99.25             | 99.55                         |
|                           | 8.0                 | 8.03                | 100.38            | 100.14                        |
|                           | 10.0                | 9.89                | 98.90             |                               |
|                           | 12.0                | 12.09               | 100.75            |                               |
|                           | 16.0                | 15.91               | 99.44             |                               |
|                           | 20.0                | 20.03               | 100.15            |                               |
| - $\bar{X} \pm \text{SD}$ |                     |                     | $100.05 \pm 0.92$ | $100.04 \pm 0.45$             |
| - Student's t-value       |                     |                     | 0.02 (2.31)       |                               |
| - Variance ratio F-test   |                     |                     | 4.18 (5.14)       |                               |

N.B.:

Each result is the average of three separate determinations.

Figures between parentheses are the tabulated t and F values, respectively, at  $p = 0.05$ <sup>25</sup>

Table 4. Validation of the proposed method for the determination of thioctic acid in pure and dosage forms

| Sample   | % Recovery<br>Repeatability<br>(12 µg mL <sup>-1</sup> ) | % Recovery<br>Intermediate<br>precision<br>(20 µg mL <sup>-1</sup> ) |
|--|--|--|
| 1- Thioctic acid<br>(pure form)                          | 99.50  | 98.82  |
|  | 99.00  | 100.00   |
|  | 100.75   | 99.26  |
|  | 99.35  | 99.56  |
|  | 99.63  | 99.41  |
| Mean found %   | 99.63  | 99.41  |
| ±SD  | 0.77   | 0.50   |
| RSD, %   | 0.77   | 0.50   |
| 2- Thiotacid tablets<br>(thioctic acid 300<br>mg/tablet) | 99.49  | 100.59   |
|  | 98.99  | 101.47   |
|  | 99.24  | 100.74   |
|  | 99.75  | 101.03   |
|  | 99.37  | 100.89   |
| Mean found %   | 99.37  | 100.89   |
| ±SD  | 0.33   | 0.46   |
| RSD, %   | 0.33   | 0.46   |
| 3- Thiotacid ampoules<br>(thioctic acid 300<br>mg/10 mL) | 101.48   | 100.78   |
|  | 100.92   | 99.22  |
|  | 101.29   | 101.64   |
|  | 99.63  | 99.26  |
|  | 100.83   | 100.23   |
| Mean found %   | 100.83   | 100.23   |
| ±SD  | 0.83   | 1.19   |
| RSD %  | 0.83   | 1.19   |

ance value of 0.54 at constant TCA concentration (16 µg mL<sup>-1</sup>). These minor changes that may take place during the experimental operation didn't greatly affect the absorbance value of the reaction product.

#### Pharmaceutical Applications

The proposed method was further applied to the determination of TCA in its tablets and ampoules.

#### Specificity

Common excipients such as talc, lactose, starch, avisil, gelatine and magnesium stearate did not interfere with the assay. The results are abridged in Table 5.

Antioxidants which are frequently added to ampoules such as ascorbic acid and ethylenediamine tetracetic acid did produce observed changes.

#### Accuracy

The results of the proposed method were statistically compared with those obtained using the reference method. Statistical analysis of the results, using Student's t-test and variance ratio F-test, revealed no significant difference between the performance of the proposed and reference methods regarding the accuracy and precision, respectively (Ta-

Table 5. Application of the proposed and reference methods to the determination of thioctic acid in dosage forms

| Pharmaceutical preparation   | µg taken | µg found | % recovery   | Reference method <sup>3</sup> |
|--|----------|----------|--------------|-------------------------------|
| 1- Thiotacid tablets <sup>a</sup><br>(thioctic acid 300 mg/tablet) | 2.0      | 1.98     | 99.00        | 100.07                        |
|  | 4.0      | 3.96     | 99.00        | 99.38                         |
|  | 8.0      | 7.93     | 99.13        | 98.42                         |
|  | 12.0     | 11.94    | 99.50        |                               |
|  | 16.0     | 15.95    | 99.69        |                               |
|  | 20.0     | 20.15    | 100.75       |                               |
| $\bar{X} \pm SD$   |          |          | 99.51 ± 0.67 | 99.29 ± 0.83                  |
| - Student's t-value  |          |          | 0.42 (2.37)  |                               |
| - Variance ratio F-test  |          |          | 1.45 (5.79)  |                               |
| 2- Thiotacid ampoules <sup>b</sup><br>(thioctic acid 300 mg/10 mL) | 2.0      | 2.03     | 101.50       | 100.63                        |
|  | 4.0      | 3.98     | 99.50        | 99.69                         |
|  | 8.0      | 7.94     | 99.25        | 100.14                        |
|  | 12.0     | 11.88    | 99.00        |                               |
|  | 16.0     | 16.07    | 100.44       |                               |
|  | 20.0     | 19.84    | 99.20        |                               |
| $\bar{X} \pm SD$   |          |          | 99.82 ± 0.97 | 100.15 ± 0.47                 |
| - Student's t-value  |          |          | 0.54 (2.37)  |                               |
| - Variance ratio F-test  |          |          | 4.26 (5.79)  |                               |

N.B.:

Figures between parentheses are the tabulated t and F values, respectively, at  $p = 0.05$ .<sup>25</sup>

<sup>a</sup> and <sup>b</sup> are products of Eva Pharma for Pharmaceutical Application, Cairo, Egypt.

ble 5).

The formation constant of the reaction product was calculated according to the following equation:

$$K_f = \frac{A/A_m}{[(1-A/A_m)^{n+1}] c^n n^n}$$

where  $A$  and  $A_m$ : are the observed maximum absorbance and the absorbance obtained from the extrapolation of the two lines obtained from Job's continuous variation method, respectively.

$n$ : is the stoichiometry (the ratio is 1:1) therefore,  $n = 0.5$

$C$ : is the molar concentration of the drug used in Job's continuous variation method

Using the above equation  $K_f$  was found to be  $2.17 \times 10^3$ .

Also, the free energy changes ( $G$ ) were calculated according to the following equation:

$$\Delta G = -2.303 R T \log K_f$$

where

$R$  = gas constant =  $8.3 \text{ joule/degree}^{-1} \cdot \text{mole}^{-1}$

$T$  = absolute temperature =  $^{\circ}\text{C} + 273$

Using the above equation  $\Delta G$  was found to be  $-1.9 \times 10^4 \text{ Kcal/Mole}$ .

The negative value of  $\Delta G$  indicates that the reaction is spontaneous.

### Mechanism of the Reaction

The stoichiometry of the reaction between TCA and  $\text{PdCl}_2$  has been determined spectrophotometrically adopting the limiting logarithmic method.<sup>26</sup> The absorbance of the reaction product was alternately measured in the presence of an excess of  $\text{PdCl}_2$  and TCA. A plot of log absorb-

ance versus  $\log [\text{PdCl}_2]$  and  $\log [\text{TCA}]$  gave straight lines; the values of the slopes were 0.96 and 1.0, respectively (Fig. 5). Hence, it is concluded that the molar reactivity of the reaction is 0.96/1.0, i.e. the reaction proceeds in the ratio of 1:1, pointing out that one molecule of the drug reacts with one molecule of  $\text{PdCl}_2$  (Fig. 5). The drug reacts via the two sulfur atoms with  $\text{Pd(II)}$  ion. Based on the obtained molar reactivity and by analogy to a previous study,<sup>23</sup> the reaction pathway is proposed to proceed as shown in the following Scheme I.

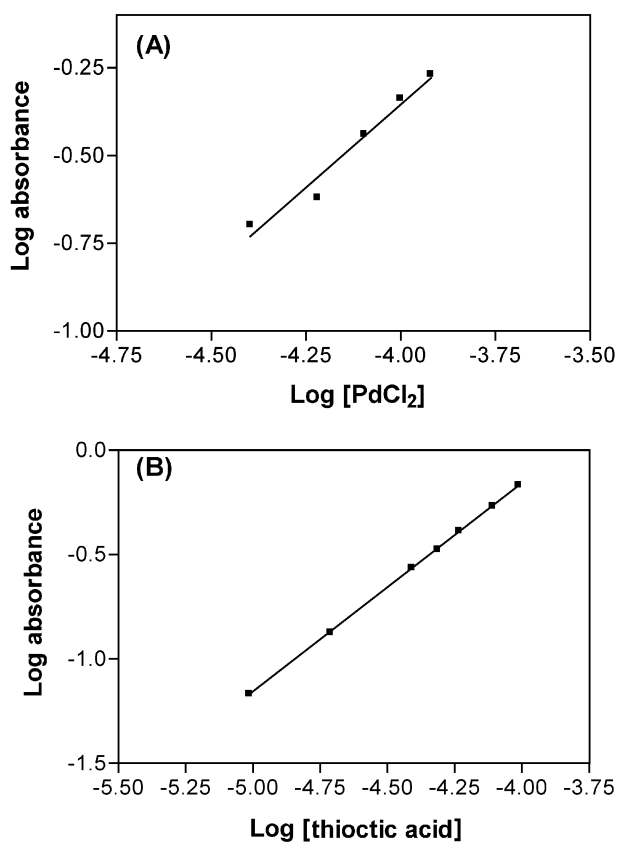
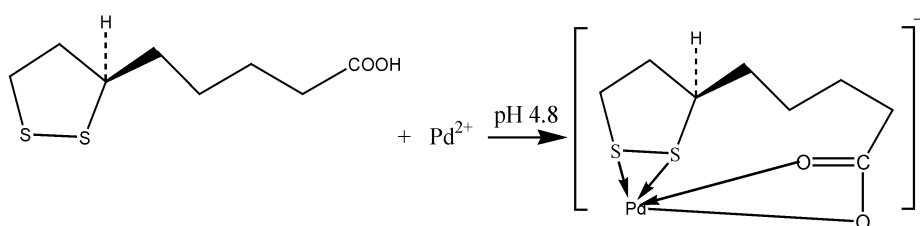


Fig. 5. Limiting logarithmic plots for the molar ratio. (A) Log A vs. Log  $[\text{PdCl}_2]$  (B) Log A vs. log  $[\text{thiocetic acid}]$ .

### Scheme I Proposal of the reaction pathway between $\text{Pd}^{2+}$ and thiocetic acid at pH 4.8



The proposed method could not be applied to the determination of TCA in biological fluids because of the resulting interference from endogenous amino acids and soluble proteins.

The proposed method has the advantages of being simple, time saving and sensitive with a minimum detection limit (LOD) of  $0.15 \mu\text{g mL}^{-1}$ . It is considered as a stability indicator, since the decarboxylated derivative of the drug which is one of its degradation products will not react with Pd(II). Moreover, the complex formed did not require a prior extraction procedure. The method is also more specific than other reported spectrophotometric methods,<sup>2,3</sup> because it depends on the presence of both a sulphur bridge and carboxylic groups.

## CONCLUSION

A simple and sensitive method has been developed for the determination of thioctic acid in pharmaceutical preparations. It can measure as low as  $0.51 \mu\text{g mL}^{-1}$  with good accuracy. The complex formed did not require a prior extraction procedure. The proposed method can be used for routine quality control and it has some distinct advantages over other existing methods regarding sensitivity, time saving and a lower detection limit.

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