

Spectrophotometric micro determination of drug promethazine hydrochloride in some pharmaceutical by chelating with Rhodium

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Abstract

The drug promethazine hydrochloride (PRZH) forms with rhodium (II) a colored chelate ($\lambda_{\max} = 472 \text{ nm}$) complex at ($\text{pH} = 2.1$) which is extractable with benzyl alcohol as organic solvent.

Under the appropriate experimental conditions a calibration plot was set up from which some analytical parameter were derived and deduced by regression. Standard addition procedure was also adopted. It has been estimated that the concentration of the drug PRZH to be 24.89 mg per unit and 24.19 mg per unit for both calibrations. Under optimal conditions, the developed method has been achieved the following characteristics:

LDR ($30 - 150 \mu\text{g ml}^{-1}$) PRZH, RSD % ($0.6 - 2.47$), sandell sensitivity ($0.0844 \mu\text{g. cm}^{-2}$), LOD ($1.66 \mu\text{gml}^{-1}$), recovery % (100.74 ± 1.34), Erel % (0.74). Stability constant ($6.4 \times 10^5 \text{ M}^{-1}$). The mole – ratio method (1: 1) approved that PRZH – Rh (II) as a structure of the complex. The developed procedure has been adapted to analyze PRZH in various pharmaceuticals.

Introduction:

Promethazine, a phenothiazine drug, is widely used as an antihistamine and a mild sedative [1].

Various methods have been reported for the determination of promethazine hydrochloride these include spectrophotometry [2, 3, 4], HPLC [5, 6], capillary zone electrophoresis [7], titrimetry [8].

In this work, a molecular spectrophotometric method for determination of drug promethazine hydrochloride (PRZH) in some pharmaceutical preparations by chelating with Rhodium (II) has been developed. The complex has a maximum absorption at (472 nm). Benzyl alcohol was used as organic solvent for extraction of chelating complex. This method can be applied successfully to pharmaceutical preparation containing promethazine hydrochloride.

Experimental

Apparatus

- all spectral and absorbance measurements were carried out on a shimadzu UV- Visible 160 a digital double - beam recording spectrometer using 1 cm silica cell.
- pH meter, Jenway 3020 .

Reagents

All chemicals used were of analytical reagent grade unless otherwise state, promethazine hydrochloride standard material was provided from the state company for drug industries and medical appliances samara – Iraq, phenergan drug was provide from the Arab pharmaceutical manufacturing Co.Ltd.,) sult – Jordan .

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Promethazine hydrochloride Stock solution (1000 $\mu\text{g ml}^{-1}$)

A 0.1gm of PRZH was dissolved in water (DIW) and diluted to 100 ml in a volumetric flask.

Rhodium Stock solution (1000 $\mu\text{g ml}^{-1}$)

A 0.2145 gm of Rh(CH₃COO)₂ was dissolved in 5ml of hydrochloride acid (3N) ,Diluted to 100 ml in a volumetric flask with deionized water .

Analytical Procedures**(A) Direct Calibration**

preparation of working calibration solutions in (30 – 150 $\mu\text{g PRZH ml}^{-1}$): A volume in range of 150 – 750 μl of 1000 $\mu\text{g PRZH ml}^{-1}$ transferred to (250 ml) separating funnels, then 1 ml of 250 $\mu\text{g Rh ml}^{-1}$ was added to each funnel and the pH of all solutions was adjusted to 2.1 using dil.HCl or NaOH solution. These solutions were set aside for 5 min, and then diluted to 5 ml with DW. Each solution was extracted with 3 ml of benzyl alcohol after shaking for 3 min , then the absorbance of organic layer was measured at ($\lambda_{\text{max}} = 472 \text{ nm}$) against blank (organic solvent) . The calibration graph was constructed and unknown PRZH concentration found by regression (Fig .1).

(B) Standard additions

An Appropriate equal volume of Drug samples solutions were add to 5 ml volumetric flask .An increase concentration of PRZH standard solution plus 1ml of 250 $\mu\text{g Rh ml}^{-1}$ were added to each flask except one flask remain without standard addition . All solution was diluted to 5 ml with DW after pH adjusted. The content of each flask was transferred to separating funnel. Then extracted processes and measurement with applied as mentioned in (A) .the concentration of drug sample was obtained from the standard addition plot by regression (Fig 2).

Results and Discussion**Absorption spectra****I- drug stock solution**

0.25 ml of (1000 $\mu\text{g ml}^{-1}$) promethazine hydrochloride standard solution , was transferred to 5 ml volumetric flask , and diluted to the mark with water , 4 ml of this solution , was transferred to absorption cell , then the absorption spectrum of this solution was measured in the region between 200 to 1100 nm using water as the reference . Fig (3) shows the two absorption maxima for the drug was 249 and 297 nm.

II – rhodium (II) stock solution

Fig (4) shows the two absorption maxima for rhodium (II) by the application of the same procedure described in (I), was at 224 and 594 nm.

III- orange – yellow complex of PRZH with Rhodium (II)

The absorption spectrum of extracted complex was measured in the region (300 to 1100) using the extracting solvent as the reference. Fig (5) shows that a wavelength maximum was 472 nm.

Optimization of Experimental Conditions**1-Effect of pH Values**

The effect of pH on the formation of PRZH – Rh (II) complex is shown in Fig. (6); from which it appears that the best pH (2.1) for the formation of chelate complex occurs at value (2.1).

2-Effect of Concentration of Rhodium (II)

The concentration (50 $\mu\text{g ml}^{-1}$) of rhodium (II) was found to be enough for the complete formation of chelating complex , Fig (7) .

3-Effect of Reaction Time

Fig (8) refers that a reaction time of (4 min) is enough for complete complex formation.

4 – Effect of temperature

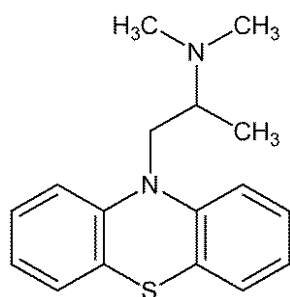
The reaction of the rhodium with PRZH was very slow and it might be take exactly one hour , so we use the temperature as catalyst to speed up the formation of the complex and inspit of using the temperature . It was found that the best temperature was 100°C is shown in Fig. (9).

5 –Organic Solvents used in the extraction

Since the method involves the measurement of complex in organic phase, it is necessary to use a solvent which will extract the chelate complex, but unreacted excess the rhodium (II) use. It was found that at pH (2.1) the PRZH is more soluble in water than in benzyl alcohol, but Rh (II) – PRZH is more soluble in benzyl alcohol than water.

6- Effect of Extraction Time

Fig (10) reveals that the complex of PRZH with rhodium (II), needed at least (1 min) of shaking to reach a state of equilibrium.



PRZH

7- Effect of Phase Ratio

An aqueous – to – organic phase of 5: 3 gives the highest extractability and highest absorbance, Fig (11).

Extraction efficiency

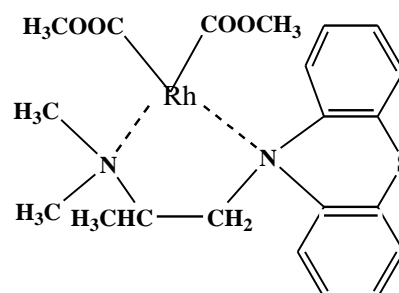
Table (1) shows molecular absorbance values for the extracted chelating complex of PRZH with rhodium (II) after the first and second extraction of the aqueous phase. The extraction efficiency (E %) was found to be 93.37 and the distribution coefficient (D = 23.47) was achieved.

The molar ratio of ligand (L) to metal (M)

The molar- ratio method at $\lambda_{max} = 472$ nm showed that a 1: 1 complex was formed. Fig (12) shows the molar ratio of ligand: metal and the stability constant (K) was calculated and equal to $6.4 \times 10^5 M^{-1}$.

Structure of the complex

Several techniques as FTIR, Molar ratio method have been used to elucidate the structure PRZH-Rh(II) complex formed at optimal conditions ,and from IR spectra and elemental analysis data, the following structure of the complex was suggested:



PRZH-Rh (II)

Calibration Graph

Fig (1) shows a calibration graph of PRZH established by plotting the absorbance of complex vs. concentration and shows that Beer's law is obeyed over the PRZH concentration of (30- 150 μgml^{-1}) at wave length (472 nm).

Statistical Calculations

All measurement can be characterized statistically. Table(2) shows the liner range of PRZH - Rh (II) and detection limit , molar absorptivity (ϵ) , sandell sensitivity (s) and confidence limits for the concentration and the absorbance . Table (3) reveals that the test statistic $t = 134.12$ is higher than critical value (2.262) in regression analysis ($r = 0.9997$). This means that the predications based on the estimated regression line $Y=0.0118x+0.0127$ should be acceptable. Therefore, all concentration of PRZH in the analyzed sample was determined from this relationship.

Table (4) shows the accuracy test in term of recovery. Recovery % was shown to be acceptable and found to be 100.74 ± 1.34 . Good precision as E_{rel} of the method was achieved and found to be 0.74 %.

Standard additions procedure was also applied (Fig. 2) for the determination of PRZH complex and all the analytical performances

were tabulated in table (5). The two samples of direct calibration and standard additions calculated was equal one, indicating the absence of interference effects and use of direct calibration is to be preferred.

Analysis of PRZH in pharmaceutical preparations with rhodium

Two procedures (direct calibration and standard additions) were used to determine PRZH in phenergan tablets at $\lambda = 472$ nm. The results are shown in table (6) and table (7). Good agreement in concentration for both calibrations was obtained compared with the stated concentration of 25 mg per unit.

Conclusions

This study has shown that the method described allows the rapid determination of promethazine. The analytical scheme of the proposed system is simpler than that of other conventional procedures. Moreover, it offers a higher sensitivity compared with other analytical methods and better recovery.

The analytical results obtained for the determination of PRZH in pharmaceuticals have shown good agreement with the given labeled quantity. The complex formed have stoichiometric ratio of 1: 1.

Table (1): absorbencies of complex after the first and second extraction

PRZH ($\mu\text{g.ml}^{-1}$)	Rh(II) ($\mu\text{g.ml}^{-1}$)	pH	A_1 (Ex. No.1)	A_2 (Ex. No.2)	A_o Blank
70	50	2.1	0.793	0.039	0.009

Table (2): analytical characteristics of result

λ_{max} (nm)	Linearity ($\mu\text{g}.\text{ml}^{-1}$)	D.L.*** ($\mu\text{g}.\text{ml}^{-1}$) (n=11)	D.L.T** ($\mu\text{g}.\text{ml}^{-1}$)	S ($\mu\text{g}.\text{cm}^{-2}$)	Conf. Limit. Conc.($\mu\text{g}.\text{ml}^{-1}$) 95% C.I	Conf. Limit. Abs. 95% C.I	ϵ ($\text{L}.\text{mol}^{-1}.\text{cm}^{-1}$)
472	30-150	1.66	1.77	83565.40	69.45±1.05	0.832±0.028	3.8x10 ³

*** Experimental

** Theoretical

Table (3) : Regression equation , correlation coefficient (r) two tailed t-test and confidence limit for the slope for the intercept at 95% confidence level and (n – 2) degree of freedom for the calibration graph .

Regre. Eq. Y=BX+A	Corr. Coef. (r)	t- test statistic	Tabulated t- test two tailed (n-2) 95% C.I	Conf. Limit. for the slope b + t _{sb}	Conf. Limit for the intercept a + t _{sa}
Y=0.0118X+0.0127	0.9997	134.124	2.262	0.0077±0.0027	0.234±0.223

Table (4): shows the relative standard deviation RSD%, E_{rel}%, recovery Rec%

Amount of PRZH taken ($\mu\text{g}.\text{ml}^{-1}$)	Amount of PRZH found ($\mu\text{g}.\text{ml}^{-1}$)	%Rec.	%Erel.	%RSD n = 5	Mean %Rec.+S.D	Mean %Erel.
40	40.57	101.11	1.1	1.42	100.74±1.34	0.74
80	80.27	100.33	0.335	0.60	-	-
120	120.95	100.79	0.79	2.47	-	-

Table (5): shows regression equation , correlation coefficient (r) two tailed t-test and confidence limit for X – Value obtained (X_E) at 95% confidence limit and (n – 2) degree of freedom for the standard additions calibration graph , recovery Rec% , E_{rel}% .

Regre. Eq. Y=BX+A	Corr. Coef. (r)	t- test statistic	Tabulated t- test two tailed n-2 95% C.I	Conf. Limit for x-value XE+tsXE	Rec. (%)	Erel. (%)
Y=0.0121X+0.3049	0.9992	63.194	2.447	28.22±0.2849	94.06	-5.9

Table (6): determination PRZH in sample of pharmaceutical preparation by direct calibration and standard additions.

Name of pharmaceutical	Type of Preparation	Stated concentration (mg per unit)	Found (direct calb.) (mg per unit)	%Erel.	Found (st. add. calb.) (mg per unit)	%Erel.
Phenergan	Tablets	25	24.89	-0.44	24.19	-3.3

Amount of PRZH taken ($\mu\text{g}.\text{mL}^{-1}$)	Amount of PRZH found ($\mu\text{g}.\text{mL}^{-1}$)	Rec. (%)	Erel. (%)	RSD (%) (n=5)	Mean Rec.%+S.D	Mean Erel. (%)
45	44.96	99.91	-0.088	1.2	98.8±3.04	-0.78
75	74.3	99.06	-0.93	1.4	-	-

105	103.6	98.6	-1.33	2.25	-	-
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Table (7): shows the RSD%, $E_{rel}\%$, recovery Rec% the calibration graph .

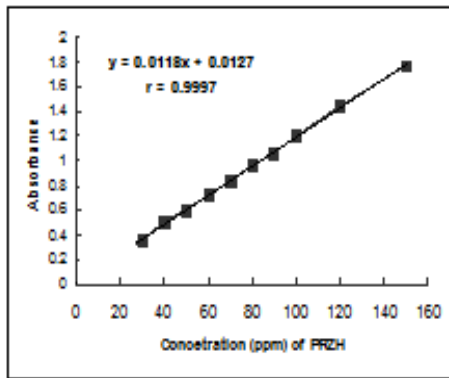


Fig1: Calibration graph for the determination of PRZH – Rh (II)

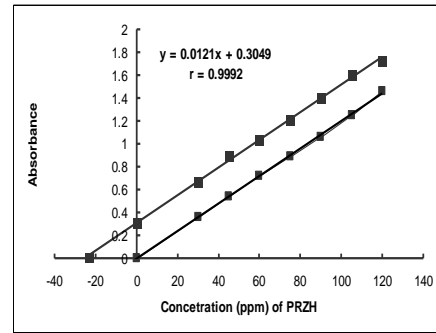


Fig.(2): Determination of PRZH s procedures in pharmaceuticals by using direct and standard additions

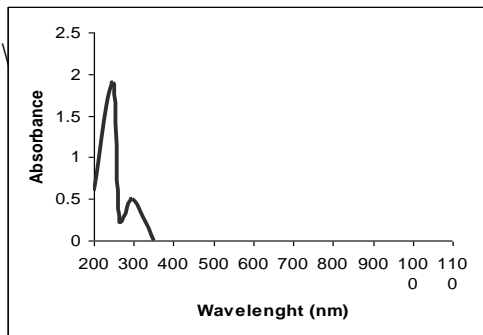


Fig3: absorption spectrum of PRZH

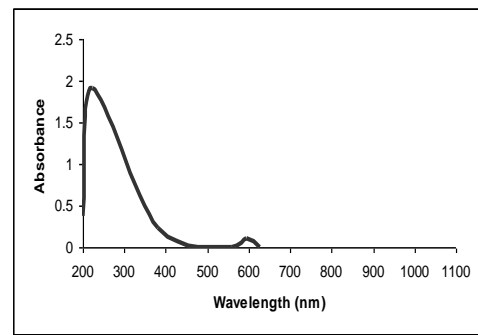


Fig4: absorption spectrum of Rh (II)

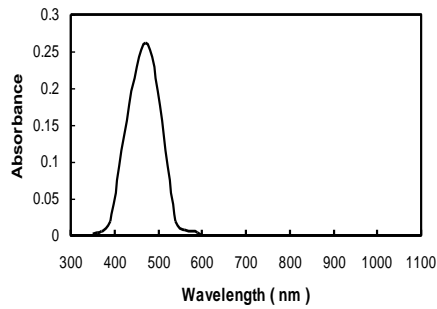


Fig5: absorption spectrum of complex PRZH – Rh (II)

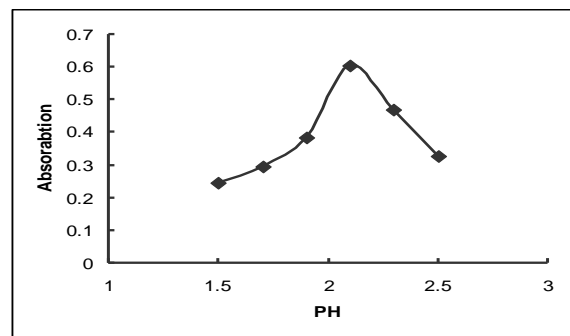


Fig.(6): Effect of pH

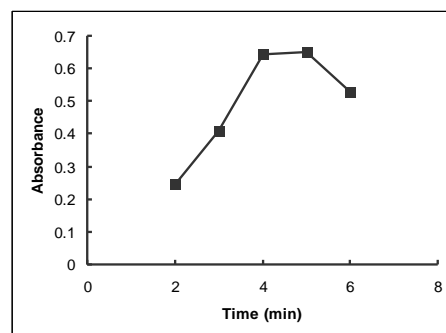
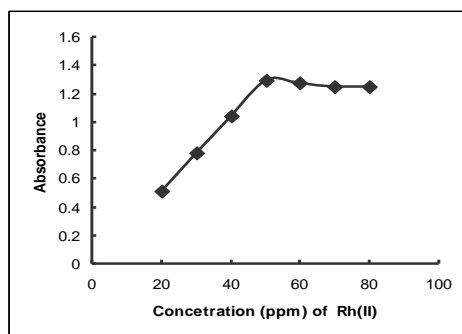


Fig. (7): Effect of Concn. of Rhodium on the determination of PRZH

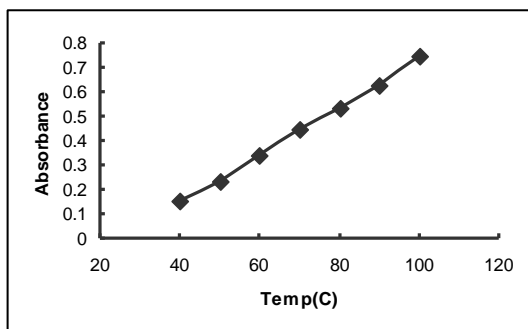


Fig.(9): Effect of temperature

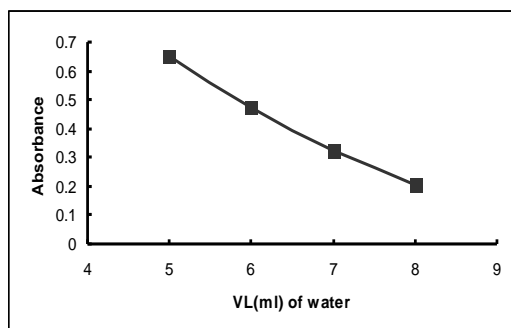


Fig.(11): Effect of phase ratio

Fig.(8): Effect of reaction time

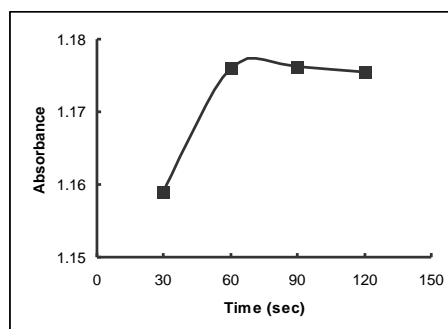


Fig.(10): Effect of extraction time

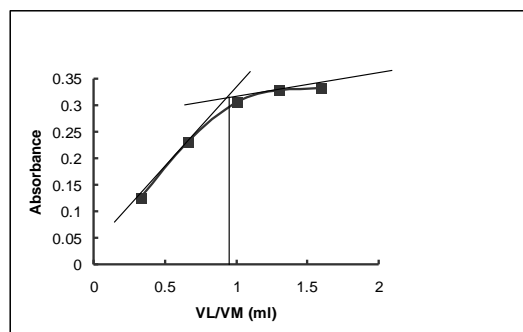


Fig.(12): Molar ratio plot , PRZH – Rh (II)

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التقدير الطيفي للدواء هيدروكلوريد البروميثازين في بعض المستحضرات الصيدلانية باستخدام فلز الروديوم كوسيط

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الخلاصة:

يتضمن البحث استحداث طريقة تحليلية جديدة في تقدير المركب الدوائي هيدروكلوريد بروميثازين (PRZH) (المستعمل في علاج الحساسية والتقيؤ) في الدواء فنزكان بطريقة الامتصاص الطيفي الجزيئي حيث تم تقدير الدواء بتكوين المعقد PRZH-Rh(II) بعد دراسة الظروف العملية المثلى: الرقم الهيدروجيني (PH=2.1) وتركيز الأيون (Rh(II)) (50 ميكروغرام.مل⁻¹) ونسبة الطور المائي إلى العضوي (3:5) وزمن التفاعل (4-5) دقائق لإكمال التفاعل قبل عملية الاستخلاص، أما أفضل زمن للاستخلاص فهو دقيقه واحده لاستخلاص المعقد الكلاسي وأفضل درجة حرارة هي درجة حرارة (100°C) باستخدام حمام مائي. إن عملية الاستخلاص لمرة واحدة كانت كافية لاستخلاص المعقد. وجد أن Benzyl alcohol هو أفضل مذيب لاستخلاص معقد PRZH-Rh(II) بدون تداخلات منشأ. وتم التقدير عند الطول الموجي ($\lambda_{max}=472\text{ nm}$)، وتمت معرفة نسبة الاتحاد المولية بين الدواء والروديوم وهي (1:1)، وكذلك تم حساب ثابت استقرارية المعقد (6.4×10^5 مولاري⁻¹)، أما مديات التركيز في تعيين الدواء فكانت (30 – 150 ميكروغرام.مل⁻¹) وحد الكشف (1.66 ميكروغرام.مل⁻¹) ومعامل الارتباط ($r=0.9997$) وحساسية ساندل (26.816 ميكروغرام.سم⁻²) والخطأ النسبي المئوي (0.74%) والدقة (0.60-2.74%) والاستردادية (100.74 ± 1.34). كما تم تعيين الدواء في المستحضر الصيدلاني بالطريقة المباشرة وطريقة إضافات القياس.