Determination Of Mtronidazole In Pharmaceutical Preparations

Hamdan Abbood Al-Hamdany
Applied Sciences Department
University of Technology

Abstract:

In this work we present the synthesis and spectroscopic determination of CuII, coordinate compound with the antibiotic metronidazole. An accurate method was chemically designated for the determination of metronidazole in pharmaceutical preparations. The green complex that was formed between copper(II) and metronidazole was studied in methanolic media. Coordination to metal ions is through its imidazolic nitrogen, while the hydroxyl and nitro groups act as supramolecular synthons. Pleated sheet or layers are formed by [Cu(metronidazole $)_2Cl(H_2O)$]Cl. The new analytical method based on measuring absorbance in UV-visible spectrum at λmax 400nm. Optimum pH and divalent copper ion concentration were estimated. Linearity(2×10^{-3}-6×10^{-7}), detection limit 6×10^{-7} M. were determined. The complex was identified with UV-visible and FT-IR spectra. The molar ratio also investigated and found 1:2(Cu: Metr).

تقدير دواء ر الميترونيدازول في المستحضرات الصيدلانية

حمدان عبود عداي الحمداني

فرع التقانات الكيميائية الاحيائية، قسم العلوم التطبيقية، الجامعة التكنولوجية

الخلاصة:

تم في هذا البحث استحداث تقدير عقار الميترونيدازول في المستحضرات الصيدلانية اعتمادا على تكوين معقد بين فلز النحاس والعقار(الميترونيدازول) على أساس أن العقار يعتبر ليكاند مخلبي لاحتوائه على عنصري الأوكسجين والنتروجين. تم حساب النسب المولية بين الفلز والدواء ووجدت أنها تساوي ٢:١، إضافة إلى حدود الكشف ١*١٠$^{-٧}$. تم تحديد شكل المعقد المتكون بين الدواء والفلز اعتمادا على النسب المولية للتفاعل إضافة إلى مطيافية الأشعة فوق البنفسجية والمرئية و مطيافية الأشعة تحت الحمراء

Introduction:

Due to the selective toxicity to anaerobic bacteria and protozoarium, metronidazole (MTZ) has been found to be clinically useful in a variety of anaerobic and protozoarium infection, particularty *Trichomonas Vaginalis* and *Amoebic Dysentery* [1]. It can kill or inhibit the majority of anaerobic bacteria when the metronidazole concentration in serum is in the range from 2 to 8 μg/ml [2]. Therefore, the determination of trace levels of MTZ is very necessary in clinics.

Various methods, such as non-aqueous titration [3], spectrophotometry [4], high-performance liquid choromatography [5], polarography [6] and adsorptive stripping voltammetry [7], have been developed for this purpose.

Experimental:

Materials and Method:

The chemicals used in this work were obtained from B.D.H. and they were all pure grade reagents. FTIR spectra were recorded using shimadzu - 8000 spectrophotometer for the range 4000 – 200 cm^{-1}. Electronic spectra were recorded using shimadzu uv –visible spectrophotometer type 160A.

Standard Solutions:

Stock solution of metronidazole (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 metronidazole then extracting the complex after each addition and measuring the absorbance at λmax = 400nm (as shown in fig.1).

2: Effect of Temperature: Optimum temperature degree for the complex were determined by changing the temperature of solution

(30 C^o to 80C^o) and extracting the complex and measuring the absorbance at λmax =400nm and pH = 4 (as shown in fig.2).

3: Molar ratio of metal to metronidazole (M:L): (By using the Mole-Ratio method), the addition of 1mL (0.002M) standard metal solution to the same concentration of metronidazole solutions (1, 1.5, 2, 2.5, 3)mL then extracting the complex and measuring the absorbance at λmax =400nm, (as shown in fig.3).

Preparation of Standard Curve:

The complex was standardized by the reaction of (0.1-1mL) 1000ppm metronidazole standard solution with 1000ppm (0.5mL) Cuppric chloride standard solution and extracting the complex and measuring the absorbance at λmax =400nm (as shown in fig.4).

Extraction Procedure:

Sample Preparation

An amount of 10 pharmaceutical tablets of MTZ were ground into powder. The resulting powder was then extracted with 25 ml of buffer solution (pH 4.3). After being extracted, the extract filtered was into a calibrated flask and then diluted to 1000 ml for determination.. The complex was synthesized by the reaction of metronidazole solution with copper ion solution, then extraction of complex by methanol and measure the absorbance at λmax,400nm.

Results and Discussion

The Copper ion react hardly with the ligand in molar ratio 1:2. The molar ratio 1:2 produce the crystal of the complex [Cu(metronidazole)$_2$ Cl(H_2O)]Cl in methanolic medium. The crystal of the complex is soluble in pH 4 and denaturated at pH 6 over .

The chemical structure of the ligand (metronidazole) has more than one coordination center because there is imidazolic nitrogen, hydroxyl and nitro groups. When we compare the IR spectrum of ligand with that of complex we found:

1: The evidence for complexation is the band at 453cm^{-1} for the conection of metal with oxygen, and there is another band at 427.5cm^{-1} for the coordination of metal with nitrogen.

2: Changing of carbonyl band from 1721cm^{-1} (in the ligand) to 1679.3cm^{-1} (for the complex) at that may be refer to the stability of the carbonyl.

3: Appear of band at 3396.7 may be refer to coordination of H_2O with the metal

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

Com.	C-H_{arom}	C-H_{alif}	C=C	C=N	C=O	Cu-O	Cu-N	NO_2
Ligand	3151.79	2981.3	1610.1	1556.61	1721	-	-	1406.15
Complex	3120.2	2870	1600	1550.9	1679.3	453	427.6	1400.2

Metronidazole react with Cu(II) in medium in molar ratio M:L_2 at the pH =4.3 to give green crystal of the complex [Cu(metronidazole)$_2$ Cl(H_2O)] Cl. The complex decomposed at pH = 6.

Table 2: The wave length and ABS of the ligand and the complex.

Compound	Wave length(nm)	Abs
Ligand Mtr.	399 310 275	0.761 2.013 1.211
Complex Cu(Met.)$_4$	524 401 360 255	0.071 0.620 2.011 1.55

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, and found to be 3.

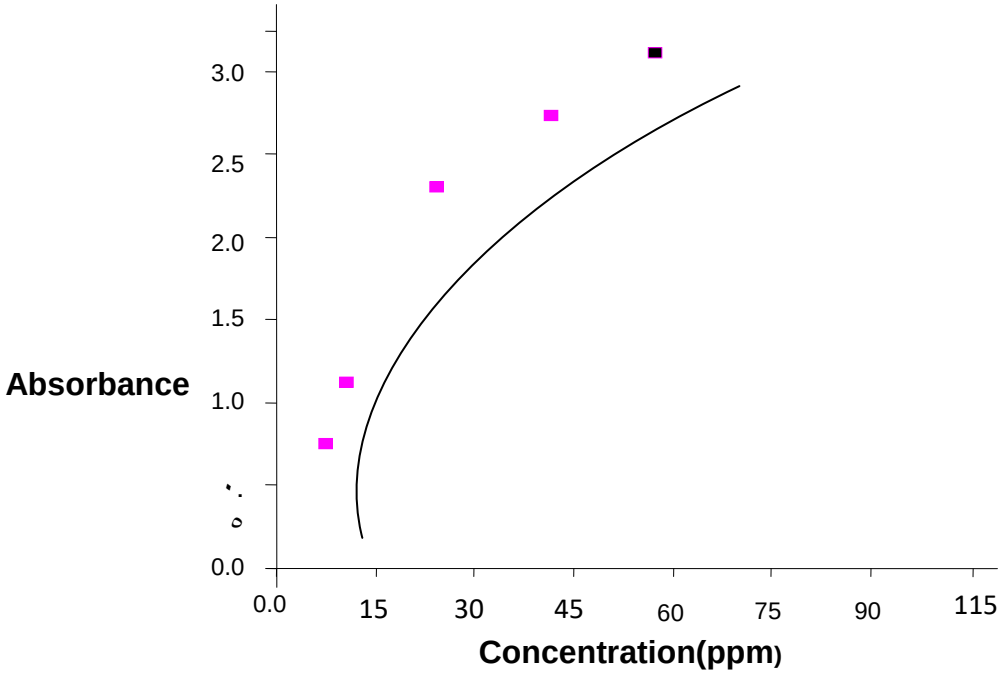

Figure 1: Concentration vs absorbance

2: **Temperature** : Optimum Temperature (C^o) of the complex formation determined as it found from Figure 2 (Temperature vs Absorbance). The best temperature (t= 30 C^0) were given from the highest absorbance

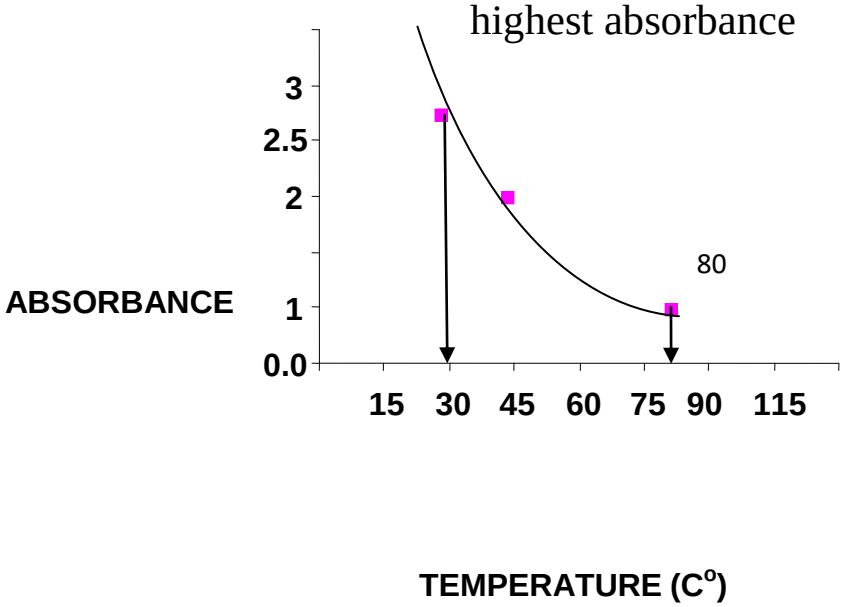

Figure 2: Temperature vs Absorbance

3: Molar ratio of metal to Metronidazole (M:L): The Mole-Ratio of metal ion to the metronidazole (in the complex) is found from Figure 3 (Volume vs Absorbance) at λmax = 400 nm

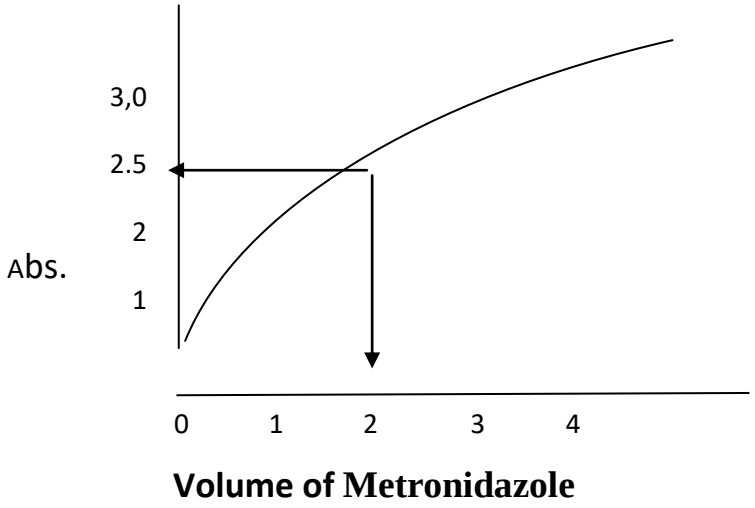

Figure 3: Molar ratio of metal to metronidazole at (2×10^{-3}M), show that M:L equal to 1:2

Standard Curve For our complex: Fig.4 represent the concentration of metronidazole vs absorbance under Beer Law, Showing the linearity.

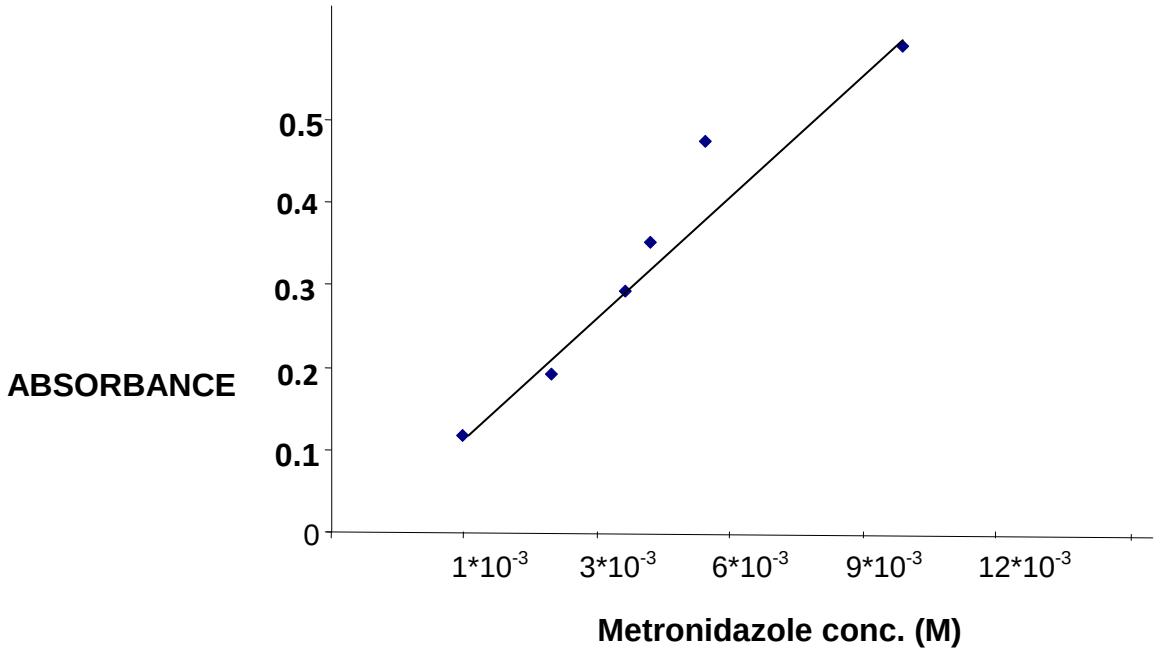

Figure 4: Standard curve or determination of metronidazole in pharmaceutical preparations at λmax =400 nm.

Table 3: The λmax, Linearity, D.L., S. And E. Of the complex.

λmax(nm)	Linearity M	Detection limit	Sensitivity
400	$1*10^{-3}$-$12*10^{-3}$	$1*10^{-3}$M	0.1

Table 4: The results of metronidazole determination in pharmaceuticals.

Pharmaceutical	Stated	Found	Recovery %
Met. indian	500mg	515mg	97%

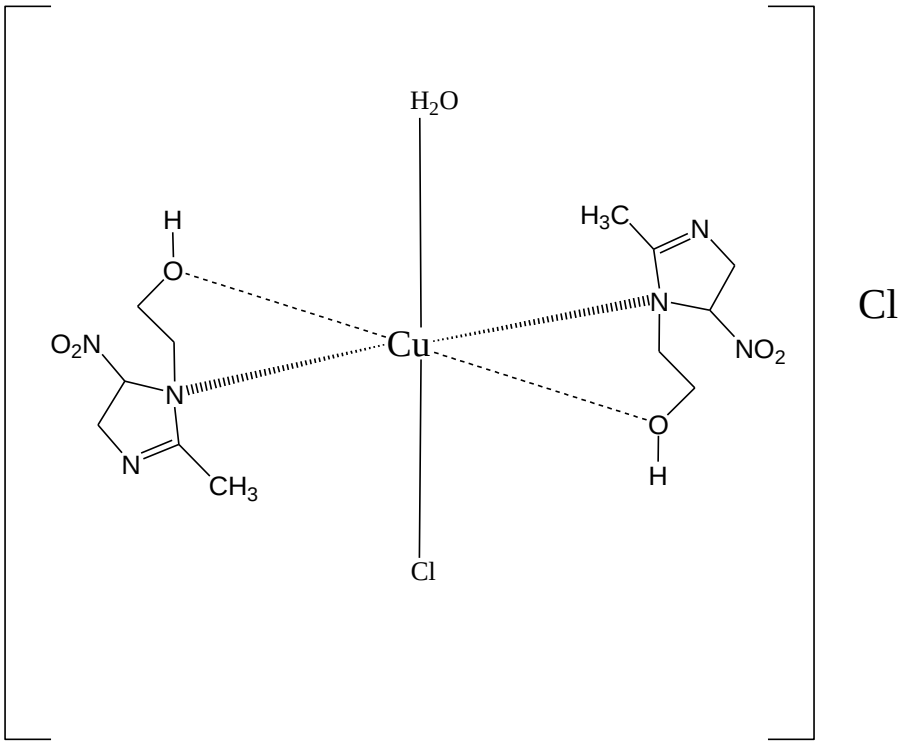

Figure 6: The complex between Couper and Meronidazole

References

1. Edwards, D. I. *J. Antimicrob. Chemother.* **1993**, *31*, 9.
2. Molav, A. *Med. Clin. North Am.* **1982**, *66*, 12.
3. *"British Pharmacopaeia"* 1988, Page 199.
4. Sanyal, A.K. *Analyst* **1992**, *1*, 117.
5. Bhoir, L.C.; Raman, B.; Sundaresan, M.; Bhagwat, A.M. *Anal. Chim. Acta* **1997**, *354*, 123.
6. Smyth, W.F.; Chabala, E.D. *Fresenius' J. Anal. Chem.* **1993**, *345*, 701.
7. Wang, Z.H.; Zhou, H.X.; Zhou, S.P. *Talanta* **1993**, *40*, 1073.