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International Journal of Pharmaceutical Research & Allied Sciences, 2021, 10(3):83-88
https://doi.org/10.51847/fXSBoyPF7i

Original Article

ISSN : 2277-3657
CODEN(USA) : IJPRPM

UV-Visible Spectrophotometric Method for Complexes Stoichiometry between Zn(II), Mg(II), Cd(II), Ca(II) and Cu(II) with Clonidine Hydrochloride

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ABSTRACT

In the present study, an accurate, rapid, and simple, UV-Visible spectrophotometric method was developed for determining complexes stoichiometry of Zn(II)-clonidine hydrochloride, Mg(II)-clonidine hydrochloride, Cd(II)-clonidine hydrochloride, Ca(II)-clonidine hydrochloride, and Cu(II)-clonidine hydrochloride. The spectra of the complexes formed between clonidine hydrochloride with Zn (II), Mg (II), Cd (II), Ca (II), and Cu (II) cations were determined at 190-400 nm and the stoichiometry of the complexes formed between clonidine hydrochloride with the mentioned metal cations was determined at maximum wavelength using the mole ratio method. The stoichiometry of Cu^{2+}-clonidine hydrochloride, Cd(II)-clonidine hydrochloride, Zn(II)-clonidine hydrochloride, and Mg(II)-clonidine hydrochloride were calculated as 1:1, but Ca(II)-clonidine hydrochloride, the complex was 1:2. The recovery was 100.8% for clonidine hydrochloride. The LOQ and LOD were 0.003 and 0.0028 µg/mL, respectively for clonidine hydrochloride. The interaction between clonidine hydrochloride with Cu^{2+}, Ca^{2+} Cd^{2+}, Mg^{2+}, and Zn^{2+} were evaluated using the UV-vis spectrophotometric method, and reasonable results were obtained.

Key words: *Clonidine hydrochloride, Cadmium(II), Copper(II), Zinc(II), Calcium(II), Magnesium(II)*

INTRODUCTION

Clonidine hydrochloride Hypertension is a type of high blood pressure or cardiovascular disease. Antihypertensive agents can decrease high blood pressure [1]. Blood pressure consists of two valves, systolic and diastolic [2, 3]. Values greater than 140mmHg for SBP and 90mmHg for DBP are considered to be high blood pressure values, that is hypertension [4, 5]. Clonidine hydrochloride is N-(2,6-Dichlorophenyl)-4,5-dihydro-1H-imidazol-2-amine hydrochloride is a centrally acting α2 agonist drug that can inhibits stimulation of the sympathetic nervous system. In addition, Clonidine hydrochloride is an antihypertensive drugs used for menopausal flushing, migraine prophylaxis and high blood pressure. This causes a decrease in heart rate and therefore decreased blood pressure [4, 6, 7].

The use of Clonidine hydrochloride is a type antihypertensive agent with a mechanism that differs from other common antihypertensive drugs. For example, Clonidine hydrochloride normalizes the blood pressure and clonidine hydrochloride is used for Tourette syndrome ADHD menopausal flushing, and migraine prophylaxis [8-11]. Clonidine hydrochloride lowers blood pressure by lowering certain blood chemicals. This causes the blood vessels to relax and the heart to slow down more slowly [12].

A low-dose administration leads to more effective control of blood pressure in both standing and supine positions in severe or moderate hypertension [9]. Also, narcotics are utilized to improve withdrawal symptoms associated with the long-term use of nicotine, benzodiazepine and alcohol [13]. In the literature review, some analytical

methods for clonidine hydrochloride have been identified, but no studies have been conducted on the determination of the stoichiometry of complexes between clonidine with Zn(II), Mg(II), Cd(II), Ca(II) and Cu(II).

MATERIALS AND METHODS

Chemicals and reagents

All reagents used were of analytical grade. The pure standard of clonidine hydrochloride was obtained from Sigma-Aldrich Co. (USA). Copper (II) nitrate trihydrate, zinc (II) nitrate hexahydrate, calcium (II) nitrate tetrahydrate, magnesium nitrate hexahydrate, cadmium (II) tetrahydrate, and methanol reagent were obtained from Merck (Germany).

Apparatus

This experimental study was performed on Shimadzu UV-2550 series spectrophotometer with a double-beam detector configuration. The absorption spectra of test and reference solutions were performed in a 1.0cm quartz cell (Germany) in a range of 190 to 400 nm.

Preparation of standard stock and titration solutions

Clonidine hydrochloride (5.0×10^{-3}M): 0.0333 g of clonidine hydrochloride was taken into 50mL volumetric flask and dissolved in 25mL methanol and the volume was made up to 50mL distilled water.

$Cu(NO_3)_2.3H_2O$ (5.0×10^{-3}M): Copper (II) nitrate trihydrate was prepared by dissolving 0.0604g copper(II)nitrate trihydrate in 50 mL mixture of water-methanol (50:50 v/v).

$Ca(NO_3)_2.4H_2O$ (5.0×10^{-3}M): Calcium(II)nitrate tetrahydrate was prepared by dissolving 0.0590g calcium(II) nitrate tetrahydrate in 50 mL mixture of water-methanol (50:50 v/v).

$Cd(NO_3)_2.4H_2O$ (5.0×10^{-3}M): Cadmium(II)nitrate tetrahydrate was prepared by dissolving 0.0771g cadmium(II) nitrate tetrahydrate in 50 mL mixture of water-methanol (50:50 v/v).

$Mg(NO_3)_2.6H_2O$ (5.0×10^{-3}M): Magnesium nitrate hexahydrate was prepared by dissolving 0.0641g magnesium nitrate hexahydrate in 50 mL mixture of methanol-water (50:50 v/v).

$Zn(NO_3)_2.6H_2O$ (5.0×10^{-3}M): Zinc(II)nitrate hexahydrate was prepared by dissolving 0.0744g zinc(II)nitrate hexahydrate in 50 mL mixture of water-methanol (50:50 v/v).

Selection of analytical wavelength of clonidine hydrochloride

For the selection of analytical wavelengths, the working test solution of bupropion hydrochloride (2.0×10^{-3}M) was scanned between 400-190 nm. The overlay spectrum of clonidine hydrochloride was recorded.

Selection of analytical wavelength of Cu^{2+}-clonidine hydrochloride and Ca^{2+} clonidine hydrochloride

Several test solutions were made by mixing different volumes of 2.0×10^{-3}M solution of each of the copper (II)nitrate trihydrate and 2.0×10^{-3}M of clonidine hydrochloride. The absorbance was scanned between 400-190 nm to determine their maximum wavelength using UV-2550 double-beam UV-visible spectrophotometer. The wavelength of the maximum absorbance and spectra were recorded.

Selection of analytical wavelength of Cd^{2+}-clonidine hydrochloride, Mg^{2+}-clonidine hydrochloride, and Zn^{2+}-clonidine hydrochloride

Similarly, the absorbance of working test solutions of Cd^{2+}-clonidine hydrochloride, Mg^{2+} -clonidine hydrochloride, and Zn^{2+}-clonidine hydrochloride complexes was scanned between 400 to 190 nm to determine their maximum wavelengths. The maximum wavelength and spectra for Cd^{2+}-clonidine hydrochloride, Mg^{2+}-clonidine hydrochloride, and Zn^{2+}-clonidine hydrochloride complexes were recorded.

Determination of the complex stoichiometry

The stoichiometries of Cu^{2+}-clonidine hydrochloride, Ca^{2+}-clonidine hydrochloride, Cd^{2+}-clonidine hydrochloride, Mg^{2+}-clonidine hydrochloride, and Zn^{2+}-clonidine hydrochloride complexes were determined by using the mole ratio method. To determine the Cu^{2+}-clonidine hydrochloride complex, several solutions were prepared such that the ratio of copper to clonidine hydrochloride was between 0-2.5, and the absorbance of these solutions was measured on UV spectrophotometer at the determined maximum wavelength.

Then, a graphic was drawn using the values between the ligand-metal mole ratio with absorbance. Similar operations were carried out in the same manner in other metal ions.

Validation

Linearity and calibration curve

For linearity and calibration curve, the working solutions were prepared at 0.066, 0.133, 0.266, 0.399, 0.533, and 0.666 µg/mL concentrations, respectively. The absorption spectra of solutions were scanned on spectrophotometer in the UV range of 400 to 190 nm, and their absorbance was recorded. The calibration curve between absorbance and concentration was drawn.

Precision

Interday and intraday variations were determined by analyzing four solutions (0.120, 0.33, 0.467, and 0.599 µg/mL) of clonidine hydrochloride within the same day and 3 different days for a week. The statistical parameters such as relative error (%RE) and relative standard deviation (%RSD) were calculated using the results obtained.

Accuracy

AThe analytical method accuracy was evaluated by the percentage recovery experiment carried out at one level equal to 100. The known amount of standard clonidine hydrochloride solution was added to the samples; absorbance was recorded and reanalyzed by the proposed method. The recovery percentage was calculated using the following formula:

n (mg) = C (mole/liter)×(molecular weight) (50,0 mL/1 tablet) × (dilution factor) =…… mg/ 1 tablet (1)

% Recovery = (Found amounts of clonidine hydrochloride) / (Known amounts of clonidine hydrochloride) × 100 (2)

LOD and LOQ

Limit of quantification (LOQ) and limit of detection (LOD) were calculated using the following formula:

LOD=C+3s and LOQ=C+10s (C: concentration, s: standard deviation) (3)

RESULTS AND DISCUSSION

The proposed method was based on spectrophotometric and mole ratio method determination of clonidine hydrochloride with metal complexes in the UV area using the mixture of water-methanol (50:50 v/v) as a solvent. The absorption spectra of clonidine hydrochloride, Cu^{2+}-clonidine hydrochloride, Ca^{2+}-clonidine hydrochloride, Cd^{2+}-clonidine hydrochloride, Mg^{2+}-clonidine hydrochloride, and Zn^{2+}-clonidine hydrochloride were found in the range of 190 to 400 nm. The curves between the absorbance and the wavelength have been shown in **Figures 1 and 2**.

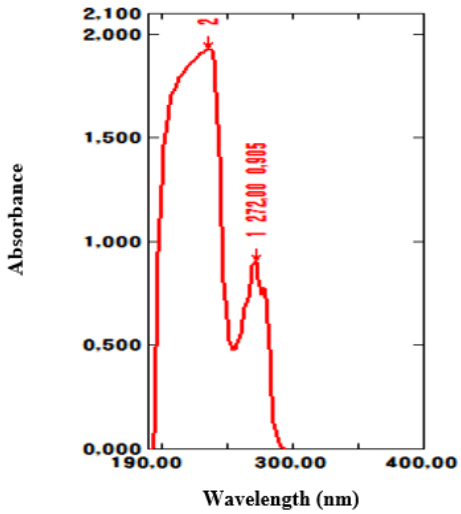

Figure 1. The spectra of clonidine hydrochloride ($2{,}0\times10^{-3}$ M) clonidine hydrochloride for lambert-beer was found to be compatible in the concentration range 0.066-0.666 µg/ml **(Figure 2)** with correlation coefficient (r^2) of 0.9992.

The linear equation of standard deviation, correlation coefficient and regression in linearity, intersection and slope were calculated and summarized in **Table 1**. **Figure 3** is the linearity plot of clonidine hydrochloride and **Figure 4** determines the composition of Ca^{2+}-clonidine hydrochloride complex by mole ratio method.

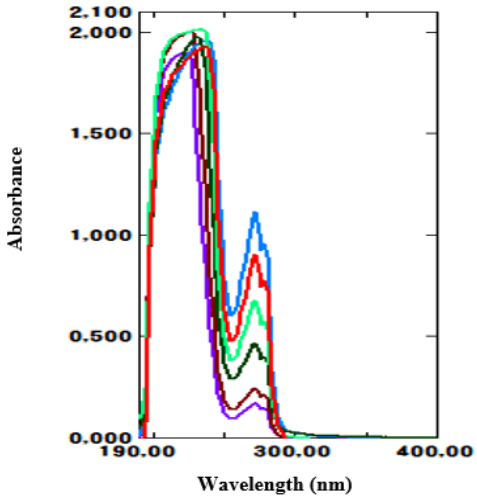

Figure 2. Absorption spectra of five different concentrations Cd^{2+}, Ca^{2+}, Zn^{2+}, Cu^{2+}, Mg^{2+} (0,066-0,666 µg/mL) of clonidine hydrochloride

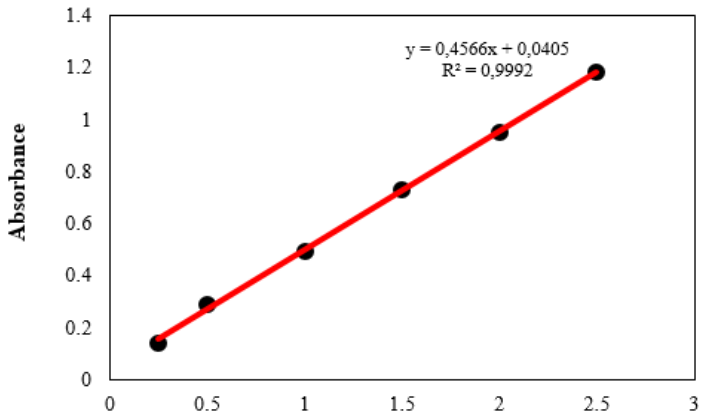

Figure 3. Linearity plot of clonidine hydrochloride

Table 1. The statistical results of clonidine hydrochloride calibration curve

Statistical parameters	Result
Wavelength	272 nm 236 nm
Linearity range	0.066-0.666 µg/mL
Regression linear equation	y=0.4566×-0.0405
r^2: Correlation coefficient	0.9992
S_a: Standard deviation on an intercept	0.738
S_b: Standard deviation on the slope	0.234

The LOD and LOQ values for Clonidine hydrochloride were found to be 0.0028-0.0039 µg/mL, respectively. RSD% and RE% day-to-day measurement results were calculated and summarized in **Table 2**.

Table 2. Intraday and interday precision measurements results

	Intraday measurement values				Interday measurement values			
Taken µg/mL	**Found µg/mL**	**x̄±s µg/mL**	**RE%**	**RSD%**	**Found µg/mL**	**x̄±s µg/mL**	**RE%**	**RSD%**
0.12	0.150 0.167	0.16±0.011	-18.5	6.79	0.152 0.183	0.17±0.019	-12.56	10.91

	0.171				0.187			
0.333	0.276 0.278 0.285	0.28±0.005	-16.2	1.718	0.277 0.286 0.305	0.29±0.014	-13.21	4.84
0.466	0.404 0.408 0.411	0.41±0.004	-12.6	0.98	0.407 0.433 0.420	0.42±0.013	-97.21	3.09
0.599	0.509 0.514 0.519	0.51±0.005	-14.19	0.97	0.519 0.530 0.536	0.53±0.008	-11.85	1.63

Recovery for clonidine hydrochloride was found to be 100.8%. Recovery percentage results are shown in **Table 3**.

Table 3. Recovery study of clonidine hydrochloride

100%	**Known amounts of clonidine hydrochloride (mg)**	**Found amounts of clonidine hydrochloride (mg)**	**Recovery %**
1	39.68	32.60	82
2	49.61	51.37	101.5
3	59.53	70.90	119.1
The mean recovery %			100.8

The stoichiometry of Cu^{2+}-clonidine hydrochloride, Mg^{2+}- clonidine hydrochloride, Cd^{2+}- clonidine hydrochloride and Zn^{2+} clonidine hydrochloride complexes were calculated as 1:1, but Ca^{2+}-clonidine hydrochloride complex was calculated as 1:2.

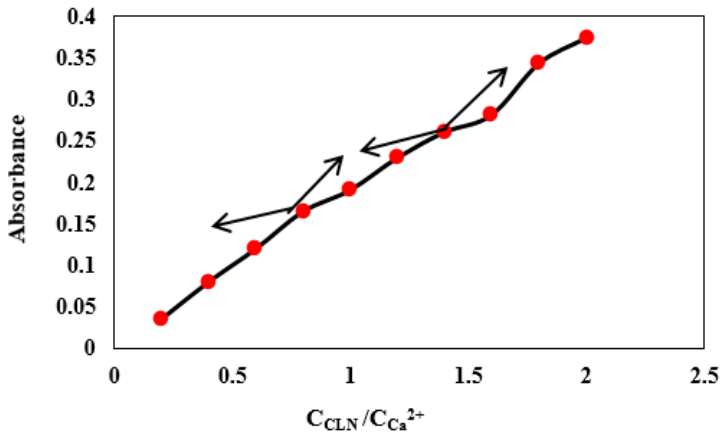

Figure 4. Determination of the composition of Ca^{2+}-clonidine hydrochloride complex by mole ratio method

CONCLUSION

In summary, in our study, the stoichiometry of the complexes formed by clonidine hydrochloride with some transition metals (Cu(II), Cd(II), Zn(II), Ca(II) and Mg(II)) was determined. The stoichiometry of Cu(II)-clonidine hydrochloride, Cd(II)-clonidine hydrochloride, Zn(II)-clonidine hydrochloride and Mg(II)-clonidine hydrochloride were calculated as 1:1, but Ca(II)-clonidine hydrochloride, complex was 1:2.

For all the values, low relative errors (RE< ±15%), high correlation coefficient (r2=0,9992) and high percentage recovery 100.8% showed the high linear relationship between the predicted and actual concentrations. The % RSD was less than 2%, without any significant difference in values for interday and intraday precision, which indicated the reproducibility of the method with high precision.

The lack of statistically significant difference between the values of the validation parameter (precision, accuracy, linearity, LOD and LOQ) for clonidine hydrochloride proved the system's suitability for the developed UV-Vis spectrophotometric method. Literature information about complexes occurring between clonidine hydrochloride

and metal cations was obtained. As a result, the precision of the analytical method was further substantiating. The proposed spectrophotometric method was rapid simple and accurate. Literature information about complexes occurring between clonidine hydrochloride and metal cations was obtained. We think that this information will contribute to the literature.

ACKNOWLEDGMENTS : The authors are thankful to Marmara University Scientific Research Projects Commission (BAPKO) for its support the project.

CONFLICT OF INTEREST : None

FINANCIAL SUPPORT : This research work has been supported by research grants from Marmara University Scientific Research Project SAG-C-YLP-110718-0440 by Marmara University Scientific Research Projects Committee.

ETHICS STATEMENT : None

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