



**SPECTROSCOPIC STUDY OF COMPLEX FORMATION BETWEEN
HYPOTENSIVE DRUG MIDRODRINE HYDROCHLORIDE WITH METAL IONS
Ag (I), Pd (II), Cd (II)**

BHARADWAJ N^{1*} AND KAUSHIK J²

1: Dean of Science, Dr. C.V. Raman University, Kota, Bilaspur, C.G., India

2: Department of Chemistry, LCIT College of commerce & science Bodri, Bilaspur, C.G.,
India

***Corresponding Author: E Mail: nbnillisweet@gmail.com**

Received 29th Oct. 2019; Revised 28th Nov. 2019; Accepted 5th Jan. 2020; Available online 1st July 2020

<https://doi.org/10.31032/IJBPAS/2020/9.7.5100>

ABSTRACT

The stability of the complex formed between the Midrodrine Hydrochloride and Metal ions Ag (I), Pd (II), and Cd (II) are evaluated. That are investigated and monitored by the UV Spectrophotometric method. Midrodrine hydrochloride react with Ag(I), Pd(II) & Cd(II) in aqueous buffer solution where by a coloured complex are formed which absorb maximally at 300 nm .The data show that stoichiometric ratio of drug with metal ions 1:1 ratio. The stability constant of complex were calculated to be Ag(I)-midrodrine -5.72 , Pd(II)-midrodrine -7.17 & Cd(II) – midrodrine - 2.24 by jobs continuous variation method.

**Keywords: Complexation, Stability Constant, Midrodrine Hydrochloride,
Spectrophotometer**

INTRODUCTION

Midodrine Hydrochloride is a Anti hypotensive drug used for the elevation of supine blood pressure. Midodrine involves the constriction of the blood vessels and increasing the blood pressure [1]. Midrodrine drug has various functional groups which can bind to receptor or

enzyme or metal ions (**Figure 1**). They forms many type of complex and can enhance the activity of drug. The metal complex of drug play an important role in drug action and metabolism [2]. The drug – metal complex are used to control growth of pathogenic and parasites which are

harmful to human [3]. Midrodrene converted to its active metabolic. This selective bind to the alpha-1- adrenergic receptor of the arteries. And venous vascular. Desglymidrodrene diffuses poorly across the blood brain barrier and is therefore not associated with effect on the central nervous system [4].

Midrodrene is 2-amino-N-[2-(2, 5-dimethoxyphenyl) hydroxyethyl] acetamide; hydrochloride chemical formula $C_{12}H_{19}ClN_2O_4$ [5]. Metal ions play a vital role in growth, overall health and maintenance of human body but at the same time can induce various diseases due to their imbalance. Electron rich ligands or drugs effectively bind and interact with metal ions to give so called “metallo drugs” and “metallo pharmaceuticals” [6]. We have synthesized midrodrene – Ag (I), midrodrene - Pd (II), midrodrene – Cd (II) complexes. The metal complex were characterized by UV visible spectroscopy .

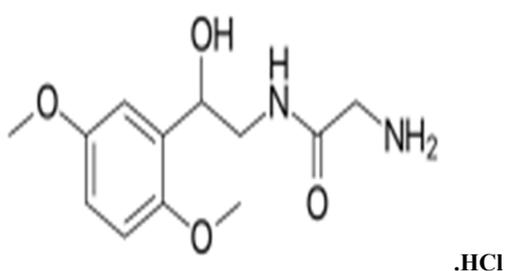


Figure 1: Structure of Midrodrene Hydrochloride

MATERIAL AND METHOD

Midrodrene – Ag (I), Pd (II), and Cd (II) metal complexes were prepared by adding corresponding aqueous solution of Ag (I), Pd (II), and Cd (II) metal salt to buffer

solution & Midrodrene. A systronic UV-Visible spectrophotometer with 1 cm quartz cell was used to measure the absorbance [7]. The pH measure with systronic pH meter measurement were performed at room temperature $35^{\circ}C$ [8]. Standard stock solution of Midrodrene Hydrochloride was prepared by dissolving 0.762 g of drug in 10 ml of methanol to get concentration of 1000 $\mu g/ml$. from which 1 ml was further diluted to 10 ml with methanol to get concentration of solution 100 $\mu g/ml$ [9]. Metal stock solution (0.01 M) was prepared by dissolving appropriate amount of silver nitrate, palladium nitrate and cadmium chloride with deionized water. The universal phosphate buffer solution of varying pH value.

A series of solutions containing up to 4.0 ml of buffer solution, 1 ml (0.01 M) of the metal ions and 0.5-4.0 ml (0.01 M) of Midrodrene was mixed in 10 ml measuring flask and then diluted up to the mark with water. The mixture was allowed to stand for 10 min. The absorbance was measured at the maximum wavelength (λ_{max}) against a blank solution prepared in the same manner but not contains metal ions [10]

Stoichiometry of Midrodrene complexes formed in the solution was determined spectrophotometrically applying the continuous variation method [11]. The obtained results revealed the formation of

1:1 (M: L) midrodrine complexes with Ag (I), Pd (II), Cd (II) metal ions respectively. The logarithmic constants ($\log \beta_n$) and the free energy changes (ΔG) of the formed complexes were calculated from the data of continuous variation methods [12] applying equations 1 and 2.

$$\beta_n = A/A_m / 1 - [A/A_m]^{n+1} C_1^n N^2 \dots \dots \dots (1)$$

$$\Delta G = -2.303 RT \log \beta_n \dots \dots \dots (2)$$

Where β_n is the stability constant of the metal chelate, A is the absorbance at ligand concentration CL, A_m is the absorbance at full color developed, n is the order of the complex formed, T is the absolute temperature and R is the gas constant.

RESULT AND DISCUSSION

When the ligand solutions are mixed with metal ions solution it is observed colour of solution was changed above the 9.2 pH. That indicates the complex formation between metal ion and ligand. The stability constant value for complex of midrodrine with Ag (I), Pd (II) and Cd (II) metal ions by spectrophotometrically. The UV region exhibits maximum absorbance at 300 nm for M/L complex (Table 1) (Table 2) (Table 3). The stability constant for midrodrine in found in the order of Pd (II) > Ag (I) > Cd (II); 7.17 > 5.72 > 2.24 respectively which obey the Irving-William order (Table 4).

Table 1: System Ag (I) – midrodrine (λ_{max} - 300 nm; pH-9.2)

Metalions (ml)	Ligand (ml)	Optical Density
0.5	3.5	2.816
1.0	3.0	2.823
1.5	2.5	2.843
2.0	2.0	2.921
2.5	1.5	2.828
3.0	1.0	2.775
3.5	0.5	2.762

Table 2: System Pd (II) – midrodrine (λ_{max} - 300 nm; pH-9.2)

Metalions(ml)	Ligand(ml)	OpticalDensity
0.5	3.5	2.809
1.0	3.0	2.874
1.5	2.5	2.893
2.0	2.0	3.008
2.5	1.5	2.945
3.0	1.0	2.931
3.5	0.5	2.901

Table 3: System Cd (II) – midrodrine (λ_{max} - 300 nm; pH-9.2)

Metalions(ml)	Ligand(ml)	Optical Density
0.5	3.5	2.004
1.0	3.0	2.029
1.5	2.5	2.048
2.0	2.0	2.596
2.5	1.5	2.721
3.0	1.0	2.245
3.5	0.5	1.948

Table 4: Spectrophotometric analytical characteristic of midrodrine complexes with Ag(I), Pd(II) and Cd(II) ions

SN	Metal ions	λ max	M/L Ratio	β_n	$-\Delta G$
1	Ag(I)	300 nm	1:1	5.72	4.47
2	Pd(II)	300 nm	1:1	7.17	5.04
3	Cd(II)	300 nm	1:1	2.24	2.07

CONCLUSION

In summary it is successfully showed by spectrophotometry technique that Midrodrine hydrochloride have binding ability with Ag(I), Pd(II) and Cd(II) metal ions. Composition of the complex was determined by using jobs continuous variation method, result shows that the stoichiometric ratio of Midrodrine –Ag, Pd, Cd (M/L) was 1:1. It is also observed that size of metal ions also affect the complex Midrodrine hydrochloride formation can be determined in pharmaceutical preparation and also in biological samples by complexation with metal ions.

The development of the new antihypotensive drug with enlarged biological activity can be possible by progress in the field of antihypotensive complexes.

ACKNOWLEDGEMENT

We are thankful to Dr. C.V Raman University Kota, Bilaspur (C.G.) for providing the laboratory facility.

REFERENCE

[1] Krishna A, Kavitha M.P, Krishnakumar K, A review on the determination of midrodrine hydrochloride in bulk and marked

formulation by using different analytical techniques, World j. of pharmaceutical research 7(14); 2013: 260-266.

- [2] Ware R, Farooqui M, Naikwade S.D, Equilibrium studies on mixed ligand complexes of Copper (II) metal ion with some antihypertension drugs and amino acids, International Journal of Emerging Technologies in Computational and Applied Sciences. 13; 2013: 123-128
- [3] Seku K, Yamala A, Kanchera M, Badathala V, Synthesis of moxifloxacin –Au (III) and Ag (I) metal complexes and their biological activities, Journal of Analytical Science and Technology, 9(1); 2018: 2-14.
- [4] Drug bank. Available from: <http://www.drugbank.ca/drugs/DB00211>. [Last accessed on 11 Jun 2016].
- [5] Jain H.K, Gujar K, Randhe V, Stability indicating RP-HPLC assey method for estimation of midrodrine hydrochloride in bulk and tablet . J.

- of pharm. And pharmaceutical sci. 8(9); 2016: 283-287.
- [6] Shah P , Shah J, Sanyal M, Shrivastav P , Complexation study of Glimepiride with Mg^{2+} , Ca^{2+} , Cu^{2+} and Zn^{2+} in methanol by conductometric, Int. J. Pharm. Pharm. science, 7(9);2015: 105-111.
- [7] Alkaya D, Karadari S, Erdogan G, Tersary complex formation of isoniazid with some transition metal and amino acid , J. Nat. Sci, 14(1); 2013: 1 -14.
- [8] Gaber M, Khedr A, Kady A, Spectrophotometric determination of norfloxacin in pure and dosage form by complexation with Fe(III) and Cu(II) , Int. Res. J. Pharm. Pharmacol, 2(5); (2012): 97-102.
- [9] Damle M.C, Salunke .S, Stability – Indicating HPTLC method for determination of midodrine hydrochloride, Eur. J. of phar. And medical sci. 3(9); 2016: 202-207
- [10] Bharadwaj N , Koshle G, Complexation of Norfloxacin with Some Transition Metal Ions - A Spectrophotometric Study, j. Chem and chem. Sci. 6 (9); 2016: 821-825.
- [11] Yoe J, Jones L, Colorimetric determination of iron with disodium -1,2 – dihydroxybenzene-3,5-disulfonate. Ana. Chem.16; 1944: 111-125
- [12] Ramteke A, Narwade M, “Spectrophotometric Studies on stability constant of chlorosubstituted pyrazoles with Cu (II) Nd (III) and Tb (III) metal ions at 0.1 M Ionic strength” Der Chemica Sinica, 3(5); 2012: 1036-1040.