The Antibacterial Activity of 1.4(amino methylene) cyclohexane Platinum (II) and Palladium (II) Dicarboxylate amino Acid Complexes

A Al-Fregi, H Abood, I Al-Saimary

Citation

A Al-Fregi, H Abood, I Al-Saimary. *The Antibacterial Activity of 1.4(amino methylene) cyclohexane Platinum (II) and Palladium (II) Dicarboxylate amino Acid Complexes*. The Internet Journal of Microbiology. 2006 Volume 4 Number 1.

Abstract

Objective: To estimate the antibacterial activity of four complexes of the type [Pt(O^O)(BAMC)]AND [Pd(O^O)(BAMC)] [O^O = dicarboxylate amino acid: Asptrate and Glutamate : BAMC = 1,4 – Bis(amino methylene) cyclo hexane] .

Methods: We conducted the study between November 2006 and April 2007. In-vitro evaluation of antibacterial activity by growth inhibition and minimal inhibition concentration (MIC)) against eight types of Pathogenic bacteria: Staphylococcus aureus, Staphylococcus epidermidis, -hemolytic streptococci, viridance streptococci, Escherichia coli, Klebsiella and Pseudomonas aeruginosa.

Results: The platinum and palladium complexes have a high antibacterial activity in (1000g/ml) except complex [II] against Staph. aureus and Staph. Epidermidis, and [IV] against Staph. aureus. All of the complexes are not effective at low concentration except complex [III] in (250g/ml) against Klebsiella.

Conclusion: We conclude that four complexes of the type [Pt(O^O)(BAMC)]AND [Pd(O^O)(BAMC)] [O^O = dicarboxylate amino acid: Asptrate and Glutamate : BAMC = 1,4 – Bis(amino methylene) cyclo hexane] have various antibacterial activity against pathogenic bacteria isolated from clinical cases.

INTRODUCTION

In recent years, a great deal of effort has been devoted to developing transition metal antitumor agent which have better therapeutic properties than the prototype drug Cis-$[PtCl_2(NH_3)_2]$([1,2,3,4,5]). The bulk of the work to date has involved investigation of the platinum complexes as potential antitumor agent; however some investigation involving palladiums have been done ([6,7,8,9]). For the most part palladium (II) complexes have shown little or no antitumor activity compared to platinum (II) complexes. This has been attributed to platinum (II) complexes ([10]).

On the other hand, it has been found that the platinum complexes which contain good leaving group are responsible for cytotoxic activity of these complexes also, it has been found that the platinum (II) complexes which be charged and water insoluble are lees biological activity and more toxicity ([3,4]).

In an effort to solve the problem including lack of stability of palladium complexes, we have adopted the approach by Gill ([8]). This approach involves the use of chelation ligand to stabilize the palladium complexes so that it can reach the cancerous cell intact to be the lack of effective as antitumor agent. On the other hand, to solve the problems of the lack of water- soluble of platinum and palladium complexes and to increase the biological activity, therefore, we chosen the dicarboxylate amino acid (Aspartate and Glutamate) which have intermediate leaving group. Generally, the complexes of amino acids with platinum (II) and Palladium (II) are well known ([11,12]) and have been of wide interest because of their biological aspect and the variety of their structure properties ([13,14,15])

We report the four complexes of 1,4-Bis (amino methyl) cyclo hexane platinum (II) and Palladium (II) containing bidantate dicarboxylate amino acid were compare the in vitro against eight type of pathogenic bacteria, to determine

the anti bacterial activity. Structure ability to destroy the bacteria of platinum (II) and palladium (II) complexes.

MATERIALS & METHODS

All the complexes in this study are listed in the table (1). All complexes were prepared by the same general procedure([16]). The method involves reaction of K_2PtCl_4 salt with KI to give K_2PtI_4 which upon reaction with 1,4-Bis - (aminomethyen) cyclohexane (BAMC) at room temperature led to formation beige precipitate to (BAMC) Pt I_2. Because of the high reduction ability of palladium (II) with KI, Na_2PdCl_4 was been reacted with (1) enquire (BAMC) directly to give (BAMC)Pd I_2 .

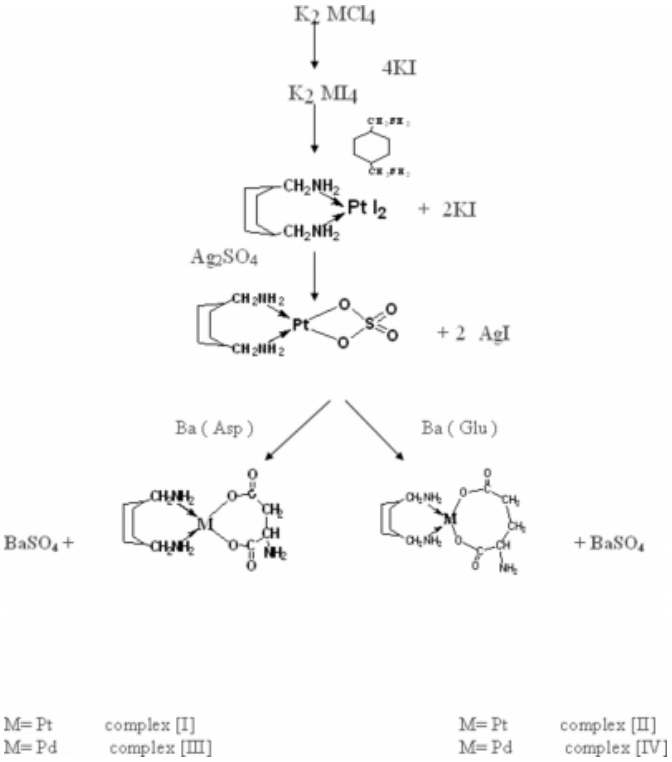
The yellow precipitate, (BAMC)Pt I_2 and (BAMC)Pd Cl_2 was collected by filtration and washed with water. Reaction of (BAMC)Pt I_2 and (BAMC)Pd Cl_2 with silver sulfate gave of (BAMC)PtSO_4 and (BAMC)Pd SO_4

After silver iodid or silver chloride was filtered off, the reaction of 1,4 (amino methylene)cyclo hexane platinum(II) sulfate or 1,4(amino methylene)cyclo hexane palladium(II) sulfate with barium salts of aspartate or glutamate ligand in aqueous solution at room temperature smoothly afforded the product.

The general synthesis method has been utilized to prepare these complexes are explain in the scheme (1).

Figure 1

Scheme 1 : methods of preparation of complexes [I]-[IV] .



ANTIBACTERIAL SUSCEPTIBILITY

Various concentration for synthesis complexes have been prepared in dimethyl sulfoxide (DMSO) (100, 250, 500, 750, and 1000 µg/ ml) and two techniques were used to determine the antibacterial activity of complexes([17,18]).

1) Plate agar diffusion method used to determinate of the growth inhibition zone millimeter (mm) by using Muller –Hinton agar (MHA).

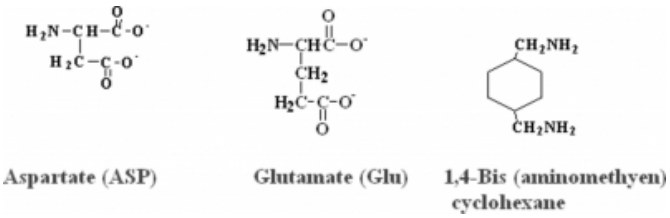
2) Tube (dilution) method used to determination minimal inhibitory concentration (MIC) of platinum and palladium complexes by using Brain – Heart Infusion (BHI).

RESULT

Four complexes of 1,4- bis (amino methylene) cyclohexane platinum (II) and palladium (II) that contain dicarboxylate amino acid have been prepared. Figure (1) illustrates the two amino acid and amino ligands used in this study. Table (1)explains some physical properties of Pt(II) and Pd(II) complexes.

Figure 2

Figure 1: Structure of the dicarboxylate amino acid and amino ligand used in Complexes



Aspartate (ASP) Glutamate (Glu) 1,4-Bis (aminomethyen) cyclohexane

Figure 3

Table 1: shown some physical properties and yield to prepared these complexes

Complex Number	Complex	Physical Properties		yeild
		Color	Meeting point(dec. c)	
[I]	(BAMC)pt(O OASP)	Beige	210 – 211	88%
[II]	(BAMC)pt(O OGlu)	Beige	225 – 227	72%
[III]	(BAMC)pd(O OASP)	Beige	175 – 176	70%
[IV]	(BAMC)pd(O OGlu)	Pale yellow	180 - 182	65%

The bacterial activity has been measured and summaries in table (2) and the point blew:

1- At (1000 µg/ml) all the synthesis complexes give ability for killed the bacteria except complex [II] against Staph. aureus and Staph. epidermidis also complex [IV] against Staph. aureus. All the complexes not affective low concentration except complex [III] in concentration (250 µg/ml) against Klebsiolla highly anti bacterial activity recorded for Gram positive bacteria, because the cell membrane of this type contain mucopolysaccharides, protein and less amount of phospholipds and have a less number of pores in the cell envelop. So, the permeability of anti bacterial agent is highly effective against cell membranes.

2-The more active complex is the complex [III] and [IV], *and [II] respectively.*

3-The complex [III] give (27 mm) against Klebsiolla at concentration (1000 µg/ml).

4-From the results in the table (2), it has been found the palladium (II) has a higher bacterial activity than other complexes.

Figure 4

Table 2:: Growth Inhibitor Zone (mm) , Minimal Inhibitory Concentration (MIC µg/ml)

Bacterial types	*Diameters Inhibitor Zones (mm), MIC (µg/ml), for different Conc. Of complexes*																	
	[I]					[II]					[III]					[IV]				
	100	250	500	750	1000	MIC	100	250	500	750	1000	MIC	100	250	500	750	1000	MIC
Staphylococcus aureus	0	0	0	0	8	1000	0	0	0	0	0	1000	0	0	0	8	16	500	0	0	0	0	0	650
Staphylococcus epidermidis	0	0	0	10	16	550	0	0	0	0	0	900	0	0	0	10	18	450	0	0	0	6	12	650
β-hemolytic *Streptococci*	0	0	0	0	10	600	0	0	0	0	6	1000	0	0	0	12	23	400	0	0	0	0	10	1000
viridance streptocci	0	0	4	9	12	550	0	0	0	0	0	900	0	0	0	16	22	400	0	0	0	0	12	600
Escherichia coli	0	0	0	10	14	500	0	0	0	0	12	750	0	0	0	11	25	350	0	0	0	6	14	800
Enterobacter	0	0	0	9	16	400	0	0	0	5	13	750	0	0	0	13	18	500	0	0	0	9	15	650
Klebsiella	0	0	0	0	14	450	0	0	0	00	9	900	0	0	4	9	18	350	0	0	0	10	22	500
Pseudomonas aeruginosa	0	0	0	3	9	650	0	0	0	0	7	900	0	0	0	0	12	500	0	0	0	0	0	750

DISCUSSION

At (1000 µg/ml) all the synthesis complexes give ability for killed the bacteria except complex [II] against Staph. aureus and Staph. epidermidis, also complex [IV] against Staph. aureus. All the complexes not affective low concentration except complex [III] in concentration (250 µg/ml) against Klebsiella highly anti bacterial activity recorded for Gram positive bacteria, because the cell membrane of this type contain mucopolysaccharides, protein and less amount of phospholipids and have a less number of pores in the cell envelop. So, the permeability of anti bacterial agent is highly effective against cell membranes.

The more active complex is the complex [III] and [IV], *and [II] respectively, and it has been found the palladium (II) has a higher bacterial activity than other complexes.*

Its necessary to our knowledge that there are no any previous studies that interested in these compounds, so its unable to compare our study with another studies, and our study was investigated Pt(II) and Pd(II) compounds as a pioneer study.

CORRESPONDENCE TO

DR.Ihsan E. Al-Saimary.assist. professor , PoBox 696 Ashar 42001, college of medicine university . of Basrah Basrah, Iraq. E-mail : IHSANALSAIMARY@yahoo.com

References

1. A.W.Prestayko , S.T.Crooke and S.K.Carter(eds.),Cisplanin : "current status and new

development", Academic prees , Newyork, 1980.
2. M.J.Cleare and P.C. Hydes, "Metal Ions in Biological System", Marcel Dekker , NewYork ,11 ,1(1980).
3. M.J.Clear , "Structure - Activity Relationships of Antitumor Agents Development in Pharmacology" Martinus Nijhoff, the hague Boston, 13, P.P 59. (1983).
4. Y.Keun, Y.S. Sohn and Y. - A Lee, Biochemistry, 68, 289 (1997).
5. A.R.Khokhar , Al. Baker, T. Brown and R.Perez - Soler, J. of midicinal chem. , 34, 325 - 329 , (1991).
6. M.m.l.Fiallo and A.Garnier - Suillerot , Biochemistry , 25 , 924 (1986).
7. A.Furlani , V.Scarcia , G. Faraglia , L. Sindellari , L.Trincia and M. Nicolini ,Eur. J. Med.chem. - chim. Ther. 21 , 261 (1986).
8. D.S. Gill , in M.P. Hacker , E.B.Doupl and I.H. Krakoff(eds.) , " Platinum Coordination Complexes in cancer Chemothaerapy" , Martinus Nijhoff , Boston P.P. 267 ,(1984).
9. A.A. Chachoyan and B.T. Garibdzhanyan , Biol. Zh. Arm. , 39 , 260(1986).
10. A.R. Khokhar and G,J, Lumetta , Inorg. Chim. Acta , 153 , 255 (1988).
11. F.R. Hartley, " The chemistry of platinum and palladium", (Applied Science , London , 1973), P.P. 205 - 209.
12. A.kokhar and GJ,Lumetta , J. Coord. Chem. , 26 ,251 - 257 (1992).
13. Djuran and M.I.Lempers , Inog. Chem. 30 , 2648(1991).
14. R.E.Norman , J.D. Ranford and P.J. Sadler , Inog. Chem.31 , 877(1992).
15. N. Hadjiliadis , H. Schollhorn and G. Trotscher , Inog. Chem.Acta. 164 ,
221 , (1989).
16. Adil A. Al-Fregi* , Haider A.A. Abood ;J ,Basrah Reasrches (Science) Vol.30,3,31-41(2004).
17. B.A. Atkinson , F. Lorian , "Antimicrobial agent susceptibility Patterens of bacterial in hospital from 1972 - 1982 , J. Clin. Luicrbial , 20 , 791 , (1984).
18. R.E Bachanon and .E. Gbbors " Bergeys Manual of Determinative Bacteriology" 18th ed. , The williams and wilkins company , Baltimore (1984).

Author Information

Adil A. Al-Fregi
Department of chemistry, College of Science, University of Basrah

Haider A.A. Abood
Department of Material Engineering, Engineering College, University of Basrah

Ihsan Edan Al-Saimary
Department of Microbiology, College of Medicine, University of Basrah