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Synthesis, Characterization and Antimicrobial Activities of Platinum(II) and Palladium(II) Complexes with Various Donor Ligands: Part (I)

SUHAIR A. SALEH*, LUAY J. RASHAN and TALAL A.K. AL-ALLAF†
Department of Clinical Pharmacy and Therapeutics, College of Pharmacy
Applied Science Private University, Amman 11931, Jordan
E-mail: suhair_suleh@yahoo.com

Several platinum(II) and palladium(II) complexes of the general formula *cis*-[MLL′X_2], M = Pt or Pd, L = L′ = DMSO, X = Cl, ½C_2O_4, ½$(OCO)_2$-$CCH_2CH_2CH_2$, ½{(OCO)CH=CH(OCO)}, $(OCO)C_6H_{11}$; M = Pt or Pd, L = DMSO, L′ = harmaline or harmine, X = Cl, ½C_2O_4, ½$(OCO)_2$-$CCH_2CH_2CH_2$; M = Pt, L = 3,5-dimethylpyrozole, L′ = harmine; and *trans*-[Pd(3,5-dimethyl-pyrazole)$_2Cl_2$)] have been prepared and characterized physico-chemically and spectroscopically. These complexes together with the antibiotic ciprofloxacin and antifungal miconazole nitrate were tested for their antimicrobial activity against the two gram-negative bacterial species, *Escherichia coli* and *Pseudomonas aeruginosa*, and the gram-positive bacterial species, *Staphylococcus aureus* and the fungal species, *Candida albicans*. The results obtained were compared with those of the platinum complexes, cisplatin, carboplatin and oxaliplatin; the known anticancer drugs.

Key Words: Synthesis, Complexes, Pt(II), Pd(II), Harmaline, Harmine, Antimicrobial Activity.

Since the accidental discovery of Rosenberg[1] that platinum complexes inhibit the growth of some bacterial species and latter cancer cells, several platinum complexes have been prepared for the same purpose[2]. Because of this, a large number of metal compounds and metal complexes were synthesized and tested for their biological activities, *i.e.*, antipathogenic bacteria and tumour cells; hence several articles and reviews have been reported[3–7]. As a continuation of our intrinsic interest in preparing metal compounds and metal complexes and studying their *in vitro* biological activities as antibacterial[8, 9], antitumour[10–14] and anti-complementary agents[15–17], several square planar platinum(II) and palladium(II) complexes were prepared (Fig. 1) and studied their antimicrobial activities against some gram-negative and gram-positive bacteria and one fungal species. Furthermore, the antimicrobial activities of the complexes, cisplatin, carboplatin and

†Department of Chemistry, College of Basic Sciences, Applied Science Private University, Amman 11931, Jordan.

oxaliplatin (Fig. 2), the known anticancer drugs, were also examined for comparisons.

Platinum(II) and palladium(II) complexes were prepared according to standard methods[10-12, 15]. The complexes were purified before using for their antimicrobial activity. The anticancer drugs cisplatin, carboplatin and oxaliplatin were prepared and their purities were checked with standard samples.

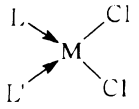
The complexes were dissolved in 10% DMSO and diluted with sterile distilled water and stock solutions of the concentration 10 μg/mL were prepared to be used in the antimicrobial activity.

Antimicrobial activity study: Fresh cultures of four standard strains of the microorganisms were used in this study, *i.e.*, *Staphylococcus aureus* ATCC (6538), *Escherichia coli* ATCC (8739), *Pseudomonas aeruginosa* ATCC (9027) and *Candida albicans* ATCC (10231). For antimicrobial study, the agar-well diffusion technique was used. A standard inoculum size of each microorganism was prepared from the fresh culture. The turbidity was standardized according to 0.5 McFarland standards[18] and the turbidity of the actively growing broth culture was adjusted with sterile saline. This resulted in a suspension containing approximately 1 to 2×10^8 CFU/mL for bacteria. Fungal suspensions were adjusted to a concentration of 1 to 2×10^6 CFU/mL. All-purpose Mueller Hinton agar media was used in this study which has been tested to meet the acceptance limits of NCCLS[18]. Mueller Hinton agar plates were evenly seeded with microorganisms using sterile cotton swabs dipped into the adjusted suspension of microorganisms. Each plate was then punched using sterile 6 holes puncher and the punched media were removed to produce (6 mm) 6 wells in each plate. To each well 50 μL from each complex was added and allowed to diffuse. Each complex was tested against each organism in three replicates. The plates were then incubated aerobically at 37°C for the bacteria strains and at 25°C for the fungus for 18 h.

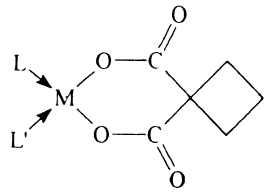
The antimicrobial activities were then tested for each complex and recorded as the mean diameter of the resulting growth inhibition zones in millimetres. Three separate sets of control containing the dissolved compound and the antibiotic ciprofloxacin and the antifungal miconazole were used. In all the experiments, the mean of each triplicate was measured.

The platinum(II) and palladium(II) complexes used in this study were chosen with various donor ligands, L and L′ and different anions (Fig. 1). They were prepared according to standard methods and purified and their identities were checked by the analytical tools, *i.e.*, CHN elemental analysis, IR and NMR spectral data.

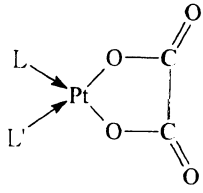
The results of antimicrobial activity of the complexes are listed in Table-1. From the data obtained, it is evident that some of these complexes exhibit an antimicrobial activity against the tested species of microorganisms with the concentration used. The complex **(8)** has shown a wide spectrum activity against the two gram-negative bacterial species, *E. coli* and *P. aeruginosa* and the gram-positive *S. auerus*. On comparison, the activity exhibited by **(8)** is considered to be significant against a problematic pathogenic and the most resistant



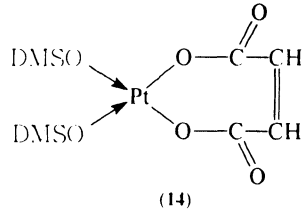
M = Pt , L = L' = DMSO (**1**)
M = Pt , L = DMSO , L' = harmaline (**2**)
M = Pd , L = DMSO , L' = harmaline (**3**)
M = Pt , L = DMSO , L' = harmine (**4**)
M = Pd , L = DMSO , L' = harmine (**5**)
M = Pt , L = Pyrazole , L' = harmine (**6**)



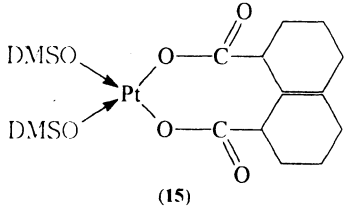
M = Pt , L = L' = DMSO (**7**)
M = Pd , L = L' = DMSO (**8**)
M = Pt , L = DMSO , L' = harmaline (**9**)
M = Pt , L = DMSO , L' = harmine (**10**)
M = Pt , L = L' = Pyrazole (**11**)



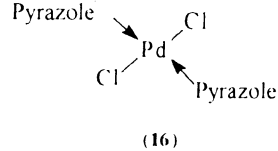
L = L' = DMSO (**12**)
L = DMSO , L' = harmaline (**13**)



(**14**)



(**15**)



(**16**)

Fig. 1. Platinum(II) and palladium(II) complexes used in this study

bacteria used in this study *i.e.*, *P. aeruginosa.* The complex **(10)** also showed a significant activity against the gram-negative bacteria *E. coli.* Although the free ligand 3,5-dimethylpyrazole showed a significant activity against *E. coli,* its complex **(6)** showed some good activity against *P. aeruginosa* and in the contrary, its complex **(11)** showed no activity against any of the bacterial species used. The rest of the complexes did not show any activity against the bacterial or fungal species used in this study, which could be due to some structure-activity relationship.

The known anticancer drugs (Fig. 2) were also examined for their antimicrobial activity as they have structures similar to the complexes tested. However, they did not show any inhibition to the bacterial species used apart of oxaliplatin which showed some weak activity against *E. coli* (Table-1).

Moreover, neither the platinum and palladium complexes used in this study nor the three anticancer drugs showed any activity against the fungal species *C. albicans.*

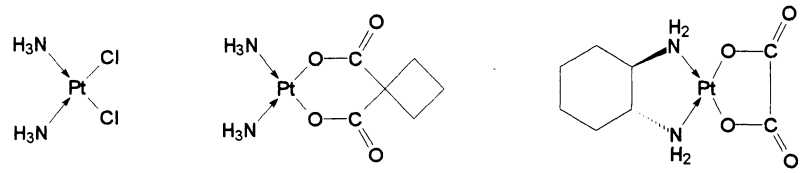


Fig. 2. The known anticancer drugs used in this study

TABLE-1
ANTIMICROBIAL ACTIVITY [INHIBITION ZONE (MM)] OF THE COMPLEXES (10 μg/mL) USED IN THIS STUDY

Compound	*E. coli*	P. aeruginosa	S. aureus	C. albicans
(1)	—	—	—	—
(2)	—	—	—	—
(3)	—	—	—	—
(4)	—	—	—	—
(5)	—	—	—	—
(6)	—	10	—	—
(7)	—	—	—	—
(8)	16	10	11	—
(9)	—	—	—	—
(10)	15	—	—	—
(11)	—	—	—	—
(12)	—	—	—	—
(13)	—	—	—	—
(14)	—	—	—	—
(15)	—	—	—	—
(16)	—	—	—	—
Pyrazole	12	—	—	—
Cisplatin	—	—	—	—
Carboplatin	—	—	—	—
Oxaliplatin	10	—	—	—
Ciprofloxacin	21	21	21	—
Miconazole	—	—	—	20

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