Research Article

From Synthesis to Biological Impact of Pd (II) Complexes: Synthesis, Characterization, and Antimicrobial and Scavenging Activity

Nitin Kumar Sharma, Rakesh Kumar Ameta, and Man Singh

School of Chemical Sciences, Central University of Gujarat, Gandhinagar 382030, India

Correspondence should be addressed to Man Singh; mansingh50@hotmail.com

Received 12 October 2015; Accepted 23 February 2016

Academic Editor: Robert J. Linhardt

Copyright © 2016 Nitin Kumar Sharma et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The Pd (II) complexes with a series of halosubstituted benzylamine ligands (BLs) have been synthesized and characterized with different spectroscopic technique such as FTIR, UV/Vis, LCMS, $^1$H, and $^{13}$C NMR. Their molecular sustainability in different solvents such as DMSO, DMSO : H$_2$O, and DMSO : PBS at physiological condition (pH 7.2) was determined by UV/Vis spectrophotometer. The in vitro antibacterial and antifungal activities of the complexes were investigated against Gram-positive and Gram-negative microbes and two different fungi indicated their significant biological potential. Additionally, their antioxidant activity has been analyzed with DPPH$^\cdot$ free radical through spectrophotometric method and the result inferred them as an antioxidant. The stronger antibacterial and antioxidant activities of the synthesized complexes suggested them as a stronger antimicrobial agent. Our study advances the biological importance of palladium (II) amine complexes in the field of antimicrobial and antioxidant activities.

1. Introduction

After a tremendous discovery of cisplatin, the synthesis and biological evaluation of new transition metal-based compounds are fields of growing interest [1]. The palladium (II) as nonplatinum metal complexes highly attracted the researchers because of its significant biological activity as well as lower side effects along with higher lipophilicity or solubility compared to cisplatin [2–5]. Palladium metal is a suitable candidate for metallo drugs because it displays structural properties similar to those of platinum and also exhibits promising in vitro cytotoxicity. Numerous Pd (II) complexes with different benzylamine ligands have been synthesized and their interesting in vitro biological activities have been reported [6, 7]. The antimicrobial activity of different palladium (II) complexes on the growth and metabolism of various groups of microorganisms has been studied and reported elsewhere. Garoufis et al. reviewed numerous scientific papers on antiviral, antibacterial, and antifungal activity of Pd (II) complexes with different types of ligands (sulfur and nitrogen donor ligands, Schiff base ligands, and different drugs as ligands) [8]. There are other interesting works which are reported recently in the literature showing different intensities of palladium complex activity on various species of bacteria and fungi [9–15]. In view of the growing cases of drug resistance of microorganisms it is urgent to search for more biospecific antifungal, less toxic agents. Metal-based drugs might answer this claim, representing an alternative therapeutic route. In this context, the discovery of nonplatinum based metal complexes came into consideration [16].

The aim of this paper is to synthesize new series of palladium (II) complexes and evaluate their in vitro antibacterial and antifungal activities against different microbes. The main aim of this research is focused on the biological impact of the newly synthesized Pd (II) complexes on different microorganism like Gram-positive and Gram-negative bacteria and different fungi. Hence, our study is an attempt to get overcome from microbial disease up to some extent. So
with the aforesaid objectives we have synthesized new Pd (II) with halo substituted BLs and analyzed in vitro antimicrobial, antifungal, and antioxidant activity.

2. Experimental Section

2.1. Materials and Methods. Palladium dichloride (PdCl₂), benzylamine ligands (BLs), DMSO, and ethanol (>99.5%) were purchased from Sigma Aldrich and used without further modifications. Elemental analysis was made with a Euro vector CHN analyzer, and UV/Vis spectra were recorded with a Spectro 2600 plus spectrophotometer over 200–600 nm in a 1 cm path length cuvette. FTIR (Perkin Elmer) spectra were taken with KBr palate where polystyrene thin film was used as a calibration standard.¹ H and ¹³C NMR spectra were recorded in DMSO-d₆ (NMR, 99.999%) with a Bruker- Biospin Avance-III 500 MHz FT-NMR spectrometer. Mass spectra were obtained with PE SCIEX API 165 with +ve ESI mode with ammonium acetate and acetonitrile in 1:9 ν/ν ratio as mobile phase. The molecular sustainability of Pd (II) complexes was determined by preparing a solution in DMSO, DMSO : water, and DMSO : phosphate buffer of pH 7.2. Buffer solution was prepared by adding 70 mL 0.1 M aequous NaOH to 0.1 M aequous KBr-P₄O₆ solution. The pH of a resultant buffer was checked with RS-232 modelled CyberScan pH 2100, EUTECH pH meter.

2.2. General Consideration for Synthesis. Initially, PdCl₂ and BLs (molar ratio 1:2, resp.) were separately dissolved in freshly prepared solvent (absolute ethanol and Milli-Q water in 1:1.5) using 1 MLH magnetic stirrer. Then, the BLs solutions were added dropwise to metal compound solution with continuous stirring at room temperature. After 10 h, the mixture turned from light red brown to greenish color and after 16 h, precipitates were formed. The precipitates were filtered off, washed several times with chilled water/ethanol in 1:1 ratio, and kept overnight in vacuum oven at room temperature for absolute dryness.

2.3. Characterization Data

2.3.1. Complex 1: C₁₄H₁₅N₂Cl₃Pd [Pd₂CBA]. Yield: 0.1492 g, 67.615%. Elemental analysis, found: C, 39.65; H, 3.57; N, 6, 61%. Calcd for C₁₄H₁₅N₂Cl₃Pd: C, 40.01; H, 3.98; N, 7.88%. IR (KBr): νmax/cm⁻¹: 3273 and 3226 (NH₂), 1497 and 1457 (Ph, C=C), 734–736 (1H, d, PhH, J = 7.3 Hz), 743–745 (1H, d, PhH, J = 6.5 Hz) and 757–759 (1H, s, PhH).¹³C NMR (125 MHz; DMSO-d₆; MeSi) δ 3.74–3.80 (2H, s, PhCH₂NH₂), 4.06–4.10 (2H, s, PhCH₂NH₂), 7.43–7.45 (1H, d, PhH, J = 7.3 Hz), 772–775 (1H, d, PhH, J = 6.5 Hz) and 732–736 (1H, t, PhH).¹ H NMR (500 MHz; DMSO-d₆; MeSi) δ 3.80–3.84 (2H, s, PhCH₂NH₂), 4.06–4.10 (2H, s, PhCH₂NH₂), 7.43–7.45 (1H, d, PhH, J = 7.3 Hz), 772–775 (1H, d, PhH, J = 6.5 Hz) and 732–736 (1H, t, PhH). ¹ H NMR (500 MHz; DMSO-d₆; MeSi) δ 3.80–3.84 (2H, s, PhCH₂NH₂), 4.06–4.10 (2H, s, PhCH₂NH₂), 7.43–7.45 (1H, d, PhH, J = 7.3 Hz), 772–775 (1H, d, PhH, J = 6.5 Hz) and 732–736 (1H, t, PhH). ¹ H NMR (500 MHz; DMSO-d₆; MeSi) δ 3.80–3.84 (2H, s, PhCH₂NH₂), 4.06–4.10 (2H, s, PhCH₂NH₂), 7.43–7.45 (1H, d, PhH, J = 7.3 Hz), 772–775 (1H, d, PhH, J = 6.5 Hz) and 732–736 (1H, t, PhH).

2.3.2. Complex 2: C₁₄H₁₅N₂Cl₃Pd [Pd₂CBA]. Yield: 0.1492 g, 67.615%. Elemental analysis, found: C, 39.88; H, 3.84; N, 6.66%. Calcd for C₁₄H₁₅N₂Cl₃Pd: C, 40.22; H, 4.93; N, 6.88%. IR (KBr): νmax/cm⁻¹: 3273 and 3226 (NH₂), 1497 and 1457 (Ph, C=C), 734–736 (1H, d, PhH, J = 7.3 Hz), 743–745 (1H, d, PhH, J = 6.5 Hz) and 757–759 (1H, s, PhH).¹³C NMR (125 MHz; DMSO-d₆; MeSi) δ 3.58–3.61 (2H, s, PhCH₂NH₂), 4.00–4.03 (2H, s, PhCH₂NH₂), 7.37–7.39 (1H, s, PhH) 7.50 (1H, d, PhH, J = 8.43 Hz, JH) 7.49–7.51 (1H, d, PhH, J = 8.23 Hz, JH).¹ H NMR (500 MHz; DMSO-d₆; MeSi) δ 4.59 (C1), 129.69 (C5), 129.47 (C4), 131.6 (C3), 136.5 (C2), and 173.6 (C6). +ve ESI-MS: 424.93 m/z [M + 1] (calc. for [C₁₄H₁₅N₂Cl₃Pd] = 424.03). UV/Vis in DMSO: λmax [ε (dm³ mol⁻¹ cm⁻¹)] = 275 (2066), 335 (265), 385 (221) nm, in DMSO : phosphate buffer (1:1): λmax [ε (dm³ mol⁻¹ cm⁻¹)] = 265 (2465) nm, in DMSO : phosphate buffer (1:1): λmax [ε (dm³ mol⁻¹ cm⁻¹)] = 265 (1514) nm.

2.3.3. Complex 3: C₁₄H₁₅N₂Cl₃Pd [Pd₃CBA]. Yield: 0.1492 g, 67.615%. Elemental analysis, found: C, 39.88; H, 3.84; N, 6.66%. Calcd for C₁₄H₁₅N₂Cl₃Pd: C, 42.85; H, 4.93; N, 6.88%. IR (KBr): νmax/cm⁻¹: 3273 and 3226 (NH₂), 1497 and 1457 (Ph, C=C), 734–736 (1H, d, PhH, J = 7.3 Hz), 743–745 (1H, d, PhH, J = 6.5 Hz) and 757–759 (1H, s, PhH).¹³C NMR (125 MHz; DMSO-d₆; MeSi) δ 45.43 (C1), 129.0 (C5), 129.2 (C4), 130.4 (C7), 132.2 (C3), 135.5 (C2), and 172.6 (C6). +ve ESI-MS: 424.93 m/z [M + 1] (calc. for [C₁₄H₁₅N₂Cl₃Pd] = 424.03). UV/Vis in DMSO: λmax [ε (dm³ mol⁻¹ cm⁻¹)] = 275 (2066), 335 (265), 385 (221) nm, in DMSO : water (1:1): λmax [ε (dm³ mol⁻¹ cm⁻¹)] = 265 (2465) nm, in DMSO : phosphate buffer (1:1): λmax [ε (dm³ mol⁻¹ cm⁻¹)] = 265 (1514) nm.

2.4. UV/Vis Spectroscopy. Electronic spectra were recorded with a Spectro 2060 plus model UV/Vis spectrophotometer from 200 to 600 nm using 1 cm path length cuvette. DMSO was used for solution preparation. The stability of compounds was determined by preparing a solution in DMSO, DMSO/water, and DMSO/phosphate buffer of pH 7.2. Buffer solution was prepared by adding 70 mL 0.1 M aequous NaOH solution to 0.1 M aequous KH₂PO₄ solution. The pH of the resultant buffer was checked with RS-232 modelled CyberScan pH 2100, EUTECH pH meter instrument. Their concentration for the UV study with DMSO, DMSO : water and DMSO : phosphate buffer of pH 7.2.

2.5. HRTEM Images and SAED Pattern. The TEM images of the Pd2MBA were taken by HRTEM JEOL JEM 2100 at different magnification. The sample analysis was done by dispersing the sample in water and then dropped on carbon coated copper grid. After complete dryness of the sample on grid, the grid was inserted in specimen and then the images were taken.
3. Biological Evaluation

3.1. Microorganism Test. The synthesized palladium (II) complexes tested against 6 microbes for their biological potential. They screened their antibacterial activities against human pathogenic bacteria, namely, Gram-negative (*Escherichia coli*; NCIM 2109 and *Pseudomonas aeruginosa*; NCIM 2036) and Gram-positive (*Staphylococcus aureus*; NCIM 2079 and *Bacillus subtilis*; NCIM 2250) bacterial strains and two fungal strains (*Candida albicans*; NCIM 3471 and *Aspergillus niger*; NCIM 545) by Kirby Beurs Disc Diffusion Method using DMSO as solvent at 200 μg mL⁻¹ on Mueller Hinton Agar media. The zone of inhibition was measured in millimetre (mm) after 24h incubation at 37°C and pH 7.4. The zones of inhibition were compared with the standard drugs chloramphenicol (10 μg) and ciprofloxacin (10 μg). Discs with only DMSO were used as positive control.

3.2. Antioxidant Activities. Antioxidant activities have been studied on free radical scavenging of stable 1-2, 5- diphenyl-2-picrylhydrazyl (DPPH∙). For this purpose stock solution of complexes and DPPH∙ (0.002%) were mixed in DMSO + water (1:1) for Pd (II) complexes. For sample preparation, the DPPH∙ solution was mixed with a complex solution in 1:1, followed by vigorous shaking, and thereafter kept for incubation of 30 min in dark. The UV absorbance was measured at 517 nm with UV/Vis spectrophotometer and a decrease in DPPH∙ absorbance was noted which indicates a radical-scavenging activity calculated with the following equation:

\[ \text{Scavenging activity}\% = \left( \frac{A_o - A_s}{A_o} \right) \times 100. \]  

4. Results and Discussion

4.1. Synthesis and Characterization. PdCl(BLs)₂ have been synthesized allowing reaction of PdCl₂ with different BLs (Figure 1) in 1:2 molar ratio over 16 h as per Reaction Scheme. The ethanol + water solution in 1:1.5 ratios was used for the synthesis of all complexes solution.

**Reaction Scheme.** Synthesis of Pd(II) complexes is as follows:

\[
PdCl_2 + 2BLs \xrightarrow{\text{Aqueous } C_2H_5OH} \text{16 h/rt} \xrightarrow{16\, h/rt} PdCl(BLs)_2
\]

The 3300 to 3119 cm⁻¹ stretching frequencies inferred presence of NH₂ of benzylamine ligands in the complexes and similarly from 1497 to 1453 cm⁻¹ predicted C=C in phenyl ring. The 495.92 to 438.78 cm⁻¹ and 380–348 cm⁻¹ bands indicate the Pd–N and Pd–Cl bands, respectively [17, 18]. In ¹HN M R, 2H of –NH₂ and PhCH₂ appeared at δ 4.03 to 4.10 and 3.58 to 3.80, respectively, with singlet for all complexes. The aromatic protons appeared with their specific peak from δ 7.32 to 7.59 (J = 7 to 8). In ¹³C NMR, the benzyl carbon (PhCH₂) appeared at δ 45.43 to 45.39 for all the (PdCl(BLs)₂) complexes [19]. The aromatic ortho, meta, and para –Cl attached carbon appeared within δ 145.72 to 128.6 for the complexes. The carbon of –Cl at ortho, meta, and para appeared at δ 132.2, 128.5, and 129.69 ppm, respectively. The +ve ESI mass spectra of Pd complexes have found [M + 1] confirming their molecular mass. The UV/Vis absorption from 265 to 270 nm and ¹HNMR coupling constant between 5 and 9 MHz have confirmed their trans geometry (Figure 2) [20–22].

4.2. Absorption Spectroscopy. To investigate a solid state structure retained in solution, the UV/Vis spectral behaviour was investigated in DMSO and DMSO + water as well as in DMSO + phosphate buffer for PdCl(BLs)₂. The overall patterns of spectra for complexes solution were found similar to different mediums to ensure their molecular sustainability.
Figure 2: Structure of synthesized Pd (II) complexes.

Figure 3: UV spectra of Pd (II) complexes in DMSO at 0.001 M.

Figure 4: UV spectra of Pd (II) complexes in DMSO : water.

Figure 5: UV spectra of Pd (II) complexes in DMSO : phosphate buffer at 7.2 pH.

4.3. SAED Pattern through HRTEM. The TEM images reports from the SAED pattern were taken at different magnification suggesting the presence of different elements which are semicrystalline and homogeneous in shape (Figure 6, ESI Figures S1 and S2 in Supplementary Material available online at http://dx.doi.org/10.1155/2016/4359375). The proper alignment is not seen in the rings which indicate that the complex is not completely crystalline but a clear formation of rings suggesting the semicrystalline nature of complexes.

4.4. Biological Potential

4.4.1. Antimicrobial Activity. Biological evaluation was made by Kirby Beurs Disc Diffusion Method as per standard procedure [24, 25]. The PdCl(BLs)$_2$ gave best response against Gram-negative (E. coli and P. aeruginosa) and Gram-positive (S. aureus and B. subtilis) microbes (Figure 7, Table 1). All Pd (II) complexes are not effective against the fungal microbes (C. albicans and A. niger) and they have not shown any zone of inhibition. The biological evaluation inferred that the PdCl(BLs)$_2$ showed greater activity against positive organisms and less activity against negative organisms.
4.4.2. Antioxidant Activities. The scavenging activities have been investigated to support the biological potential of PdCl(BLs)₂ [26, 27]. The antioxidant activities have been studied with analyzing the decrease in absorbance or scavenging effect of a stable free DPPH⁻ as per standard procedure for the PdCl(BLs)₂ [28, 29]. The percentage scavenging activity of Pd (II) complexes has been determined in a concentration-dependent mode in comparison to the DPPH⁻ absorption at 517 nm [30–32]. The DPPH⁻ free radical’s absorption at 517 nm with DMSO was 0.906 for Pd (II) complexes. From 50 to 250 μM with an interval of 50 μM, complexes have expressed a decrease in absorption (Figure 8) that characterized them as an antioxidant.

The highest 94.49, 72.36, and 70.79% for Pd2CBA, Pd3CBA, and Pd4CBA, respectively, inferred Pd2CBA a strong antioxidant among them. The obtained values also compared with the control ascorbic acid which inferred that the results are very closer to control range. Thus, the antioxidant activities of Pd complexes have inferred their significance in medicinal as well as material sciences.

5. Conclusion

Genome studies have provided a better understanding of the closer distance between the microbial kingdom and the human species. The synthesized PdCl(BLs)₃ complexes showed selective and moderate activity against different microbes and the interesting results were obtained for Gram-positive species, which are common in the environment. Apart from their microbial studies, the complexes have also expressed significant free radical-scavenging activities acting as antioxidants and could be used for medicinal purposes. However, in present study, we have focused on their antimicrobial and antioxidant activities and their other activities relevant to medical, biophysical, and biochemical processes are being pursued. The anticancer activity on suitable cell line
Figure 7: Antimicrobial studies of Pd (II) complexes.

Figure 8: Free radical-scavenging activities of synthesized complexes.
against solid tumours, apoptosis, and DNA binding studies are under progress.

**Competing Interests**

The authors declare that there are no competing interests regarding the publication of this paper.

**Acknowledgments**

The authors are thankful to Central University of Gujarat, Gandhinagar, for financial and infrastructural support and experimental facilities.

**References**

[1] B. Taqui Khan, K. Najmuddin, S. Shamsuddin, K. Annapoorna, and J. Bhatt, "Synthesis, antimicrobial, and antitumor activity of a series of palladium(II) mixed ligand complexes," *Journal of Inorganic Biochemistry*, vol. 44, no. 1, pp. 55–63, 1991.

[2] L. Tušek-Božič, A. Furlani, V. Scarcia, E. Clercq, and J. Balzarini, "Spectroscopic and biological properties of palladium(II) complexes of ethyl 2-quinoxylmethylphosphonate," *Journal of Inorganic Biochemistry*, vol. 72, no. 3-4, pp. 201–210, 1998.

[3] M. Galanski, "Recent developments in the field of anticancer platinum complexes," *Recent Patents on Anti-Cancer Drug Discovery*, vol. 1, no. 2, pp. 285–295, 2006.

[4] E. Gao, C. Liu, M. Zhu, H. Lin, Q. Wu, and L. Liu, "Current development of Pd(II) complexes as potential antimutagen agents," *Anti-Cancer Agents in Medicinal Chemistry*, vol. 9, no. 3, pp. 356–368, 2009.

[5] K. S. Prasad, L. S. Kumar, S. Chandan, R. M. Naveen Kumar, and H. D. Revanasiddappa, "Palladium(II) complexes as biologically potent metallo-drugs: synthesis, spectral characterization, DNA interaction studies and antibacterial activity," *Spectrochimica Acta. Part A*, vol. 107, pp. 108–116, 2013.

[6] C. Navarro-Raninger, F. Zamora, J. R. Masaguer, J. M. Pérez, V. M. González, and C. Alonso, "Palladium(II) compounds of putrescine and spermine. Synthesis, characterization, and DNA-binding and antitumor properties," *Journal of Inorganic Biochemistry*, vol. 52, no. 1, pp. 37–49, 1993.

[7] I. Brudzińska, Y. Mikata, M. Obata, C. Ohtsuki, and S. Yano, "Synthesis, structural characterization, and antitumor activity of palladium(II) complexes containing a sugar unit," *Bioorganic and Medicinal Chemistry Letters*, vol. 14, no. 10, pp. 2533–2536, 2004.

[8] A. Garoufsis, S. K. Hadjikakou, and N. Hadjiliadis, "Palladium coordination compounds as anti-viral, anti-fungal, anti-microbial and anti-tumor agents," *Coordination Chemistry Reviews*, vol. 253, no. 9-10, pp. 1384–1397, 2009.

[9] W. Guerra, E. de Andrade Azevedo, A. R. de Souza Monteiro et al., "Synthesis, characterization, and antibacterial activity of three palladium(II) complexes of tetracyclines," *Journal of Inorganic Biochemistry*, vol. 99, no. 12, pp. 2348–2354, 2005.

[10] L. M. M. Vieira, M. V. de Almeida, M. C. S. Lourenço, F. A. F. M. Bezerra, and A. P. S. Fontes, "Synthesis and antituber-bercular activity of palladium and platinum complexes with fluoroquinolones," *European Journal of Medicinal Chemistry*, vol. 44, no. 10, pp. 4107–4111, 2009.

[11] D. Kovala-Demertzzi, A. M. Demertzis, J. R. Miller, C. Papadopoulos, C. Dodorou, and G. Filouis, "Platinum(II) complexes with 2-acetyl pyridine thiosemicarbazone: synthesis, crystal structure, spectral properties, antimicrobial and antitumour activity," *Journal of Inorganic Biochemistry*, vol. 86, no. 2-3, pp. 555–563, 2001.

[12] R. R. Coombs, M. K. Ringer, J. M. Blacquiere et al., "Palladium(II) Schiff base complexes derived from sulfanilamides and aminobenzothiazoles," *Transition Metal Chemistry*, vol. 30, no. 4, pp. 411–418, 2005.

[13] I. Kiziclik, Y. D. Kurt, B. Akkurt et al., "Antimicrobial activity of a series of thiosemicarbazones and their Pd(II) complexes," *Folia Microbiologica*, vol. 52, no. 1, pp. 15–25, 2007.

[14] N. M. Aghatabay, M. Somer, M. Senel, B. Dulger, and F. Gucin, "Raman, FT-IR, NMR spectroscopic data and antimicrobial activity of bis[µ2-(benzimidazol-2-yl)-2-ethanethiolato-N,N,S,S-chloro-palladium(II)] dimer, [{µ2-CH2CH2NHNCC6H5}2PtCl2], C2H4OH complex," *European Journal of Medicinal Chemistry*, vol. 42, no. 8, pp. 1069–1075, 2007.

[15] M. K. Biyala, K. Sharma, M. Swami, N. Fahmi, and R. V. Singh, "Spectral and biocidal studies of palladium(II) and platinum(II) complexes with monobasic bidentate Schiff bases," *Transition Metal Chemistry*, vol. 33, no. 3, pp. 377–381, 2008.

[16] K. Lemma, S. K. C. Elmoth, and L. I. Elding, "Substitution reactions of [Pt(dien)Cl]2, [Pt(dien)(GSMe)]2+ , cis-[PtCl3(NH3)2] and cis-[Pt(NH3)4(GSMe)2]+ (GSMe = S-methylglutathione) with some sulfur-bonding chemoprotective agents," *Journal of the Chemical Society. Dalton Transactions*, no. 7, pp. 1281–1286, 2002.

[17] Y. Sun, S. Gou, R. Yin, and P. Jiang, "Synthesis, antiproliferative activity and DNA binding study of mixed ammine/cyclohexylamine platinum(II) complexes with 1-(substituted benzyl) azetidine-3, 3-dicarboxylates," *European Journal of Medicinal Chemistry*, vol. 46, no. 10, pp. 5146–5153, 2011.

[18] A. D. Allen and C. V. Senoff, "Preparation and infrared spectra of some ammine complexes of ruthenium(II) and ruthenium(III)," *Canadian Journal of Chemistry*, vol. 45, no. 12, pp. 1337–1341, 1967.

[19] N. D. Ball, J. W. Kampf, and M. S. Sanford, "Synthesis and reactivity of palladium(II) fluoride complexes containing nitrogen-donor ligands," *Dalton Transactions*, vol. 39, no. 2, pp. 632–640, 2010.

[20] L. E. Mihajlović, A. Savić, J. Poljarević et al., "Novel methylene modified cyclohexyl ethylenediamine-N′,N′-dicarboxylates and their platinum (IV) complexes. Influence on biological activity," *Journal of Inorganic Biochemistry*, vol. 109, pp. 40–48, 2012.

[21] H. Varbanov, S. M. Valiahdi, A. A. Legin et al., "Synthesis and characterization of novel bis(carboxylato)dichloridobis(ethylamine)platinum(IV) complexes with higher cytotoxicity than cisplatin," *European Journal of Medicinal Chemistry*, vol. 46, no. 11, pp. 5456–5464, 2011.

[22] M. Navarro, W. Castro, A. R. Higuera-Padilla et al., "Synthesis, characterization and biological activity of trans-platinum(II) complexes with chloroquine," *Journal of Inorganic Biochemistry*, vol. 105, no. 12, pp. 1684–1691, 2011.

[23] L. Trynda, D. Kwiatkowska, and W. Tyran, "Platinum complexes and pyruvate kinase activity," *General Physiology and Biophysics*, vol. 17, no. 1, pp. 25–36, 1998.

[24] N. K. Sharma, R. K. Ameta, and M. Singh, "Biological impact of Pd (II) complexes: synthesis, spectral characterization, in vitro anticancer, CT-DNA binding, and antioxidant activities,"
[25] N. K. Sharma, R. K. Ameta, and M. Singh, "Synthesis, characterization, anticancer, DNA binding and antioxidant studies of benzylamine supported Pd (II) complex," Cancer Medicine & Anti Cancer Drugs, vol. 1, article 101, 2015.

[26] D. Meyerstein, "Comment on the section: "Antioxidant measurements and hydroxyl radical scavenging activity" in synthesis, characterization, DNA binding, and antioxidant activities of four copper(II) complexes containing N-(3-hydroxybenzyl)-amino amide ligands, by Zhi Li-Hua, Wu Wei-Na, Wang Yuan, Sun Guang, J. Coord. Chem., 66, 227 (2013)," Journal of Coordination Chemistry, vol. 66, no. 12, pp. 2076–2078, 2013.

[27] K. Jomova, S. Baros, and M. Valko, "Redox active metal-induced oxidative stress in biological systems," Transition Metal Chemistry, vol. 37, no. 2, pp. 127–134, 2012.

[28] Z. A. Taha, A. M. Ajlouni, W. Al Momani, and A. A. Al-Ghzawi, "Syntheses, characterization, biological activities and photophysical properties of lanthanides complexes with a tetradentate Schiff base ligand," Spectrochimica Acta. Part A, vol. 81, no. 1, pp. 570–577, 2011.

[29] R. Trivedi, S. B. Deepthi, L. Giribabu et al., "Synthesis, crystal structure, electronic spectroscopy, electrochemistry and biological studies of ferrocene–carbohydrate conjugates," European Journal of Inorganic Chemistry, vol. 13, pp. 2267–2277, 2012.

[30] D. Suh and J. B. Chaires, "Criteria for the mode of binding of DNA binding agents," Bioorganic and Medicinal Chemistry, vol. 3, no. 6, pp. 723–728, 1995.

[31] F.-H. Li, G.-H. Zhao, H.-X. Wu et al., "Synthesis, characterization and biological activity of lanthanum(III) complexes containing 2-methylene–1,10-phenanthroline units bridged by aliphatic diamines," Journal of Inorganic Biochemistry, vol. 100, no. 1, pp. 36–43, 2006.

[32] M. E. Howe-Grant and S. J. Lippard, "Aqueous platinum (II) chemistry: binding to biological molecules," Metal Ions in Biological Systems, vol. 20, pp. 63–125, 1980.