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Platinum(II) complexes of S-benzyldithiocarbazate based Schiff base ligand: Green synthesis, characterization, cytotoxic and antioxidant assay

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In the present work, benzyl-2-((5-methylthiophen-2-yl)methylene)hydrazine-1-carbothiolate ligand and its platinum(II) complexes have been prepared by conventional and microwave assisted methods. Structural elucidation of the ligand and its Pt(II) complexes have been performed by elemental analysis, conductance measurements, mass spectrometry, powder XRD, FT-IR and ^{1}H NMR spectroscopic methods. On the basis of analytical and spectral data, a square planar geometry has been suggested for the metal complexes. Starting material ($PtCl_2$), Ligand (LH), metal complexes $[Pt(L)_2]$ and $[Pt(LH)_2]Cl_2$ have been screened for *in vitro* cytotoxic and antioxidant activity. Cytotoxic activity has been performed by MTT[3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay against cervical cancer (HeLa) cell line and human breast adenocarcinoma (MCF-7) cell line. Cisplatin has been used as the standard drug. $[Pt(LH)_2]Cl_2$ complex have shown better cytotoxicity in comparison to ligand and other complex with IC_{50} values of 72.76 µM and 59.93 µM against HeLa and MCF-7 respectively. The antioxidant activity has been measured in terms of radical scavenging ability using the stable radical DPPH. Ascorbic acid has been used as positive control and methanol is used as negative control. The ligand shows excellent antioxidant activity with 70.82% DPPH inhibition.

Keywords: S-Benzyldithiocarbazate, Pt(II) complexes, Cytotoxic activity, Antioxidant activity

Schiff bases are prepared by condensation reaction between an aldehyde and primary amine. These are characterized by the presence of an imine group[1]. Platinum complexes of Schiff base ligands have played a significant role in the progress of coordination chemistry[2]. Nirogen-Sulphur/Oxygen containing Schiff bases have been widely studied since they show important biological and pharmacological activities[3-10]. In recent years, several studies have been carried out on metal complexes possessing sulphur and nitrogen donor ligands due to their extraordinary structural and biological properties. S-Methyldithiocarbazate and S-benzyldithiocarbazate ligands due to their specific structure and presence of sulphur and nitrogen atoms in them show many biological applications like anticancer, antifungal, antibacterial, antioxidant and many others[11-18]. When these ligands combine with metal ions enhancement in the biological properties have been observed which is due to the formation of five or six membered chelate rings[19]. Eco-friendly synthesis and green applications of Schiff bases and its metal complexes are continuously being explored by the researchers all over the world. The green microwave assisted method is an energy efficient process, required less reaction time and solvent as well as yield of the products is high in comparison to thermal method[20-22]. In cancer, a group of cells start replicating in an uncontrolled fashion after mutation in genetic makeup of normal cells. It affects all body organs and systems and has been observed in all age groups. It has been a major concern to develop cytotoxic drugs. After the discovery of cisplatin, interest in metal based cytotoxic drugs have been increased[23]. Acylpyrazone – based Schiff base ligands and their Pt(II) complexes were prepared, the complexes were found to show cytotoxicity against human breast cancer cell lines SKBR3 and MDA-MB-231(Ref.24). Platinum complexes were prepared from 4-aminoantipyrine and a few substituted aldehydes. The cytotoxic activities of the complexes were studied against human cervical cancer cell line (HeLa), colon cancer cells (HCT116) and epidermal carcinoma cells (A431). Platinum complex of {(E)-4-[4-bromobenzylideneamino]-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one} ligand was found to be most active towards the cancer cell line[25]. During oxidative metabolism, reactive oxygen species are produced.

ROS are free radicals which can attack on biomolecules and induce their oxidation that result into oxidative damage such as change in protein structure, inhibition of enzymatic activity, and breakage of DNA strains. So, they need to be scavenged by cellular constituents. Antioxidants are capable of inhibiting the synthesis of free radicals as well as delaying the lipid per oxidation leading to the spoilage of food and pharmaceutical products while processing and storage stage. Antioxidants can protect the human body from ROS. Antioxidants are extensively used for food products to prevent radical chain reactions causing the deterioration of food[26-29]. Four new transition metal complexes, $[M(PPh_3)(L)].CH_3OH$ (M = Ni(II) (1), Pd(II) (2)) $[Pt(PPh_3)_2(HL)]Cl$ (3) and $[Ru(CO)(PPh_3)_2(L)]$ (4) (H_2L = 2,4-dihydroxybenzaldehyde-S-methyldithiocarbazate, PPh_3 = triphenylphosphine) have been synthesized and tested for antioxidant activity. The complex (4) exhibited the highest scavenging activity among all compounds[30].

In view of this, it was considered worthwhile to synthesize and characterize S-benzyldithiocarbazate based ligand and its platinum(II) complexes. Their cytotoxic activity was measured against HeLa and MCF-7 cancerous cell lines and antioxidant activity was studied using stable DPPH radical.

Experimental Section

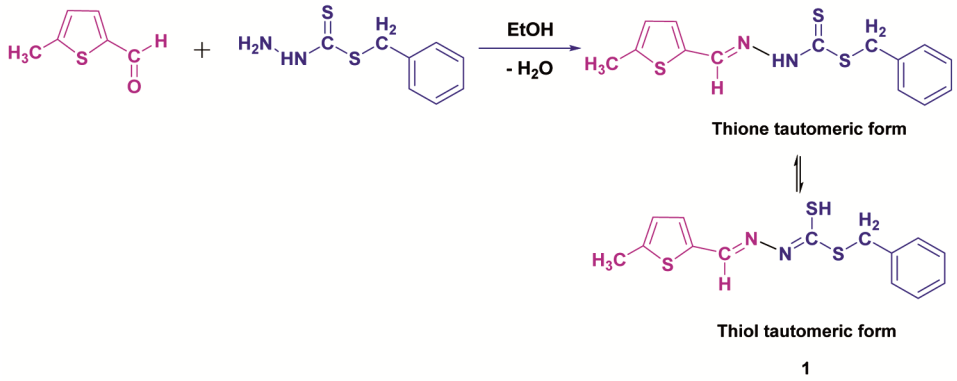
Analytical methods and physical measurements

All the chemicals and reactants used were of analytical grade. The starting material of platinum(II), $PtCl_2$ was obtained from Alfa Aesar and used as such. 5-methylthiophene-2-carbaldehyde was obtained from TCI and used as such. Ethanol was distilled and dried before use. Elemental analysis of carbon(C), hydrogen(H), Sulphur(S) and Nitrogen (N) was performed by Elemental-analyzer Model Elementar, UNICUBE at IIT Jammu. Pt(II) was estimated gravimetrically. Chlorine was estimated by Volhard's method. Mass spectra, FT-IR, ^{1}H NMR and powdered XRD were recorded from Materials Research Centre(MRC), MNIT, Jaipur . Mass spectra of the ligand and metal complexes were recorded on a Xevo G2-S Q Tof (waters, USA). ^{1}H NMR spectra of the ligand and metal complexes were obtained from an ECS 400 MHz (JEOL) NMR spectrometer. IR Spectra of the ligand and metal complexes were recorded as KBr pellets on a FT-IR Spectrum 2(Perkin Elmer) of range 4100 to 400 cm^{-1}. Powdered XRD was recorded on an X-ray diffractometer Panalytical X Pert-Pro. UV-visible spectra of metal complexes were recorded on a Shimadzu UV-2600 universal spectrophotometer from Manipal University, Jaipur. Conductance measurements were made with a conductivity meter- model cc-601. Microwave assisted synthesis was performed in a microwave oven model CEM Discovery 2.0 from Rajasthan University, Jaipur.

Conventional Synthesis

Synthesis of the ligand(LH), 1

Benzyl hydrazinecarbothioate was synthesized as reported procedure[31]. Benzyl hydrazinecar bothioate(0.98g, 4.98mmol) and 5-methylthiophene-2-carbaldehyde (0.64g, 4.98mmol) were dissolved in ethanol(100mL) in 1:1 molar ratio. The mixture was heated under reflux until the final volume reduced to 1/3rd of the original volume (~ 2h). Light yellow coloured product formed, which was filtered, recrystallized with ethanol and then dried in vacuum over anhydrous $CaCl_2$. The schematic representation of the synthesis of ligand (1) is shown in Scheme 1.



Scheme 1 — Schematic representation of synthesis of ligand(**1**) (Where EtOH = Ethanol)

Benzyl-2-((5-methylthiophen-2-yl)methylene) hydrazine-1-carbothiolate, 1

Light yellow solid. Yield 78%. m.p.165°C. IR: 1586 (C=N), 1094 (C=S), 1025 cm^{-1} (N-N); ^1H NMR: δ 2.44 s (3H, Me), 4.46 s (2H, SCH_2), 6.84 - 7.42 m (aromatic protons), 8.31 s (1H, HC=N), 13.25 bs (1H, NH); MS: *m/z* $[M + H]^+$: 307.04(M+1).

Synthesis of Platinum(II) Complexes

Substitution Product, $[Pt(L)_2]$, 2

The substitution complex of platinum(II) was synthesized by refluxing $PtCl_2$(0.1g, 0.37mmol) with **1** (0.23g, 0.75 mmol) in 1:2 molar ratio in 1:1 ethanol/water solvent in the presence of few drops of NH_3 solution until the *p*H become cal. 8 for 4 h. Light orange solid was formed which was filtered, washed with ethanol/water and then dried in vacuum over anhydrous $CaCl_2$.

Di{Benzyl-2-((5-methylthiophen-2-yl)methylene) hydrazine-1-carbothiolate} platinum(II)

Light orange solid. Yield 74%. m.p.200°C. IR: 1579 (C=N), 1027 cm^{-1} (N-N); ^1H NMR: δ 2.41 s (6H, Me), 4.61 s (4H, SCH_2), 7.23- 7.82 m (aromatic protons), 8.42 s (2H, HC=N); MS: *m/z* $[M+ H]^+$ 806.91 (M+1).

Addition Product, $[Pt(LH)_2]Cl_2$, 3

The addition complex of platinum(II) was synthesized by stirring $PtCl_2$(0.1g, 0.37mmol) with LH(0.23g, 0.75 mmol) in 1:2 molar ratio in 1:1 ethanol/water in the presence of few drops of HCl for 5 h. Dark orange solid was formed which was filtered, washed with ethanol/water and then dried in vacuum over anhydrous $CaCl_2$.

Di{Benzyl-2-((5-methylthiophen-2-yl)methylene) hydrazine-1-carbothiolate} platinum(II) chloride

Dark orange solid. Yield 72%. m.p.215°C. IR: 1580 (C=N), 1028 cm^{-1} (N-N); ^1H NMR: δ 2.41 s (6H, Me), 4.61 s (4H, SCH_2), 7.24- 7.85 m (aromatic protons), 8.45 s (2H, HC=N); MS: *m/z* $[M + H]^+$ 879.90(M+1). Proposed structure of metal complexes (**2,3**) is given in Fig. 1.

Microwave Assisted Synthesis

The products(**1**,**2**) were also prepared by microwave assisted method. The reactions carried out by microwave assisted method completed in short duration and produced higher yield of products. A Comparison between conventional and microwave assisted synthesis is given in Table 1.

Synthesis of ligand, (LH), 1

The ligand Benzyl-2-((5-methylthiophen-2-yl)methylene)hydrazine-1-carbothiolate (**1**) was synthesized by microwave irridating 5-Methylthiophene-2-carboxaldehyde (0.02g, 0.142mmol) with S-benzyldithiocarbazate (0.028g, 0.141mmol) in microwave oven in 1:1 molar ratio in 4mL absolute ethanol for ~ 5 min. Light yellow product formed, which were filtered, washed with ethanol and then dried in vacuum over anhydrous

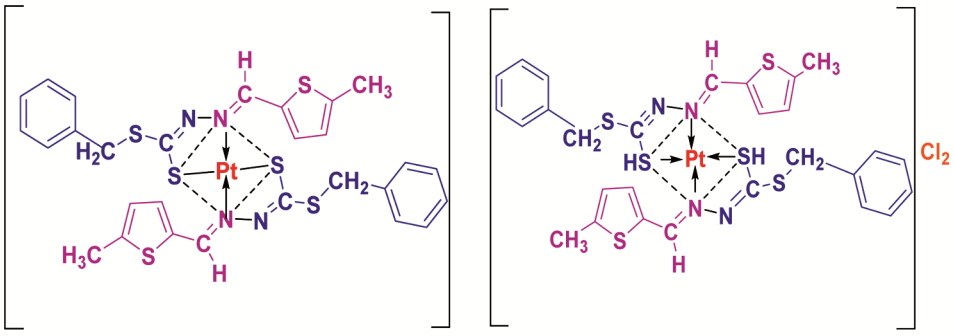


Fig. 1 — Proposed structure of metal complexes(**2**,**3**)

Table 1 — Comparison between conventional synthesis and microwave assisted synthesis

Compd	Yield (%)		Solvent (mL)		Duration (h/min)	
	Conventional	Microwave	Conventional	Microwave	Conventional (h)	Microwave (min)
1	78	86	100	4	2	5
2	74	84	40	3	4	4
3	72	82	40	3	5	5

Table 2 — Physical and analytical data of ligand **1** and metal complexes **2**, **3**

Compd	Empirical Formula	Colour	Molecular Weight Found (M+1) (Calcd)	m.p. (°C)
1	$C_{14}H_{14}N_2S_3$	Light Yellow	307.04	165
	–	–	(306.46)	–
2	$C_{28}H_{26}N_4PtS_6$	Light Orange	806.91	200
	–	–	(805.99)	–
3	$C_{28}H_{28}Cl_2N_4PtS_6$	Dark Orange	878.90	215
	–	–	(879.90)	–

Table 3 — Elemental analysis of ligand **1** and metal complexes **2**, **3**

	Elemental Analysis Found % (Calcd)					
Compd	C	H	N	S	Pt	Cl
1	54.87	4.60	9.14	31.38	–	–
	(54.85)	(4.58)	(9.12)	(31.36)		
2	41.73	3.25	6.95	23.87	24.20	–
	(41.70)	(3.23)	(6.93)	(23.85)	(24.18)	
3	38.26	3.21	6.37	21.89	22.20	8.07
	(38.25)	(3.18)	(6.35)	(21.87)	(22.19)	(8.05)

$CaCl_2$. The yield of the ligand formed from microwave assisted is 86%.

Synthesis of substitution product, $[Pt(L)_2]$, 2

The substitution complex of platinum(II) was synthesized by microwave irridating $PtCl_2$(0.01g, 0.03mmol) with LH(0.02g, 0.07 mmol) in 1:2 molar ratio in 1:1 ethanol/water in the presence of NH_3 solution until the *p*H become ~8 for 4 min. Light orange solid was formed which was filtered, washed with ethanol and then dried in vacuum over anhydrous $CaCl_2$. The yield of the substitution product formed from microwave assisted is 84%.

Synthesis of addition product, $[Pt(LH)_2]Cl_2$, 3

The addition complex of platinum(II) was synthesized by microwave irridating $PtCl_2$(0.01g, 0.03mmol) with LH(0.02g, 0.07mmol) in 1:2 molar ratio in 1:1 ethanol/water in the presence of the presence of few drops of concentrated HCl for 5 min. Dark orange solid was formed, which was filtered, washed with ethanol/water and then dried in vacuum over anhydrous $CaCl_2$. The Yield of the addition product formed from microwave assisted synthesis is 82%.

Physical and analytical data of ligand(**1**) and metal complexes(**2**,**3**) is given in Table 2. Elemental analysis of ligand(**1**) and metal complexes(**2**,**3**) is given in Table 3.

Results and Discussion

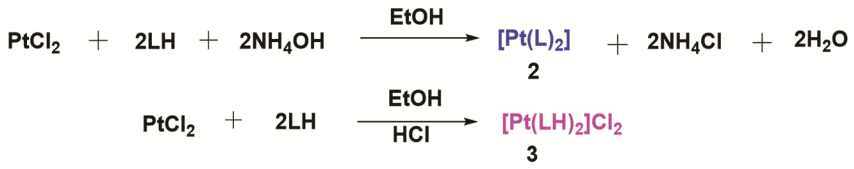
The Reactions of Benzyl-2-((5-methylthiophen-2-yl)methylene)hydrazine-1-carbothiolate(**1**) with $PtCl_2$ were performed in 1:2 molar ratios in 1:1 ethanol and water solutions. $PtCl_2$ combines with ligand in the presence of NH_3 solution to form complexes of the type $[Pt(L)_2]$ Whereas $PtCl_2$ combines with ligand in the presence of few drops of concentrated HCl to form complexes of the type $[Pt(LH)_2Cl_2]$. Synthetic outline of formation of metal complexes is given in Scheme 2.

Compounds **1**, **2**, and **3** obtained from both conventional and microwave methods were characterized separately for comparison purposes. The spectral data obtained from both the methods were found to be same.

The metal complexes are obtained as colourful solids. These are found soluble in dimethylformamide(DMF) and dimethylsulphoxide (DMSO) and insoluble in common organic solvents like methanol and ethanol. The non electrolytic behavior of substitution product of platinum is suggested due to molar conductivity values in 10^{-3}M solutions which are in the range 15-17 $ohm^{-1}cm^2mol^{-1}$ in dry DMF. The electrolytic behaviour of addition product of platinum which is 1:2 electrolytes is suggested due to molar conductivity values in the range 215-220 $ohm^{-1}cm^2mol^{-1}$in dry DMF.

FT-IR spectra

As KBr pellets, the FT-IR spectra of ligand(**1**) and its metal complexes (**2**,**3**) were scanned. An examination of the **1**, **2**, and **3** IR spectra was done in comparison, confirming the formation of metal complexes. The broad, medium-intense absorption



Scheme 2 — Synthetic outline of Metal complexes

Table 4 — UV-visible spectral data of metal complexes **2**, **3**

Complexes	Transitions	Spectral Bands (cm^{-1})	Δ_1	Δ_2	Δ_3	ν_2/ν_1
2	$^1A_{1g}\rightarrow{}^1A_{2g}$	17,182	19,282	5,523	5,442	1.28
	$^1A_{1g}\rightarrow{}^1B_{1g}$	21,505	–	–	–	–
	$^1A_{1g}\rightarrow{}^1E_{1g}$	27,247	–	–	–	–
3	$^1A_{1g}\rightarrow{}^1A_{2g}$	18,348	20,448	5,323	4,777	1.26
	$^1A_{1g}\rightarrow{}^1B_{1g}$	22,471	–	–	–	–
	$^1A_{1g}\rightarrow{}^1E_{1g}$	27,548	–	–	–	–

band in the **1**'s IR spectra is located at 3092 cm^{-1} and is indicative of ν(NH) vibrations. In the metal complex spectra, this band disappeared(**2**, **3**). In the spectrum of **1**, the azomethine group ν(C=N) has a strong and sharp band that can be seen at 1586 cm^{-1}. In metal complexes, this band shifted towards lower frequency indicating coordination by the nitrogen atom of azomethine to platinum. A doublet at 2950-2837 cm^{-1} can be assigned to ν_{symm} and ν_{asymm} vibrations of –CH of S-CH_2-C_6H_5 group in **1**. The shift in the ν(N-N) stretching frequency from 1025cm^{-1} in ligand to 1027-1028 cm^{-1} in the complexes is another indication of involvement of azomethine nitrogen in complexation (Fig.S1 and Fig.S2).

Mass spectra

The molecular weight of the ligand(**1**) and its metal complexes(**2**,**3**) determined by electron impact mass spectrum are given in Table 2. In Schiff base ligand(**1**) molecular ion peak at m/z 307.04(M+1) which corresponds to $C_{14}H_{14}N_2S_3^+$. In substitution and addition complexes of platinum(**2**,**3**) molecular ion peaks at m/z 806.91(M+1), 879.90(M+1) corresponds to $C_{28}H_{26}N_4PtS_6^+$, $C_{28}H_{28}Cl_2N_4PtS_6^+$ suggesting bidentate complexes of **1**.(Fig.S3, Fig.S4 and Fig.S5).

^{1}H NMR spectra

The ^{1}H NMR spectra of benzyl-2-((5-methylthiophen-2-yl)methylene)hydrazine-1-carbothiolate ligand(**1**) and its platinum(II) complexes(**2**,**3**) were recorded in DMSO-d_6 taking TMS as an internal standard. The broad singlet appeared at δ13.25 ppm(bs) assigned to the -NH proton in **1**. This –NH signal disappeared in the spectra of metal complexes. The signal at δ8.31ppm(s) assigned to azomethine (HC=N) proton in **1**. This signal shifted slightly downfield in the metal complexes due to involvement of azomethine nitrogen in the complex formation. The signal δ4.46ppm(s) is assigned to –SCH_2 protons in **1**. The signals for aromatic protons appeared in the range from δ6.84 to 7.42ppm(m) in **1**. Signal of –CH_3 protons appeared at δ2.44ppm(s) in **1**. All of these signals shifted slightly downfield in the metal complexes which suggest noninvolvement of these groups in the complex formation. (Fig.S6, and Fig.S7).

UV-Visible spectra

The spectra of the metal complexes(**2**,**3**) were recorded in distilled DMSO. Table 4 summarizes the UV-visible spectral data of complexes. Three d-d spin allowed transitions are observed in the Pt(II) complexes. These are corresponding to transitions from $^1A_{1g}$ to $^1A_{2g}$, $^1A_{1g}$ to $^1B_{1g}$ and $^1A_{1g}$ to ^1E_g in the order of increasing energy. The d-d transitions appeared in the region 17,182 – 18,348, 21,505 – 22,471, 27,247 – 27,548 cm^{-1}. Three orbital parameters Δ_1, Δ_2 and Δ_3 were calculated by using Slater-Codon interelectronic repulsion parameters(F_2 and F_4), F_2 = 10 and F_4 = 600 cm^{-1}. The calculated values of ν_2/ν_1 are found to be extremely close to the reported values for square planar geometry[32].

Powder X-ray diffraction

Due to the solubility constraints, attempts to obtain crystals of suitable quality for an X-ray structure determination were unsuccessful for these complexes,

So an X-ray powder diffraction pattern was obtained for complex **2** to detect the degree of crystallinity in metal complex. No Sharp and distinct peak was observed for the complex. Hence the complex shows an amorphous nature. The X-ray powder diffraction data were recorded for the complex **2** over 2Θ = 0° - 100°, scan type = continuous, scan step time(s) = 0.60.

Cytotoxic Activity

The MTT Cell proliferation assay measures the cell proliferation rate and conversely, when metabolic events lead to apoptosis or necrosis, the reduction in cell viability. starting material($PtCl_2$), Ligand(**1**), metal complexes(**2**,**3**) were screened for cytotoxic activity *in vitro* by[3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide(MTT) assay against cervical cancer(HeLa) cell line and human breast adenocarcinoma (MCF-7) cell line. Cisplatin was used as the standard drug.

Preparation of test compound

Test compounds were weighed individually and dissolved in DMSO for the MTT assay. The cells were treated with a range of concentrations from 10 to 100 µg/mL, with media made up to the final concentration of 1 mg/mL.

Principle

The MTT assay is used to quantify how much mitochondrial succinate dehydrogenase reduces yellow 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT). The assay is based on the quantity of cells present and the presumption that tetrazolium cannot be reduced by dead cells or their byproducts. When MTT enters cells, it travels through the mitochondria and becomes insoluble, forming dark purple formazan crystals. The released solubilized formazan reagent is then measured spectrophotometrically at 570 nm after the cells have been solubilized in DMSO.

Procedure

Three separate experiments were conducted using triplicates of six different drug doses to assess cell viability using the MTT test. To determine the viability of the cells in cell suspension, trypsinization and the tryphan blue test were carried out. Cell counts were performed using hemocytometers. In 96-well plate culture media, 100 µL of medium is used to seed cells at a density of 5.0×10^3 cells/well, and the cells are then incubated overnight at 37°C.

Following incubation, old medium was disposed of and 100µL of fresh medium containing various test compound concentrations was added to the wells that were represented in 96-well plates. The drug solution was disposed of after 48 h, and each well was filled with fresh medium containing 0.5 mg of MTT solution per well. The plates were then incubated for 3 h at 37°C. Precipitates form at the end of the incubation period as a result of the cells with metabolically active mitochondria reducing the MTT salt to the chromophore formazan crystals. Using a microplate reader, the optical density of solubilized crystals in DMSO was determined at 570 nm. To calculate the percentage growth inhibition, the following formula was used:

$$\%\ Inhibition = \frac{100(\text{Control} - \text{Treatment})}{\text{Control}}$$

By using Linear regression equation *i.e.* y = mx+c, IC_{50} values were determined. y= 50, m and c values were derived from the viability graph. The viability graph shows the cytotoxicity effect of $PtCl_2$, 1, 2 and 3 on MCF-7 and HeLa cell line are given in Fig. 2 and Fig. 3. The IC_{50} values of $PtCl_2$, 1, 2 and 3 on MCF-7 and HeLa cell lines are given in Table 5 and Table 6.

Antioxidant Activity

DPPH free radical scavenging assay

The antioxidant activity of starting material($PtCl_2$), ligand(LH), metal complexes $[Pt(L)_2]$ and $[Pt(LH)_2]Cl_2$ were determined using a colorimetric assay based on the discoloration of the oxidized form of 2,2-diphenyl-1- picrylhydrazyl radical (DPPH) violet to its reduced form yellow. A higher concentration of antioxidant result into yellower solution. The absorbance at 517nm was calculated after 30 min incubation period.

The percentage of DPPH inhibition was estimated by the following formula.

$$\%\ Inhibition = \frac{(\text{Absorbance of Control} - \text{Absorbance of Sample})}{(\text{Absorbance of Control})}$$

Procedure

Using the stable radical DPPH, the antioxidant activity was quantified in terms of its capacity to scavange radicals. The Blois method was used to conduct the experiments[33]. A drop in absorbance at 517 nm coincides with the radical's reduction. Test tubes were filled with a volume of 3 mL of 0.1 mM DPPH methanolic solution, and 100 µL of sample

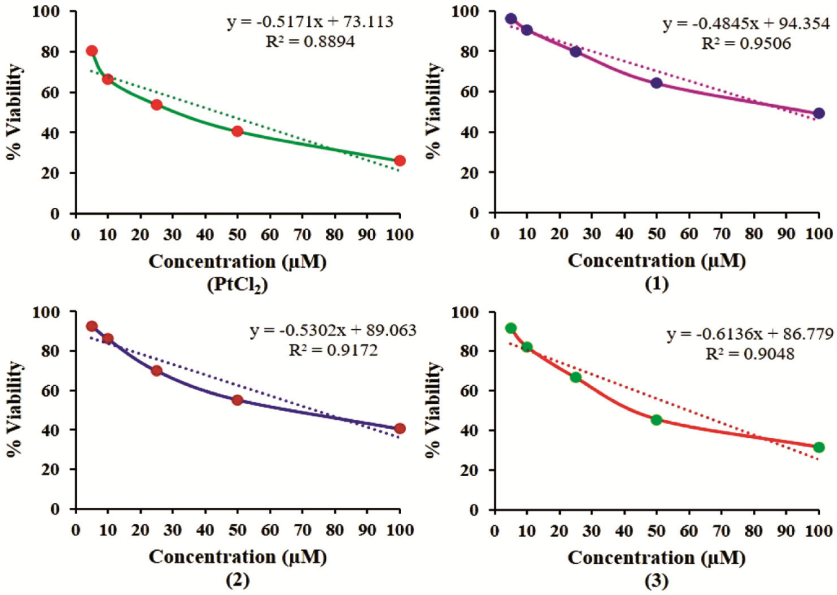


Fig. 2 — Cytotoxicity effect of $PtCl_2$, **1, 2, 3** on MCF-7 cell line

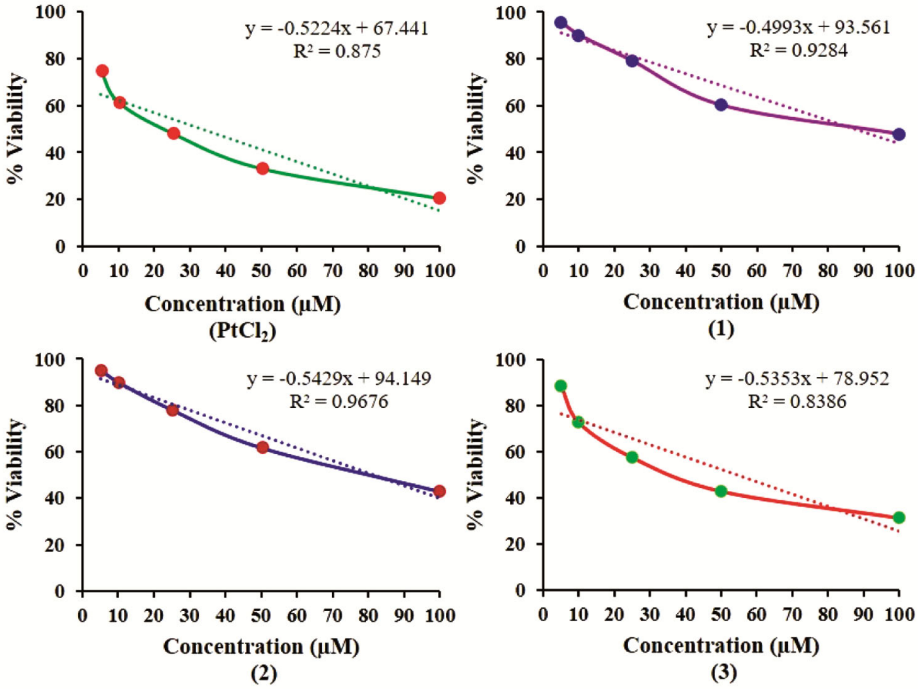


Fig. 3 — Cytotoxicity effect of $PtCl_2$, **1**, **2** and **3** on HeLa cell line

was added. The reaction tubes were stored at 300°C for 30 min in the dark while they were wrapped in aluminum foil in triplicate. When antioxidants are present, the violet/purple colour that DPPH produces in methanol solution fades to shades of yellow. Every measurement was made in dim light. A UV/VIS spectrophotometer was used to perform spectrophotometric measurements at 517 nm. Ascorbic acid was used as positive control and Methanol as negative control. The results were expressed as percentage inhibition of DPPH after 30 min of incubation. Antioxidant activity of ligand and metal complexes as percentage inhibition is given in Fig. 4. Compound **1** was showing maximum value of percentage inhibition(70.82) among all the tested compounds.

Table 5 — IC_{50} values of $PtCl_2$, **1**, **2** and **3** on the HeLa cell line

Compd	IC_{50} (μM)
$PtCl_2$	33.38
1	87.24
2	81.32
3	72.76
Cisplatin	5.62

Table 6 — IC_{50} values of $PtCl_2$, **1**, **2** and **3** on the MCF-7 cell line

Compd	IC_{50}(μM)
$PtCl_2$	44.69
1	91.54
2	73.67
3	59.93
Cisplatin	7.53

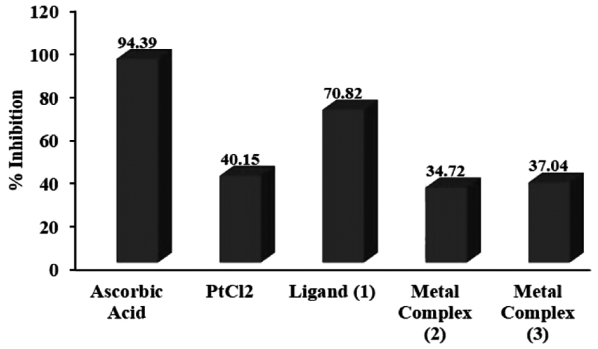


Fig. 4 — Antioxidant activity of ligand(**1**) and metal complexes **2** and **3**

Conclusions

Square planar complexes of Pt(II) were synthesized from benzyl-2-((5-methylthiophen-2-yl)methylene) hydrazine-1-carbothiolate Schiff base. Ligand(**1**) and the products(**2**,**3**) were screened for cytotoxic and antioxidant activities. Starting material of platinum($PtCl_2$), ligand, addition and substitution products of platinum were screened for cytotoxic activity against cancer cell lines, MCF-7 and HeLa. The metal complexes were showing better cytotoxic activity in comparison to ligand. Starting material of platinum, ligand, addition and substitution product of platinum were also screened for antioxidant activity against stable radical DPPH. The ligand was showing maximum activity with 70.82% inhibition. The ligand can be further investigated as a potential antioxidant agent.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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