

Synthesis, spectroscopic study of Pt (IV), Au (III), Rh(III), Co(II) and V (IV) complexes with sodium[5-(p-nitro phenyl) -¹4- phenyl-1,2,4-triazole-3-dithiocarbamato hydrazide] and cytotoxicity assay on rhabdomyosarcoma cell line of heavy metals

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Abstract :

All the prepared metal complexes of Pt (IV), Au(III), Rh (III), Co (II) and V(IV) with new ligand sodium [5-(p-nitro phenyl)-¹4-phenyl-1,2,4-triazole-3-dithiocarbamato hydrazide] (TRZ.DTC) have been synthesized and characterized in solid state by using flame atomic absorption, elemental analysis C.H.N.S, FT-IR ,UV-Vis Spectroscopy, conductivity and magnetic susceptibility measurements. The nature of the complexes formed in ethanolic solution has been studied following the molar ratio method also was studied stability constant and found to be stable in molar ratio 1:1 of VL (IV) and CoL(II) while Pt(IV), Au(III) and Rh(III) complexes stable in molar ratio 1:2 as well as the molar absorptivity for these complexes were calculated. From the previous analyses, octahedral geometry was suggested for Pt (IV), Rh (III) and Co (II) complexes, square planar was suggested for Au(III) complex while V(IV) complex has a square pyramidal. Cytotoxic effect of PtL, AuL and RhL as well as ligand has been evaluated against RD cell line by using four different concentrations (500, 250, 125 & 62.5 µg/ml) respectively in three exposure times 24, 48 and 72 hrs and compared this effect with control positive Cis-Pt.

Keywords: 5-(P-nitro phenyl), ¹4- phenyl-1,2,4-triazole, 3-dithiocarbamato hydrazide, molar absorptivity, cytotoxic, RD cell line, exposure times, control positive.

Introduction:

Dithiocarbamates(DTC) represent a large and interesting class of inorganic compounds [1], the dithiocarbamato group (Rdtc-) of ligands has been found to act usually as uninegative bidentate ligands, coordinated through both sulfur atoms with many metal ions [2]. Transition metal complexes with these ligands have been extensively investigated which are of interest in many fields: as flotation agents and antifungal agents [1,2], in industry, they are used in water-cooling system, in sugar and paper manufacturing. Other

commercial applications are such as accelerators in vulcanization[3]. Because of their chelating properties, they are used as scavengers in water-waste treatment [3], in medicine, in the treatment of alcoholism and rheumatism, some dithiocarbamates salts are used as antidotes [4]. Large quantities of water-soluble dithiocarbamato complexes are used in agriculture as fungicides or pesticides, and have been also tested in various medical applications [4]. Additional several applications in chemistry such as supermolecular chemistry due to

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the fact that the dithiocarbamate ligand is an attractive structural motif for metal-directed self-assembly to polymetallic including cages, ladders, racks and grids have been constructed [5]. The optical and electrochemical properties of dithiocarbamate complexes can be used to construct sensors for the guest molecules [5]. The major advantage of using the small bite-angle of dithiocarbamate moiety as a stabilizing chelating ligand is its unique property to remain intact under a variety of reaction conditions [5]. In the present paper we attempted to introduce the dithiocarbamate moiety in presence of triazole ring and hydrazide in the same structure which was known to possess a pharmacologically important one, in a vast number of drug structure, and to investigate the coordination behavior of the new ligand toward some transition metal ions.

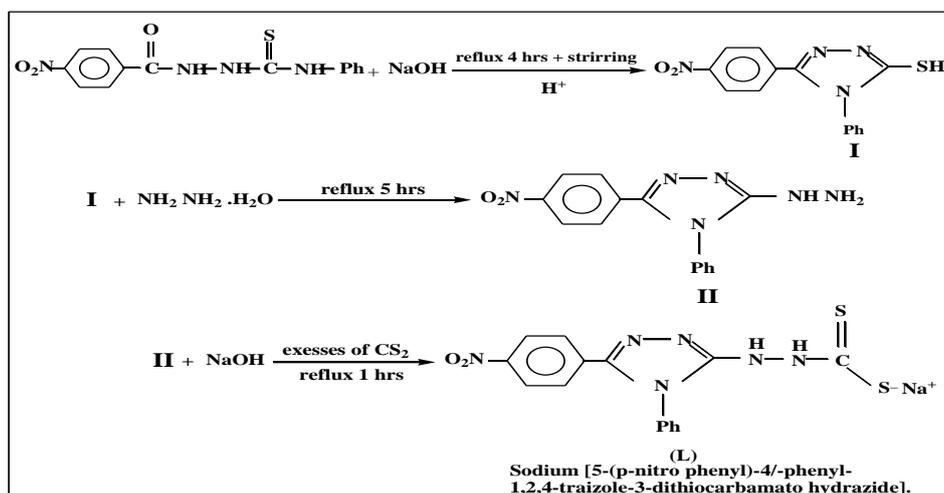
Materials and methods:

All the chemicals used were analytical analar and of highest purity available. The metal analysis of the separated solid chelates for metal content was performed by using AA-680 Shimadzu Atomic Absorption Spectrophotometer. The elemental Analysis (C.H.N.S) of all compounds has been carried out by using EM-017. The electronic spectra of the prepared compounds have been recorded on a Shimadzu UV-160 Spectrophotometer. FTIR spectra of the samples were recorded using IR Prestige-21 Spectrophotometer as CsI discs. Magnetic susceptibility measurements of the complexes in solid state were determined using

Burker BM6 instrumentation at room temperature. The molar conductance of the complexes has been measured in DMF as a solvent at room temperature using WTW conductmeter type. Melting point apparatus of Gallen Kamp M.F.B-60 was used to measure melting points of all prepared compounds. Optical density of each well in cell culture plates in cytotoxic assay was read by using micro ELISA reader ASYS, Austria at a transmitting wave length on 492nm, Plates of cell culture were incubated at 37°C by using incubator SANYO, Japan.

Synthesis of Sodium [5-(p-nitro phenyl)-4-phenyl-1,2,4-triazole-3-dithiocarbamate hydrazide] as ligand (L):

A mixture of compound 1-Phenyl-4-(p-nitro benzoyl) thiosemicarbazide (0.0006mole, 0.2gm) with 15 ml of 2M sodium hydroxide solution was refluxed with stirring for 4 hrs. After cooling, the solution was acidified with hydrochloric acid and the precipitate was filtered. (0.01mole) of this precipitate and 15 ml of hydrazine hydrate in 15 ml of absolute ethanol was refluxed for 5 hrs. After cooling, the mixture was filtered off. To (0.1mol, 16.5gm) of the previous mixture in ethanol and excess of carbon disulfide was added in the presence of NaOH in ethanolic solution and the mixture was refluxed for one hour. The excess of solvent and carbon disulfide was then distilled off, the resulting solid recrystallized from acetone, and the physical properties are listed in Table (1). The structure of the proposed ligand is shown in Scheme (1).



Scheme (1): General steps of preparation the new TRZ. DTC ligand (L)

Synthesis of complexes:

New (TRZ.DTC) complexes under investigation have been synthesized as follows: The ligand dissolved in (15 ml) of absolute ethanol followed by addition (5 ml) of metal salt drop by drop in ethanolic solution. The reaction molar ratio for vanadium and cobalt complexes is (1:1) and (1:2) for platinum, gold and rhodium complexes.

The resulting precipitate has been filtered and washed with water and recrystallized from ethanol then dried by using oven at 50°C for 1 hour. The physical properties are shown in Table (1).

Table (1): Physical data of new ligand (L) and its metal complexes.

Comp.	Colour	M.P. °C	Yield %	Molar ratio M:L	M.Wt g.mol ⁻¹	elemental analysis found(Calc.)				Metal percentage	
						C	H	N	S	found	Calc.
L	Light orange	66	88.5%	---	394.4	45.85 (45.63)	3.05 (2.78)	21.99 (21.29)	16.80 (16.22)	---	---
PtL	Dark brown	320	57.40%	1:2	1072.87	32.88 (35.20)	1.95 (2.98)	14.65 (15.65)	12.22 (11.93)	17.25	18.17
AuL	Dark Orange	104	75.04%	1:2	993.26	36.59 (36.24)	2.86 (2.41)	17.43 (16.91)	13.12 (12.88)	20.14	19.82
RhL	Brown	140	70.88%	1:2	1083.24	41.35 (42.09)	4.92 (4.43)	16.15 (15.50)	12.55 (11.81)	9.26	9.49
CoL	Dark green	124	70.05%	1:1	694.33	38.58 (39.75)	5.52 (5.04)	13.95 (14.11)	8.75 (9.21)	8.68	8.48
VL	Olive green	130d	56.35%	1:1	535.34	34.15 (33.62)	2.55 (2.24)	16.22 (15.69)	18.60 (17.93)	10.39	9.51

d= decomposition degree

Study of complexes formation in solution:

Complexes of new TRZ.DTC ligand with metal ions have been studied in solution using ethanol as a solvent, in order to evaluate the ratio of metal to ligand in complex using molar ratio method [6]. A series of solutions have been prepared having a constant concentration 10⁻³ M for each metal ion

and ligand. The ratio have been determined from the relationship between the absorption of the absorbed light and molar ratio of (M:L) at λ_{max} of maximum absorption.

Stability constant of the (TRZ.DTC) complexes:

In this study, the molar ratio plot was obtained by adding an increased amount of ligand (0.25-5.0 ml) of 10^{-3} M to a constant amount of metal ion (1ml) of 10^{-3} M in a final volume of (10 ml) absolute ethanol. Absorbance measurements were made against blank prepared for each concentration of chelating agents at a maximum wavelength of the formation complex. The absorbance (A_s and A_m) of the solution, have been measured at λ_{max} of maximum absorption. The stability constant (K) (eq. 1,2) and the molar absorptivity (ϵ_{max}) (eq.3) were calculated using the following equations:

$$K = \frac{1 - \alpha}{\alpha^2 C} \quad \dots (1)$$

when M:L is (1:1)

or

$$K = \frac{1 - \alpha}{4\alpha^3 C^2} \quad \dots (2)$$

when M:L or L:M is (2:1)

Given

$$A_m = \epsilon_{max} bc \quad \dots (3)$$

Where:

A_m = Absorbance of the solution containing an excess constant amount of ligand.

A_s = Absorbance of the solution containing stoichiometric amount of ligand metal ion.

b = Cell constant ($b = 1\text{cm}$).

c = Molar concentration.

Cytotoxic assay:

The *in vitro* cytotoxic assay has been carried out on Rhabdomyosarcoma cell line, RD. The cells were cultured in minimum essential media supplemented with 10% fetal calf serum, 50 mg/ml streptomycin and 1000U/L penicillin. Cell line was grown as a monolayer in humidified atmosphere at 37°C with 5% CO_2 . The experiments were performed when cells

were healthy and at logarithmic phase of growth. The assay of each concentration for each compound, i.e. (L, PtL, AuL and RhL) was performed in triplicate. Cis-platinum added as a positive control, only cells incubated with culture media represented the negative control, and then the 96-well cell culture plate incubated at 37°C in an incubator supplemented with (5%) CO_2 for three different times 24, 48 and 72 hrs.

Results and Discussion:

A. Chemistry

Stable complexes have been isolated in all cases based on the metal analysis data, elemental analysis C.H.N.S, FT-IR, UV-Vis Spectroscopy, conductivity and magnetic susceptibility measurements, the general formula of the complexes can be depicted as; $[\text{ML}_2(\text{H}_2\text{O})_x(\text{Cl})_y](\text{Cl})_z \cdot n\text{EtOH}$ where $M = \text{Rh}$ and Pt ; $x = 1, 2$; $y = 1, 0$; $Z = 0, 2$; and $n = 4, 1$ respectively in addition to $[\text{AuL}_2]\text{Cl} \cdot \text{H}_2\text{O}$, $[\text{CoL}(\text{H}_2\text{O})(\text{NO}_3)] \cdot 4\text{EtOH}$ respectively and $\text{Na}^+[\text{VOSO}_4\text{L}]$.

FTIR Spectra:

As expected, FT-IR gave good informations about the complex behaviour of the ligand with various metal ions. The characteristic frequencies of free ligand and its metal complexes have been readily assigned in comparison with the literature values [7]. In metal dithiocarbamate complexes, the region $(950-1050)\text{cm}^{-1}$ is considered as a characteristic of the nature of binding of the dithiocarbamate moiety. According to the criterion of Bonati and Ugo [8], the presence of a solitary band in the above region is due to symmetrical bidentate coordination of the dithiocarbamate group while the splitting of this band within a narrow range of $\pm 20\text{cm}^{-1}$ is due to the asymmetrical ambidentate or monodentate nature of the

dithiocarbamate group shown above. The bands in the region (940-1010) cm^{-1} have been attributed to the stretching mode of the C-S bond. The position of this band has been used by several authors [9,10] as a criterion for symmetric or asymmetric coordination of dithiocarbamate group. The singlet in the infrared spectrum of dithiocarbamate ligand confirms the equivalence of the S-atoms, but the splitting in the infrared spectrum indicates non-equivalence of the S-atoms in these compounds. In the present work, the bands appeared in this region of the ligand and its complexes are splitting which refer to ambidentate binding of dithiocarbamate group according to the data reported in literature [9,11]. The ligand exhibited band at (995) cm^{-1} which refers to stretching frequency of $\nu(\text{C-S})$ band [11], this band undergoes a shift toward lower frequencies in all complexes, another band appeared at (1041) cm^{-1} indicate to the stretching frequency of $\nu(\text{C=S})$ band of the free ligand which undergoes shift toward higher frequencies in all complexes except Co(II) and Rh(III) complexes undergoes a shift toward lower frequencies. The band of $\nu(\text{C-N})$ mode appeared in the region (1450-1550) cm^{-1} indicate to thioureide band [11], this band is characteristic for the

(S_2) C=NR_2 bond. The $\nu(\text{C}=\text{N})$ can appear outside the region proposed in the literature at lower frequencies, especially when the S_2CN group attached to the N atom is an aryl or H [12]. A $\nu(\text{C}=\text{N})$ band at (1438-1465) cm^{-1} region was observed, which matches well with the literature values [12], while the band at (1496) cm^{-1} of $\nu(\text{N-N})$ mode remained without change in all complexes, except Pt(IV) and Au(III) complexes which showed a slight increase toward higher frequencies, which did not support the coordination ligand with central metal ion by this group. The stretching vibration of $\nu(\text{NH})$ that appeared at (3380) cm^{-1} undergoes a slight shift about (3) cm^{-1} in some complexes. On the other hand, the bending vibration of $\delta(\text{NH})$ at (1652) cm^{-1} exhibited a shift toward lower frequencies in all complexes about (2-4) cm^{-1} which also refers did not coordination with central metal ion by this group. A band observed around (3444-3468) cm^{-1} in the spectra of metal complexes, assigned to the $\nu\text{-OH}$ which refer to presence of EtOH or H_2O uncoordination or out of sphere. This absorption was further indicated by the appearance of $\nu(\text{M-S})$ and $\nu(\text{M-X})$ respectively, Table (2).

Table (2): Most diagnostic FTIR bands of the ligand and its metal complexes in (cm^{-1}).

Comp.	$\nu(\text{NH})_{(1,2)}$	$\delta(\text{NH})_{(1,2)}$	$\nu(\text{C=S})$	$\nu(\text{C-S})$	$\nu(\text{N-N})$	$\nu(\text{C-N})$	M-S	M-O	Others
L	3380 3380	1652 1652	1041	995	1496	1438	---	---	---
PtL	3382 3382	1650 1650	1053	968	1500	1458	428	---	Coord. $\delta\text{H}_2\text{O} = 894$ $\nu(\text{OH(EtOH)}) = 3460$
AuL	3380 3380	1649 1649	1045	952	1500	1454	416	---	$\nu(\text{OH(H}_2\text{O)}) = 3444$
RhL	3382 3382	1649 1649	1029	952	1496	1465	420	520	$\nu(\text{Rh-Cl}) = 324$ Coord. $\delta\text{H}_2\text{O} = 894$ $\nu(\text{OH(EtOH)}) = 3468$
CoL	3383 3383	1648 1648	1033	950	1492	1438	412	501	Coord. $\delta\text{H}_2\text{O} = 860$ $\nu(\text{ONO}_2) = 1369, 1249, 1002$ $\nu(\text{OH(EtOH)}) = 3464$
VL	3380 3380	1650 1650	1049	964	1496	1450	462	513	$\nu(\text{V=O}) = 945$ $\nu(\text{SO}_4) = 1141, 1118$

Electronic spectra:

The electronic spectra of metal complexes were recorded as solutions in DMF in the range (190-1100) nm at room temperature. The electronic spectrum of free ligand (L) exhibited three main bands which can be assigned to the chromospheres group NCS_2 [13,14]. The first absorption band appeared at 266 nm (37593.98 cm^{-1}) due to interligand ($\pi \rightarrow \pi^*$) transition located on the . The second absorption band located at 312 nm (32051.28 cm^{-1}) also arises from ($\pi \rightarrow \pi^*$) transition, but within the group . The third absorption band attributed to ($n \rightarrow \pi^*$) electronic transition located on the sulphur atoms which appeared at 353 nm (28328.61 cm^{-1}) [13,14]. PtL: The platinum complex is a diamagnetic as expected [15], the ground state suggested spin-paired octahedral stereochemistry geometry. The atomic ground state is ^5D . Two principle spin-allowed absorption bands are to be expected corresponding to the transition from the $^1\text{A}_{1g}$ ground state to the $^1\text{T}_{1g}$ and $^1\text{T}_{2g}$ excited states in addition, two bands assigned to the spin-forbidden singlet-triplet transition may be observed at lower energies than the spin allowed transition [15]. The spectrum of the prepared brown platinum complex shows three bands in the visible region assigned to the $^1\text{A}_{1g} \rightarrow ^1\text{T}_{1g}$, $^1\text{A}_{1g} \rightarrow ^1\text{T}_{2g}$, $\text{L} \rightarrow \text{PtCT}$ transitions . The transition observed at (10928.96 cm^{-1}) is assigned to the spin- forbidden transition $^1\text{A}_{1g} \rightarrow ^3\text{T}_{1g}$ [1,16]. Conductivity measurement shows that the complex is to be conducting. AuL: Gold (III) complex is in high crystal field effect due to the large size of gold (III) ion, being in the third transition series in addition to the high oxidation state of this ion. Therefore, spectrum of such ion is characterized by charge transfer bands,

which dominate the ligand field transition. This mean that the charge transfer bands appears at longer wavelength, at the same time ligand field transition are expected to appears at shorter wavelength. These results in an overlap between the two absorption bands, which make the interpretation of the spectra more difficult [16,17]. In this work, the gold complex showed three bands, Table (3), one at (29411.76 cm^{-1}) which refer to $^1\text{A}_{1g} \rightarrow ^1\text{E}_g$ transition and the other appeared at (26385.22 cm^{-1}) , which refer to $^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}$ in a square planar geometry. The band at (31347.96 cm^{-1}) may be due to charge transfer. RhL: In the spectrum of Rh (III) complex a weak band is observed at (11467.88 cm^{-1}) which is attributed to the $^1\text{A}_{1g} \rightarrow ^3\text{T}_{1g}$ transition which may occur when the promoted electron changes its spin and be the two T terms $^3\text{T}_{1g}$ and $^3\text{T}_{2g}$. These transition are indeed observed in some cases in the region of ($10000-14000 \text{ cm}^{-1}$) [1]. Values of B^1 , 10Dq and β were calculated by using Tanabe-Sugano diagram for d^6 system by fitting ratio of the frequencies (ν_2/ν_1) of the observed spin-allowed bands to the Tanabe-Sugano diagram, which produce value of the interelectronic repulsion parameter B^1 as well as of the crystal field splitting energy 10Dq . Conductivity measurements showed that the complex is non-ionic Table(3). CoL: The value of the magnetic measurement (4.53) B.M indicates that the dark green Co(II) complex to be paramagnetic and is characteristic of high spin tetrahedral cobalt ion species [18]. The color of present Co(II) in DMF was change from dark green to light brown during dissolution the solid compound , therefore, it was postulated that two DMF molecules coordinate with the compound to give distorted octahedral

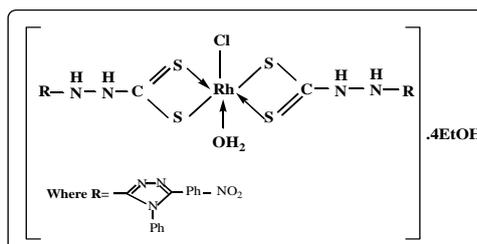
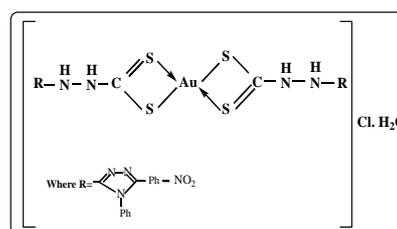
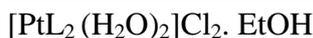
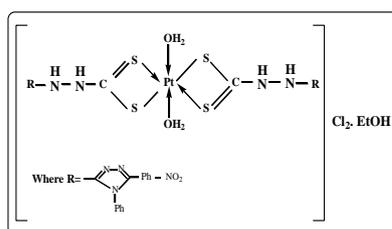
structure. In the present work, three bands are appeared Table (3); one at $(10235.41)\text{cm}^{-1}$ and the two others at $(19841.26)\text{cm}^{-1}$ and $(25641.02)\text{cm}^{-1}$ which were assigned to the transitions of ν_1 , ν_2 and ν_3 respectively [19].VL: The electronic spectrum of this complex, Table (3), shows prominent (d-d) absorption bands, the first one is a band at $(12893)\text{cm}^{-1}$ and the second at $(19531.25)\text{cm}^{-1}$ but the third bands appeared at $(28735)\text{cm}^{-1}$. These bands

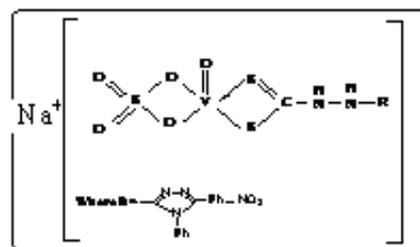
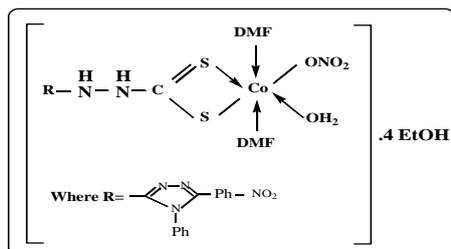
can be attributed to the following transitions; ${}^2B_{2g} \rightarrow {}^2E_g$, ${}^2B_{2g} \rightarrow {}^2B_{1g}$, and ${}^2B_{2g} \rightarrow {}^2A_{1g}$, respectively [16]. The magnetic moment (1.98) BM is higher than spin value of the vanadium ion only this result indicates a higher orbital contribution [16]. These transitions and the magnetic moment value came in accordance with the published data for square pyramid vanadium complexes [16].

Table (3): Electronic spectra, conductance in DMF solvent and magnetic moment (B.M) for the prepared ligand and its metal complexes.

Comp.	Absorption Bands(cm^{-1})	Assignment	B°	B'	β	Dq/B'	10Dq	15B'	μ_{eff} B.M.	μsm^{-1}	Suggested geometry
PtL	10928.96 14749.26 18535.68 26315.78	${}^1A_{1g} \rightarrow {}^3T_{1g}$ ${}^1A_{1g} \rightarrow {}^1T_{1g}$ ${}^1A_{1g} \rightarrow {}^1T_{2g}$ $L \rightarrow \text{PtCT}$	---	---	---	---	---	---	-0.9	121	O.h
AuL	26385.22 29411.76 31347.96	${}^1A_{1g} \rightarrow {}^1B_{1g}$ ${}^1A_{1g} \rightarrow {}^1E_g$ $L \rightarrow \text{AuCT}$	---	---	---	---	---	---	-0.43	168.5	Square planar
RhL	11467.88 14492.75 22421.52	${}^1A_{1g} \rightarrow {}^3T_{1g}$ ${}^1A_{1g} \rightarrow {}^1T_{1g}$ ${}^1A_{1g} \rightarrow {}^1T_{2g}$	720	609.38	0.84	2.9	17672.16	9140.7	0.00	37.2	O.h
CoL	10235.41 19841.26 19773.17(cal.) 25641.02	${}^4T_{1g} \rightarrow {}^4T_{2g}$ ${}^4T_{1g} \rightarrow {}^4A_{2g}$ ${}^4T_{1g} \rightarrow {}^4T_{1g(p)}$	1128	980.53	0.86	1.15	11276.15	14776.05	4.53	9.1	O.h
VL	12893 19531.25 28735	${}^2B_{2g} \rightarrow {}^2E_g$ ${}^2B_{2g} \rightarrow {}^2B_{1g}$ ${}^2B_{2g} \rightarrow {}^2A_{1g}$	---	---	---	---	---	---	1.98	67.2	Square pyramidal

Suggested structure and molecular formula of new prepared metal complexes:





Solution study:

Molar ratio method was followed to determine the M:L ratio. The results of complexes in ethanol solution, suggested that the metal to ligand ratio was (1:1) for cobalt and vanadium complexes and (1:2) for platinum, gold and rhodium complexes, which were comparable to those obtained from

isolated solid state study, high stability constant obtained in complexes of molar ratio (1:2) contrast to the other values obtained with (1:1) while the value of molar absorptivity was change between the high values and low values according to the size of metal ion, type of coordination, geometry and oxidation state. Table (4).

Table (4): Stability constant and molar absorbtivity of dithiocarbamato complexes at room temperature.

Compound	A_s	A_m	α	$K \text{ L.mol}^{-1}$	$\epsilon \text{ L.mol}^{-1} \text{ cm}^{-1}$	$\lambda_{\text{max/nm}}$
PtL	0.243	0.33	0.263	$1.02 \times 10^7 (\#)$	3300	500
AuL	1.123	1.39	0.192	$2.88 \times 10^7 (\#)$	13900	430
RhL	0.336	0.396	0.075	$9.25 \times 10^8 (\#)$	3960	370
CoL	0.336	0.386	0.129	5.24×10^4	3860	450
VL	0.41	0.423	0.031	1.00×10^6	4230	390

Where: (#) $\text{L}^2.\text{mol}^{-2}$.

B. Cytotoxic assay

The results obtained in this work showed the cytotoxicity effect of new dithiocarbamate ligand and its complexes PtL(IV), AuL(III) and Rh(III) on RD cell line (*in vitro*) may lead to suggest a mechanism of action of this new ligand according to literature; dithiocarbamates can form coordination complex with metal ions in which the two adjoining sulfur atoms are bound to the same metal ion including platinum (II), palladium (II), gold (III), tin (IV) and other common transition metal ions. On the other hand, the dithiocarbamate anti-

neoplastic activity suggested that the anti-neoplastic was attributed to pro-apoptotic redox-related mitochondrial membrane permeabilization [20]. A large number of analogs of cisplatin have been tested and it has been reported that many active complexes could react with DNA and inhibit its synthesis [21]. Octahedral platinum (IV) complexes undergo ligand substitution reactions that are slow relative to those of their platinum (II) analogues. They have been considered as the compounds which are unable to react directly with DNA. The antitumor activity of platinum (IV)

compounds has been suggested to require *in vivo* reduction to the kinetically more labile, and therefore reactive, platinum (II) derivatives [22]. The cytotoxic effect exhibited in our study of new platinum(IV) dithiocarbamate complex may refer to reduction of Pt(IV) to Pt(II) inside the cell, this effect show in figure (2). Because gold (III) is isoelectronic with platinum (II), and because four coordinate gold (III) complexes are in the same square-planar geometries as cisplatin [23], the anticancer activity of gold (III) compounds has been investigated. Although the mechanism of cisplatin is well understood, the mechanism responsible for gold (III) complex induced cytotoxicity remained unclear. It has been suggested by Fricker and et al [24] that proteins, rather than DNA, might be the main target for gold (III) complexes. They found that gold (III)

dithiocarbamate complex showed a clear preference for S-donor ligands, such as glutathione and cysteine, with only limited reactivity against nucleosides and their bases [24]. They act fast, inhibit DNA and RNA synthesis, and show only a minimal cross-resistance with cisplatin, suggesting a different mechanism of actions. Vesna Milacic and et al [25] suggest that the primary target for gold (III) dithiocarbamates is the proteasome and that inhibition of the proteasomal activity by gold (III) dithiocarbamates is associated with apoptotic cancer cell death. Vesna Milacic found that the effect of gold (III) dithiocarbamates compound could be completely blocked by two different S-donor ligands (dtc) [25]. In the present study, the gold (III)

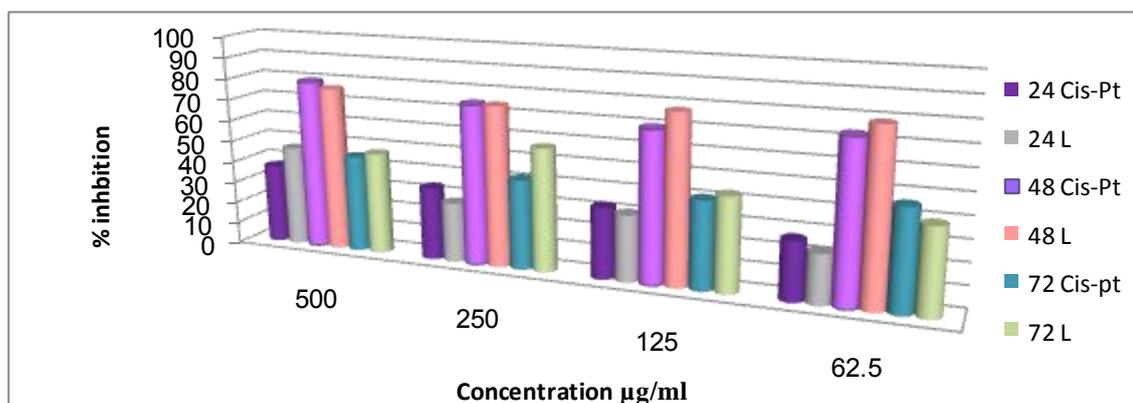


Fig (1): Shows the percentage inhibition rate in RD cell line after exposure to (TRZ.DTC) ligand at different times (24, 48 and 72 hrs) comparable to control positive (Cis-Pt) and ligand.

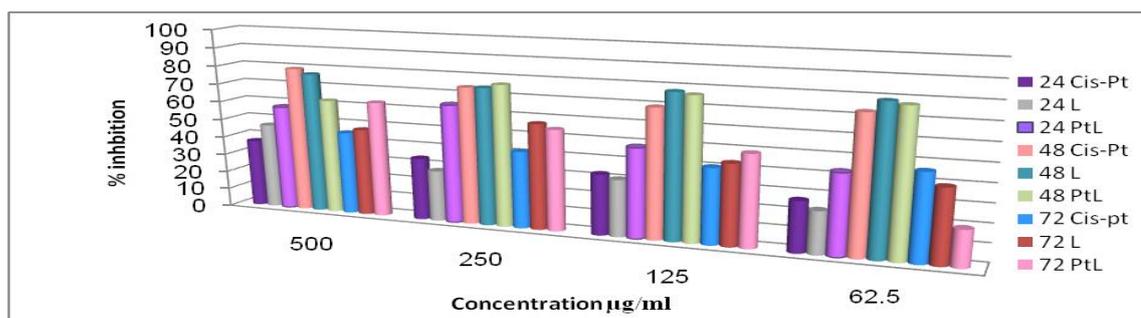


Fig (2): Shows the percentage inhibition rate in RD cell line after exposure to PtL complex at different times (24, 48 and 72 hrs) comparable to control positive (Cis-Pt) and ligand.

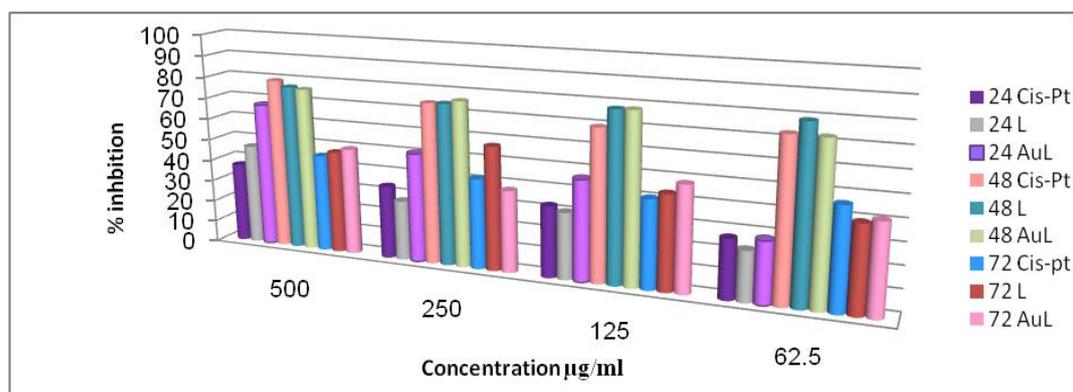


Fig (3): Shows the percentage inhibition rate in RD cell line after exposure to AuL complex at different times (24, 48 and 72 hrs) comparable to control positive (Cis-Pt) and ligand.

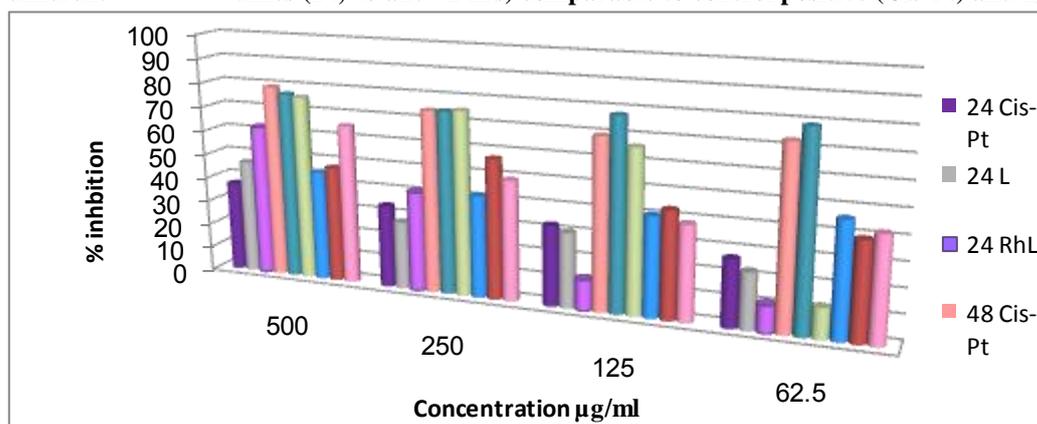


Fig (4): Shows the percentage inhibition rate in RD cell line after exposure to RhL complex at different times (24, 48 and 72 hrs) comparable to control positive (Cis-Pt) and ligand.

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تحضير ودراسة طيفية لمعقدات V ، Co (II), Rh(III), Au(III), Pt (IV) مع صوديوم [5- (بارا نايترو فنييل)-4- فنييل-1,2,4- ترايزول-3- ثنائي ثايوكاربميت هيدرازيد] وتجربة التأثير السمي الخلوي على الخط الخلوي السرطاني لسرطان العضلة لمعقدات الأيونات الثقيلة

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الخلاصة:

تم تحضير وتشخيص الليكاند الجديد صوديوم [5- (بارا نايترو فنييل)-4- فنييل-1,2,4- ترايزول-3- ثنائي ثايوكاربميت هيدرازيد] ومعقداته مع بعض الأيونات الفلزية باستخدام الطرائق الفيزيائية المناسبة كتقنية الامتصاص الذري اللهيبي و التحليل الدقيق للعناصر وأطياف الأشعة تحت الحمراء وفوق البنفسجية – المرئية وقياسات التوصيلية الكهربائية فضلاً عن الحساسية المغناطيسية. تم كذلك دراسة طبيعة المعقد المتكون في محلول الايثانول باتباع طريقة النسبة المولية، كما درست ثوابت الاستقرار للمعقدات المحضرة ووجد بأنها مستقرة عند النسب المولية 1:1 بالنسبة لمعقدي الكوبلت والفناديوم و2:1 بالنسبة لمعقدات الذهب و البلاتين والروديوم بالإضافة إلى ذلك تم حساب قيم الممتصية المولارية لجميع المعقدات المحضرة. ومن التحاليل السابقة تم اقتراح شكل ثماني السطوح بالنسبة لمعقدات الكوبلت و الروديوم والبلاتين و شكل مربع مستوي بالنسبة لمعقد الذهب بينما معقد الفناديوم يمتلك شكل هرم مربع القاعدة. كما درس التأثير السمي لبعض المعقدات المحضرة (PtL & AuL , RhL) بالإضافة إلى الليكاند ضد الخط الخلوي السرطاني نوع RD باستخدام أربع تراكيز مختلفة (500, 125, 250, 62.5 مايكرو غرام/مل) على التوالي، و بثلاث أوقات تعريض 24، 48 & 72 ساعة وتم مقارنة هذا التأثير مع العقار المضاد لسرطان سيز- بلاتين.