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Biological Applications of Metal Complexes of Dithiocarbamates

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Abstract

Dithiocarbamates are organosulphur ligands and form chelate compounds with metals. Their uses are reported in the field of accelerating vulcanization, pesticide, material science, organic synthesis, etc. Recent research demonstrated the potential of metal complexes of these ligands as good antifungal, antibacterial, and antitumor agents. Dithiocarbamate complexes have also been reported to use as a plasmonic sensor, as an inhibitor of proteasome, and for antioxidant and antileishmanial activity. This brief review presents the biological activities of metal complexes of dithiocarbamate.

Keywords

Biological; Antibacterial; Antifungal; Antitumor; Antioxidant; Antileishmanial.

1. Introduction

Dithiocarbamates are organosulfur ligands [1] and can form chelate compounds in monodentate and bidentate mode or can act as bridging ligands [2]. The resonating structure of dithiocarbamate is as shown in Figure 1 [3]. These monoanionic chelating ligands have high versatility and ability to form stable complexes with transition series elements and most of the elements of main group, lanthanide series and actinide series of periodic table [4-8]. Dithiocarbamates can be prepared easily from primary and secondary amines [4,9]. They can be classified into two types: monoalkyl- and dialkyl- dithiocarbamate.

The type of the dithiocarbamate formed depends on the type of amine used in its synthesis [4,9]. Dithiocarbamates are primarily used as fungicides in agriculture [10]. They were first time commercially used as fungicides in World War II [11]. A variety of other applications occurred historically in the field of accelerating vulcanization or as accelerators in rubber industry [12], pesticide (in agriculture) [13], organic synthesis [14], biology [15], analytical chemistry [16-18], photo-stabilizing polymer [19], material science, protecting radiators [20,21], medicine [22,23], pharmaceutical industry [24] and precursors for creating

sulfide film semiconductors [7,25]. Dithiocarbamate ligands and their metal derivatives possess aptitude to modulate key proteins that participate in various biological processes including apoptosis, transcription, oxidative stress, and degradation [26,27]. They also found to have applications, as antibacterial and antifungal agents [28,29], antioxidant [30], for possible treatment of AIDS and treatment of cancer [31]. Increase in the discovery of widespread and serious invasive fungal infections and their rates and the decrease in the effectiveness of available antifungal agents against certain fungal strains due to the emergence of drug resistivity in them, discovery of alternative drugs has become vitally important [32].

It was also reported that coordinated dithiocarbamates possess potential chemo protective function and antitumor property [33]. It has been proposed that the dithiocarbamate compounds possess antitumor activity due to complex formation with tumor cellular copper that cause binding of the proteasome and its inhibition that in order inhibits tumor cell- specific apoptosis [26]. The available chemotherapeutic agents have high toxicity thus their usefulness in the eradication of tumors is very limited [26]. This encourages the synthesis of novel compounds as effective proteasome inhibitor agents with reduced toxicity and therefore better anticancer agents. The interest in dithiocarbamate complexes is growing not only because of anticancer activity but also their use in treatment of cocaine addiction and viral infections [34,35]. Progress made in previous research in the synthesis and applications of dithiocarbamate compounds lead researchers to synthesize novel dithiocarbamate compounds as well as study their applications, especially in medicine. The purpose of this paper is to discuss the work done on the synthesis and biological applications of metal complexes of dithiocarbamates.

In last two decades many novel dithiocarbamate derivatives of Sn, Zn, Au and Ni have been prepared. Some Co, Cu, Mn, Hg, Pd, Pt , and Ru dithiocarbamates have also been synthesized. Biological activities of the synthesised metal dithiocarbamates were investigated against various test microbes. In some cases, the synthesized compounds showed better antimicrobial activities than the standard drugs. Au dithiocarbamates were mainly investigated for antitumor activity against various cancer cell lines. Antioxidant activity of some of the metal dithiocarbamates have also been reported. Some of the synthesized metal dithiocarbamates and their biological study have been described briefly in following sections.

2. Study of Biological Applications of Metal Dithiocarbamates

2.1. Sn dithiocarbamates

Awang et al. prepared six novel organotin(IV)dithiocarbamate compounds: dibutyltin (IV) ethylphenyldithiocarbamate (1), diphenyltin (IV) ethylphenyldithiocarbamate (2), triphenyltin (IV) ethylphenyldithiocarbamate (3), dibutyltin (IV) butylphenyldithiocarbamate (4), diphenyltin (IV) butylphenyldithiocarbamate (5), and triphenyltin (IV) butylphenyldithiocarbamate (6) [36].They carried out a micro-dilution test involving two-fold dilution with the highest concentration of 5 mg/ml to screen the synthesized compounds against test microbes: B. cereus, B. subtilis, Methicillin-Resistant S. aureus, S. aureus, S. pneumonia, A. baumanni, E. coli, Klebsiella sp., Shigellannei, V. cholera, A. fumigates, A. niger, C. albicans, and S. cerevisiae [36]. Results elucidated that compound 3 and compound 6 had antimicrobial activity against most

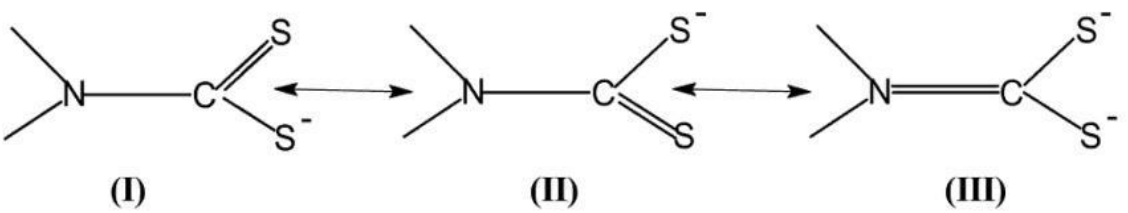


Figure 1. Resonating structures of dithiocarbamate ligand.

of the test microbes [36]. The obtained MIC value was 39 µg mL-1 for triphenyltin (IV) ethylphenyldithiocarbamate (3) against V. cholera and triphenyltin (IV) butylphenyldithiocarbamate (6) against A. baumanni [36]. Nevertheless, all synthesized compounds showed the bacteriostatic or fungistatic effect as reported by the authors [36]. Ferreira et al. synthesized organotin(IV) dithiocarbamate complexes: $[SnPh_3\{S_2CNR(R^1)\}]$ **(1)**, $[SnCy_3\{S_2CNR(R^1)\}]$ **(2)**, $[SnMe_3\{S_2CNR(R^2)\}]$ **(3)**, $[SnPh_3\{S_2CNR(R^2)\}]$ **(4)** and $[SnCy_3\{S_2CNR(R^2)\}]$ **(5)** (where R= CH_3, R^1 = $CH_2CH(OMe)_2$ and R^2 = 2-Methyl-1,3-dioxolane) (Figure 2a) and characterized by IR, ^1H,^{13}C, and ^{119}Sn NMR, and ^{119}Sn Mossbauer spectroscopy and X-ray crystallography [37]. The antifungal activity of synthesized compounds was screened against A. flavus, A. niger, A. parasiticus and P. citrinum, in terms of IC_{90} (µ mol/L) and IC_{50} (µ mol/L) [37]. In terms of IC_{50}, compound **1** and compound **4** showed noticeable activity and displayed very low inhibition concentration in case of all four test microbes [37]. Menezes et al. synthesized some pyrrolidine dithiocarbamate complex of Sn (IV) ion: $[Sn\{S_2CN(CH_2)_4\}_2Cl_2]$ **(1)**, $[Sn\{S_2CN(CH_2)_4\}_2Ph_2]$ **(2)**, $[Sn\{S_2CN(CH_2)_4\}\ Ph_3]$ **(3)**, $[Sn\{S_2CN(CH_2)_4\}_2(n\text{-}Bu)_2]$ **(4)**, and $[Sn\{S_2CN(CH_2)_4\}\ Cy_3]$ **(5)** [38]. The antifungal activity of the synthesized compounds was investigated against C. albicans (a human pathogenic fungi), using agar disk diffusion [38]. Results showed remarkable antifungal activity for all the compounds in the concentration of 0.025, 0.050, 0.100, 0.200, 0.400, 0.800, 1.600, and 3.200 mM with inhibition zone ≥ 11 mm, intermediate inhibition zone 11-9 mm and resistant zone ≤9 mm [38]. Most of the complexes were moderately active. Compounds **1** and **4** showed highest activity [38]. Similarly, Awang et al. prepared three novel organotin (IV) dithiocarbamate compounds with general molecular formula $R_mSn[S_2CN(CH_3)\ (C_6H_{11})]_{4\text{-}m}$ (where m=2, R = CH_3 **(1)**; m=2, R= C_4H_9 **(2)**; m = 3, R = C_6H_5 **(3)**) (Figure 2b) by in situ method [39]. Characterization of all the three compounds was done by elemental analysis and, IR and, NMR (^1H and ^{13}C) spectroscopic techniques [39]. The compounds were screened against bacterial strains: S. aureus, S. typhimurium, P. auruginosa, and B. subtilis [39]. Only compound **3** showed activity against S. aureus and S. typhimurium as reported by the authors [39]. Awang et al. also synthesized six organotin (IV) dithiocarbamate complexes: methyltin (IV) methylcyclohexyl dithiocarbamate **(1)**, butyltin (IV) methylcyclohexyl dithiocarbamate **(2)**, phenyltin(IV)methylcyclohexyl dithiocarbamate **(3)**, methyltin(IV)ethylcyclohexyl dithiocarbamate **(4)**, butyltin(IV)ethylcyclohexyl dithiocarbamate **(5)**, and phenyltin(IV)ethylcyclohexyl dithiocarbamate **(6)** [40]. The synthesized complexes were screened against E. raffinosus, S. aureus, Klebsiella sp., A. baumanni, P. auruginosa, and E. aerogenes [40]. Result elucidated bacteriostatic effect for compounds **1-6** at the minimum bactericidal [40]. Compound **3** showed activity against most of the test microbes with an inhibition range of 10-15 mm and MIC value of 2.5 mg/ml, similar to ampicillin [40]. Thus compounds **3** and **6** possessed best antibacterial activity and potential as an antibacterial agent [40]. Sainorudin et al. prepared four novel organotin (IV) dithiocarbamate complex: dibutyltin (IV)di-2-ethylhexyldithiocarbamate $[Bu_2Sn(C_{16}H_{34}NCS_2)_2]$, triphenyltin (IV) di-2-ethylhexyldithiocarbamate $[Ph_3SnC_{16}H_{34}NCS_2]$, dibutyltin (IV)N-methlbutyldithiocarbamate $[Bu_2Sn(C_5H_{12}NCS_2)_2]$, and triphenyltin (IV) N-methlbutyldithiocarbamate $[Ph_3Sn(C_5H_{12}NCS_2)]$ by use of insitu insertion method [41]. The characterization of compounds was done by determining melting point, elemental analysis and FT-IR and UV-visible spectroscopic techniques [41]. The screening of the compounds was done against test microbes: E. coli, S. aureus, S. typhi, and B. cereus [41]. Penicillin and Streptomycin were used as positive and negative control respectively. Results showed broad-spectrum activity towards Gram-positive and Gram-negative bacteria for all complexes [41]. Compound **4** showed better antibacterial activity then the other compounds as reported by the authors [41]. Adli et al. prepared five organotin (IV) dithiocarbamate compounds: dibutyltin (IV) 1-methylpiperazinedithiocarbamate, dimethyltin (IV) 1-methylpiperazinedithiocarbamate, triphenyltin (IV) 1- methylpiperazinedithiocarbamate, dibutyltin (IV) N-methylcyclohexyldithiocarbamate, dimethyltin (IV) N-methylcyclohexyldithiocarbamate, and triphenyltin (IV) N-methylcyclohexyldithiocarbamate [42]. The synthesized compounds were screened towards S. aureus, B. cereus, S. typhi, and E. coli by disc-diffusion method [42]. The results illustrated the great potential of synthesized complexes as antimicrobial agents except for triphenyltin (IV) N-methylcyclohexyldithiocarbamate [42]. Adeyemi et al. prepared five novel organotin (IV) N-

methyl-N-phenyldithiocarbamate compounds: $C_4H_9(Cl)SnL_2$ **(1)**, $C_6H_5(Cl)SnL_2$ **(2)**, $(CH_3)_2SnL_2$ **(3)**, $(C_4H_9)_2SnL_2$ **(4)**, and $(C_6H_5)_2SnL_2$ **(5)** (where L= N-methyl-N-phenyldithiocarbamate) (Figure 3a) [43]. Characterization was done by FT-IR and (^{1}H, ^{13}C and ^{119}Sn) NMR spectroscopy, and elemental and thermal (TGA and DTG) analysis techniques [43]. The compounds were screened for in vitro antibacterial activity towards the test microbes: S. aureus, B. cereus, E. coli, P. aeruginosa, and K. pneumonia [43]. Results showed good to moderate activity for compounds against test microbes. Compound **5** showed highest activity with an inhibition diameter ranging between 10-21 mm [43]. The least antibacterial activity was obtained for compound **3** with inhibition diameter ranging between 8-15 mm [43]. The cytotoxicity of a series of phenyltin (IV) ditiocarbamate compounds with general formula $Ph_{4-n}Sn(S_2CNEt_2)_n$ (where n = 1 to 3) was investigated towards the L1210 mouse leukemia cell line [44]. The investigated compounds showed a high cytotoxic effect compared to cisplatin and carboplatin [44]. Some binuclear diphenyl tin (IV) dithiocarbamate macrocyclic complexes with general formula $[(Ph_2Sn^{IV})_2$-μ^2-bis{κ^2S, S-$S_2CN(R)CH_2CONHC_6H_4)_2O$}] (where R = i Pr **(1)**, s- Bu **(2)**, n-Bu **(3)**, Cy **(4)**, 2-furfuryl **(5)** and benzyl **(6)**) were prepared by Kadu et al. and characterized by microanalysis and relevant spectroscopic techniques [45]. In-vitro cytotoxicity of the synthesized compounds was evaluated against HEP3B (heptatoma) and IMR32 (neuroblastoma) cell lines by use of (4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromide assay [45]. All the compounds showed extreme activity against test cell lines with 16-fold potency than the standard (cisplatin) [45].

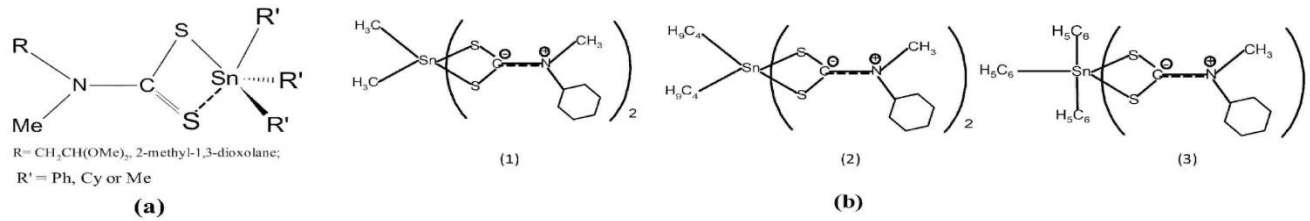


Figure 2. Structure of (a) $[SnPh_3\{S_2CNR(R^1)\}]$, $[SnCy_3\{S_2CNR(R^1)\}]$, $[SnMe_3\{S_2CNR(R)\}]$,$[SnPh_3\{S_2CNR(R^2)\}]$ and $[SnCy_3\{S^2CNR(R^2)\}]$; **(b)** Organotin(IV) dithiocarbamate compounds.

Eng. et al. prepared triorganotin(IV) dithiocarbamate compounds having formula $R_3SnS_2CNR'_2$ (where R= Cy or Ph and NR'_2= NEt_2, N(n-Bu)$_2$, N(i-Bu)$_2$, N(i-Pr)$_2$, $N(CH_2)_5$, NH(n-Pr), NH(n-Bu) or NH(i-Bu) [46]. The characterization of the compounds was done using IR, Mossbauer and NMR spectroscopic techniques and insecticidal activity of the compounds was investigated towards the second larval instar of the Anopheles stephensi Liston and Aedes aegypti (L) mosquitoes [46]. Promising insecticidal activities of the compounds has been reported against the test species [46]. Ali et al. prepared organotin (IV) dithiocarbamates: $(n\text{-}Bu_2SnCl)_2L$ **(1)**, $(n\text{-}Ph_2SnCl)_2L$ **(2)**, $(Ph_3Sn)_2L$ **(3)**, and $(Bz_3Sn)_2L$ **(4)** (where L= 4,4-trimethylenedipiperidine-1-carbodithioate) [47]. The compounds were investigated by FT-IR and ^{1}H and ^{13}C NMR spectroscopy and X-ray single crystal analysis and screening was done against the pathogenic Leshmania major using standard Amphotericine B (o.342 µg ml^{-1}) [47]. All the compounds showed promising anti-leishmanial activity [47].

2.2. Zn dithiocarbamates

Ekennia et al. prepared mixed- ligand organozinc (II) complex: ZnMDBz **(1)** and ZnEDBz **(2)** (where MD= N-methyl-N-phenyl dithiocarbamate and Bz= benzoate) [48]. The characterization was done using elemental analysis, magnetic and conductivity measurements, IR and electronic spectroscopy, and quantum chemical calculations [48]. The synthesized complexes were screened against different test microbes. Results elucidated moderate to high antimicrobial activity. The compound **1** showed better antimicrobial activity than the compound **2** [48]. The compounds were also investigated for anti-inflammatory and antioxidant activities by use of Bovine Serum Albumin Denaturation assay and DPPH and ferrous chelating assay respectively

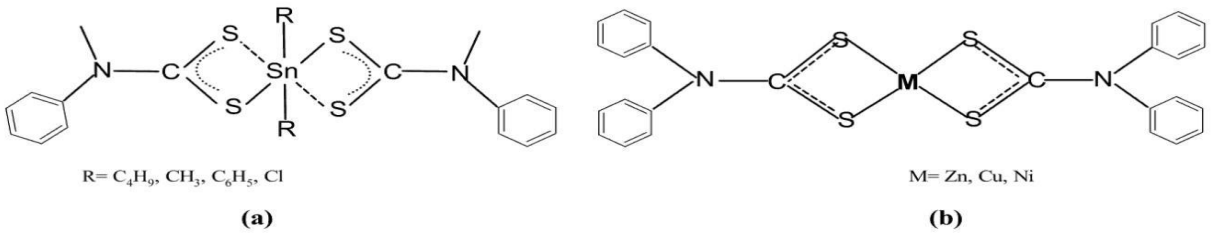


Figure 3. Chemical structure of (a) organotin(IV) N-methyl-N-phenyldithiocarbamate compounds, (b)Ni[$S_2CN(C_6H_5)_2$], Zn[$S_2CN(C_6H_5)_2$], and Cu[$S_2CN(C_6H_5)_2$]

[48]. The compounds had the potency to be anti- inflammatory and antioxidant agents as reported by the authors [48]. Khan et al. synthesized Zn (II) complexes of diphenyl dithiocarbamate: Zn[$S_2CN(C_6H_5)_2$] (Figure 3b) [49]. The complex was characterized using elemental analysis, magnetic susceptibility, conductivity measurements, and mass, IR, NMR, and UV- visible spectroscopy and screened against Aspergillus niger, Aspergillus flavous, Candida albicanes, and Acetomyceta [49]. Results showed better antifungal activities as compared to the standard drug (fluconazole) [49]. The compound also showed better antibacterial potential as compared to diphenyl dithiocarbamate and the standard, ampicillin and remarkable antioxidant potential as compared to standard butylated hydroxytoluene [49]. Mathew et al. synthesized mixed- ligand organozinc (II) complex with molecular formula [M(mordtc)(1,10-phe)], where M= Zn (II) and mordtc = morpholine dithiocarbamate and characterized it using elemental analysis and IR and electronic spectroscopic techniques [50]. The compound was investigated against Gram- negative bacteria: E. coli and K. subtilis and Gram- positive bacteria: S. aureus and S. pneumonia using the agar –disc diffusion method [50]. Result showed significant antibacterial activity against the test microbes [50]. Milacic et al. investigated proteasome inhibition activity of Cu $(PyDTC)_2$ [bis (1-pyrrolidinedithiocarboato-kS, kS') copper (II)] **(1)** and Zn $(PyDTC)_2$ [bis(1-pyrrolidinedithiocarboato-kS, kS')zinc(II)] **(2)** against the purified 20S proteasome [51]. The result showed 40% inhibition of proteasomal chymotrypsine-like activity at 50 µmol/L concentration [51]. Both the compounds showed 90% inhibition of MDA-MD-231(breast cancer) cells at 20 µ mol/ L concentration.Compound 1 exhibited higher activity the n compound 2 [51]. They also reported the more than 90% inhibition activity of the synthesized complexes against other cancer cell lines including DCIS and MCF7 (estrogen receptor α-positive breast cancer) and PC3 (androgen receptor independent – human prostate cancer) at 20 µ mol/L concentration [51]. Janabi et al. prepared the Zn (II) complexes: [Zn (κ^1 -PipDT)$_2$(Bipy)], [Zn(κ^1 -PipDT)$_2$(Phen)], and[Zn(κ^1 -PipDT)$_2$(3Apy)$_2$] (Figure 4) where PipDT= piperidine dithiocarbamate, Bipy= 2,20-bipyridine, Phen= 1,10-phenantroline and 3Apy=3-aminopyridine [52]. The characterization of the compounds was carried out using spectroscopic techniques and elemental analysis [52]. The compounds were investigated against pathogenic bacterial strains: E. coli, S. pyogenes and S. aureus and fungal strains: A. niger and C. albicans [52]. Moderate to good activity of the compounds then the standard drug had been reported by the authors [52].

Odularu et al. reported mixed ligand complexes of Zn (II) and oxovanadium (IV) ions: [Zn(sfz)(ai-dtc) and [VO(sfz)(ai-dtc) where sfz=suifadiazine and ai-dtc= aniline dithiocarbamate [53]. The characterization was done using UV-vis, FT-IR and ^{1}H and ^{13}C NMR spectroscopy [53]. The compound showed modest activity during in vitro antibacterial study against Gram negative bacterial strains: P. aeruginosa and E. coli [53]. The Zn (II) dithiocarbamate complex: (ZnLL')·$2H_2O$, where L=N-methyl-N-phenyldithiocarbamate and L'=benzoylacetone, has been prepared and characterization was carried out using IR and UV-visible spectroscopy, elemental analysis, magnetic susceptibility and electrical conductance measurement techniques (Figure 5a) [54].The antimicrobial activity of the compound was investigated. The reported activity of the compound was 83.7% compared to streptomycin towards E. coli and 72% and 80.5% compared to fluconazole towards A. niger and A.candida, respectively [54]. $(AHPDTC)_2$ Zn, where AHPDTC is dithiocarbamate ligand derived from 2-amino-3-hydroxyperidine with carbon disulphide (2–amino–3–hydroxypyridine + CS_2), has been synthesized and screened against Gram- positive bacteria: Bacillus subtilis and

Gram-negative bacteria: Klebsiella pneumoniae and Escherichia coli [55]. The complex showed better anti-bacterial activity

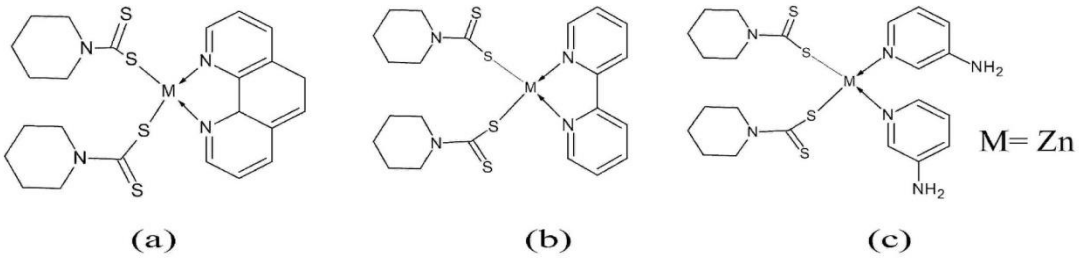


Figure 4. Chemical structures of (a) $[Zn(\kappa^1\text{-PipDT})_2(Phen)]$ (b) $[Zn(\kappa^1\text{-PipDT})_2(Bipy)]$ (c) $[Zn(\kappa^1\text{-PipDT})_2(3Apy)_2]$

than the ligand [55]. Mixed ligand complexes of Zn (II) with pentamethylene dithiocarbamate (pmdtc) and amines: ethylene diamine (en), diethylenetriamine (dien) and triethylene triamine (trien), have been prepared, characterized and investigated for antibacterial, antifungal and anticancer activities [56]. Reasonable activities were reported for all the compounds [56].

2.3. Au dithiocarbamates

Novel dithiocarbamate complexs of Au(III) ion: $[Au(DMDT)Cl_2]$, $[Au(ESDT)Cl_2]$, $[Au(DMDT)Br_2]$, and $[Au(ESDT)Br_2]$ (where DMDT= N,N-dimethyl dithiocarbamate and ESDT= ethylsarcosine dithiocarbamate) (Figure 5b and 5c) [57] were synthesized and found to inhibit cisplatin-induced nephrotoxicity. The in-vitro cytotoxicity of all the compounds was investigated towards various human- tumor cell lines. Results elucidated more in vitro cytotoxicity compared to cisplatin with 1-4 fold lower IC_{50} value. The tested compounds also showed cytotoxicity against the cisplatin resistance cell-lines [57,58]. Similarly, Keter et al. synthesized dithiocarbamate complexes of Au(I) ion: $[AuL(PPh_3)]$ **(1-3)**, $[Au_2(L)_2(dppp)]$ **(4-6)**, and $[Au_2(L)_2(dpph)]$ **(7-9)**, where dppp= 1,3-bis(diphenylphosphino)propane and dpph= 1,6- bis(diphenylphosphino)hexane; L= pyrazolyldithiocarbamate (L_1), 3,5-dimethylpyrazolyldithiocarbamate (L_2), or indazolyldithiocarbamate (L_3) [59]. Characterization was done using mass, IR and NMR spectroscopies and microanalysis techniques and screened against HeLa (human cervical epithelioid carcinoma) cells [59]. The result showed the highest activity for compound **7** (IC_{50} value 0.51 µM) and compound **8** (IC_{50} value 0.14 µM) [59]. Compound **10** and compound **11** showed more selectivity (25.0 and 70.5 times, respectively) towards tested cells than the normal cells [59]. Similarly, Altaf et al. prepared novel Au(I) dithiocarbamate complex: $[(t\text{-}Bu)_3PAuS_2CN(C_7H_7)_2]$ **(1)**, $[(DPPM)Au_2\{S_2CN(CH_3)_2\}_2]$ **(2)**, $[(DPPM)Au_2\{S_2CN(C_2H_5)_2\}_2]$ **(3)**, and $[(DPPM)Au_2\{S_2CN(C_7H_7)_2\}_2]$ **(4)** (where DPPM= 1,1-bis(diphenylphosphino)methane and C_7H_7= benzyl) [60]. In-vitro cytotoxicity of the complexes was investigated towards various human cancer cell lines (HeLa, HCT15, and A549) [60]. Results elucidated that the order of cytotoxicity was (2)> (3)> cisplatin> (1)> (4). Compound **2** and **3** had been found most effective against HeLa cells [60].

Kailasa et al. prepared nanoparticals of gold derivative of 4-hydroxy-6-methyl-3-nitro-2-pyridone-dithiocarbamate and investigated its use in simple and compitative detection of diafenthiuron (insecticide) in food and water sample [61]. The result demonstrated high selectivity of the designed plasmonic sensor towards diafenthiuron with a lower detection limit (7. 1 nM) than the permissible limit of difenthiuron [61]. Sim et al. investigated in vitro antibacterial activity of three phosphinogold(I) dithiocarbamate compounds with general formula $[R_3PAu\{S_2CN(i\text{-}Pr)CH_2CH_2OH\}]$ (where R= Ph **(1)**, Cy **(2)** or Et **(3)**) (Figure 6a) [62] against various Gram-positive and Gram-negative pathogenic bacterial strains namely A. hydrophilla, A. baumanni, B. cereus, B. subtilis, C. freundii, E. cloacae, E. aerogenes, E. faecalis, E. faecium, E. coli, K. pneumonia, L. monocytogenes, P. mirabilis, P. vulgaris, P. aeruginosa, S. paratyphi A,, S. typhimurium, S. flexneri, S. sonnei, S. aureus, methicillin-resistant S. aureus (MRSA), S. saprophyticus, S. maltophilia, S. pyogenes, and V. parahaemolyticus, by disc diffusion method, minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) determination and time-kill assay [62]. Results

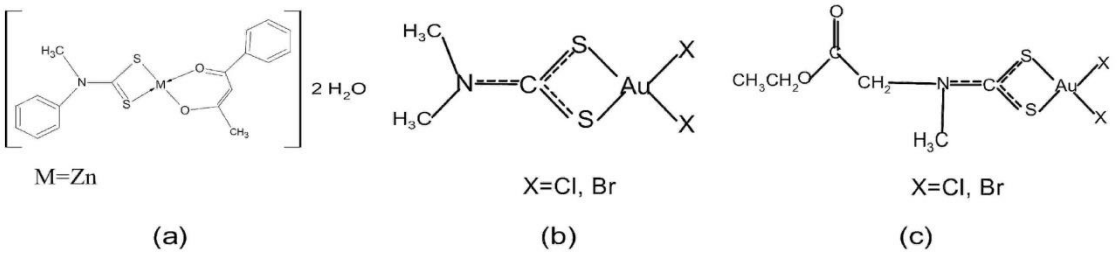


Figure 5. Chemical structure of **(a)** $[ZnC_{18}H_{17}NS_2O_2]\cdot 2H_2O$; (b) $[Au\{DMDT)Cl_2]$, $[Au(DMDT)Br_2]$; (c) $[Au(ESDT)Cl_2]$, $[Au(ESDT)Br_2]$

showed that complex **1** and **2** possessed activity towards test bacteria (Gram-positive) with MIC values in the range 7.81-125 µg/mL [62]. Compound **3** showed activity towards 24 test microbes with MIC values between 0.98-1000 µg/mL. The activity towards MRSA and B. subtilis was similar to that of standard (ciprofloxacin) [62]. The time kill assay studies elucidated that the compounds possessed bacteriostatic and bactericidal activity towards susceptible strain similar to that determined by MBC and MIC techniques [62]. $[Au(L)_2(H_2O)Cl]$ (where L= 5-cyano-3-formyl-1H-1-indole-1-carbodithioate) has been synthesized, characterized (Figure 6b) and screened against S. aureus, E. coli, and C. albicans [63]. The result elucidated good antimicrobial activity [63]. Two anti-neoplastic agents, $[Au(III)Br_2\{dtc\text{-}Sar\text{-}Gly\text{-}O(t\text{-}Bu)]]$ and $[Au(III)Br_2\{dtc\text{-}Sar\text{-}Aib\text{-}O(t\text{-}Bu)\}]$ had been prepared and investigated towards cisplatin resistant MDA-Mb-231 (human breast cancer) cell cultures and xenografts [64]. In-vivo and in-vitro studies proteasome was the main target [64]. The results showed 53% inhibition of breast tumor growth in mice after 27 days and 85% inhibition in most responsive mice, with tumor

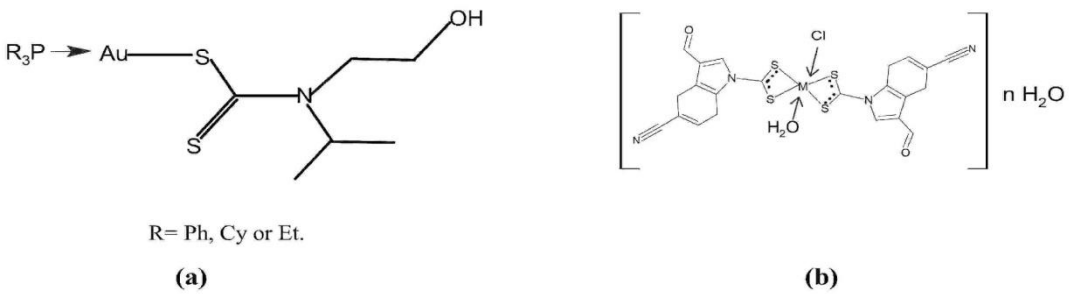


Figure 6. Chemical structure of (a) (Phosphanegold(I) dithiocarbamate compounds, (b) $[Au(L)_2(H_2O)(Cl)]$

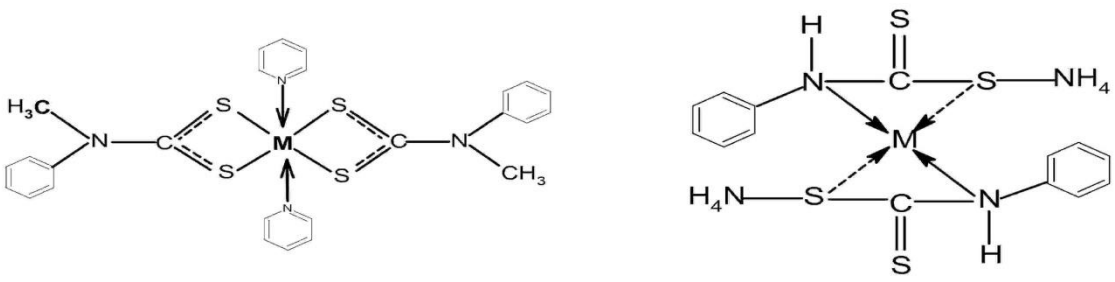
shrinkage in some animals after 13 days [64]. Altaf and coworkers synthesized bipyridineAu(III) dithiocarbamate complexes having fascinating anticancer activity towards cisplatin resistant cancer cells independent of p53 status [65]. High cytotoxicity of the compounds towards prostate, breast, ovarian and Hodgkin lymphoma cancer cells, with IC_{50} value less than cisplatin, has been reported [65]. The compounds were also screened towards panel of lung cancer cell lines. The result demonstrated significant cytotoxicity independent of p53 status [65]. Two novel linear Au(I)dithiocarbamate complexes: $[Au\{p(t\text{-}Bu)_3\}(S_2CN(CH_3)_2]$ and $[Au\{p(t\text{-}Bu)_3\}(S_2CN(C_2H_5)_2]$ were prepared and their structures had been studied using FT-IR and NMR spectroscopy, elemental analysis, cyclic voltammetry, and X-ray diffraction [66]. The compounds were screened for in vitro cytotoxicity against human cancer cell lines: MCF7(breast), A549(lung), and HeLa(cervical) [66]. The result elucidated strong in-vitro cytotoxicity [66]. The investigation of the cytotoxicity on the basis of IC_{50} data demonstrated the high effectiveness of the compounds, particularly toward HeLa cells and better cytotoxicity than cisplatin [66].

Novel phosphane gold(I) dithiocarbamate compounds: $[Au(PR_3)(S_2CNR'_2)]$ (where, R=methyl, ethyl or isopropyl; R'=methyl or ethyl) were prepared and characterization was done using FT-IR and multinuclear NMR spectroscopic and elemental analysis

techniques [67]. In the investigation of in-vitro cytotoxicity against human cancer cells: A549 and HepG2, the compounds exhibited 4-6 fold potency towards A549 and 3-5 fold potency towards HepG2 compared to cisplatin [66]. The study of in-vitro DNA-binding ability was carried out using UV-visible titration, fluorescence spectroscopy, and circular dichroism techniques [67]. The compounds had very high intrinsic binding constant values ($3.90X10^4$, $4.74X10^4$, $6.81X10^4$, 8.53X104, and $2.48X10^4$ M^{-1} respectively) [67]. The molecular docking studies elucidated that the compounds bind to the adenine- thymine residues in the minor groove of the DNA, as reported by the authors [67].

2.4. Ni dithiocarbamates

Mixed-ligand complexes of Ni(II): NiEDBz and NiMDBz (where Bz=benzoate, ED= N-ethyl_N-phenyldithiocarbamate, MD=N-methyl-N-phenyldithiocarbamate) have been synthesized using benzoic acid and sodium salt of N-alkyl-N-phenyldithiocarbamate [48]. The compounds were screened against different test microbes. The methyl-substituted complexes exhibited better antimicrobial activity [48]. The study of the anti-inflammatory activity using Bovine serum albumin denaturation assay and antioxidant activity using DPPH and ferrous chelating assays demonstrated the potential of the compounds to be anti-inflammatory and antioxidant agents [48]. $Ni[S_2CN(C_6H_5)_2]$ has been synthesized, characterized (Figure 3b) [49] and investigated towards fungal strains: Aspergillus niger, Aspergillus flavous, Candida albicans, and Acetomyceta and bacterial strains: Actinomyses viscous, Rhodococcus, Bacillus subtilis, and Escherichia coli [49]. The compound exhibited better antifungal and antibacterial activities than the Fluconazole and Ampiciline, respectively [49]. The compound also possessed antioxidant potential [49]. Sharma et al. synthesized 1;1 adducts of bis(moropholinedithiocatbamate) complex of VO(IV) and 1:1 adducts of bis(morpholinedithiocarbamate) complexes of Ni(II) and Cu(II) ions : $[VO(morphdtc)_2L].H_2O$, $Ni(morphdtc)_2.L$, $Cu(morphdtc)_2.L$, $Ni(morphdtc)_2.L_2$, and $Cu(morphdtc)_2.L_2$ (where, morphdtc= morpholinedithiocarbamate, L= morpholine and piperidine) [2]. Characterization of the synthesized adducts was done using elemental analysis, molar conductance, magnetic susceptibility, IR and UV-vis spectroscopy and TGA? DTA techniques [2]. The antifungal activity of all the five adducts with morpholine was investigated towards pathogenic fungal strain, Fusarium oxysporium by the Poisoned Food Technique [2]. The results elucidated a linear relationship between activity and concentration [2]. Ekkenia et al. prepared mixed ligand complexes of Ni(II),Co(II), Cu(II), and Mn(II) ions having formula $[ML_2(py)_2]$, where M= Ni(II), Co(II), Cu(II) or Mn(II) ions, py= pyridine, L= N-methyl-N-phenyl dithiocarbamate (Figure 7a) [68]. The compounds were characterized using elemental analysis, FT-IR and UV spectroscopy, magnetic moment, thermo-gravimetric and conductance analysis and screened in-vitro against fungal strains: A. niger, C. albicans, and A. flavous [68]. The Co(II) complex exhibited the highest antifungal activity [68].Ingle et al. prepared and characterized novel Ni(II) complex of ammonium phenyl dithiocarbamate (Figure 7b) [69].



(a) (b)

Figure 7. Structure of (a) mixed ligand dithiocarbamate of Ni(II), Co(II), Cu(II) and Mn(II) ; (b) Cu(II), Ni(II), Co(II) and Hg(II) complexes of ammonium phenyl dithiocarbamate

The in-vitro antibacterial activity was investigated against bacterial strains: E. coli, S. aureus, P. vulgaris, and P. auruginosa by cupplate agar diffusion method [69]. Results elucidated that the synthesized compound showed prominent activity against all the test microbes [69]. Mixed ligand complexes of Ni(II): [Ni(mordtc)(1,10-phe)], where, mordtc= morpholine dithiocarbamate and 1,10-phe= 1,10-phenanthroline has been synthesized and investigated for antibacterial activity [50]. The compound showed significant antibacterial activity against the test microbes [50]. Similarly Ni(II) and Pd(II) complexes: $[Ni(PDTC)_2]$ and $[Pd(PDTC)_2]$ (where PDTC= pyrrolidine dithiocarbamate) were synthesized by Islam et al. Structures of the compounds were studied using elemental, physiochemical and spectroscopic methods and antibacterial activity was investigated towards Gram-positive bacteria (B. cereus) and Gram-negative bacteria (E. coli, V. cholera, S. pneumonia) using agar disc diffusion method. The result showed higher antibacterial activity of compounds than the ligand [70]. Bis-(N-methyl-N-phenyl dithiocarbamate) complex of Ni(II) has been synthesized and screening against various Gram-positive and Gram-negative bacterial strains showed that the complex possessed antibacterial activity [71]. Alias et al. prepared Ni(II) and Co(II) dithiocarbamate complexes with novel mixed ligands synthesized from [5-(p-nitrophenyl)-4-phenyl-1,2,4-triazole-3-dithiocarbamatohydrazide)] (primary ligand) and [2,2'-bipyridyl] (co-ligand) [72]. The in-vitro cytotoxic behavior of the complexes was investigated towards HepG2 cell line, using cisplatin as positive control [72]. The complexes displayed more in-vitro anti-oxidant potential than the standard drug [72]. $(AHPDTC)_2Ni$, where AHPDTC is dithiocarbamate ligand derived from reaction of 2 –amino–3–hydroxypyridine with CS_2, was synthesized and characterized using elemental analysis and FT-IR and NMR spectroscopy [55]. The investigation of antibacterial activity against different test microbes revealed that the complex is better anti-bacterial agent than the ligand [55]. Ni(II) mixed ligand complexes: $[Ni(II)(en)(mophdtc)_2]$, $[Ni(II)(dien)(morphdtc)_2]$, and $[Ni(II)(trien)(morphdtc)_2]$ were screened against fungal strains: C. albicans, A. niger, and Rhizopus spp.and bacterial strains: S. aureus, E. coli, P. aeruginosa, A. hydrophila, and Vibrio spp. [73]. The complexes exhibited reasonable activity against test fungal strains (except Rhizopus spp.) and moderate antibacterial activity (at high concentration) [73]. The trien complex exhibited excellent activity against S. aureus [73]. Mixed ligands complexes of Ni(II): $[Ni(L^x)_2(L^3)_1]$ and $[Ni(L^x)_1(L^3)_2]Cl$ (x= 1or 2) have been synthesized (where L^1= pyrrolidine-1-carbodithioate, L^2= piperidine-1-carbodithioate and L^3= 1,10-phenanthroline) and characterized using FT-IR, UV-visible, and ^1H NMR spectroscopy (Figure 8) [74]. Screening against various test microbes demonstrated that the complexes possessed moderate and selective antimicrobial activity [74]. $[Ni\ (L)_2(H_2O)_2]H_2O$ (where= l= 5-cyano-3-formyl-1H-indole-1-carbodithioate) has been synthesized and characterized using FT-IR, UV-visible, mass, and flammable atomic absorption spectroscopies, molar conductivity, magnetic sensitivity, solubility, and product microanalysis (Figure 9) [63]. The compound showed antimicrobial activity [63]. Mixed ligand complexes of Ni(II) with pentamethylenedithiocarbamate and amines (ethylenediamine, diethylenetriamine, and triethylenetetramine) have been reported [56]. The complexes were characterized using elemental, thermal and magnetic analysis and UV-visible, IR, NMR, and ESR spectroscopic techniques [56]. Study of antibacterial, antifungal, and anticancer activities has been done [56]. The complexes exhibited reasonable activity [56]. Ni(II) and Zn(II) dithiocarbamate complexes: $[Ni(f^1prdtc)_2]$ **(1),** $[Ni(f^1prdtc)(PPh_3)(NCS)]$ **(2)**, $[Ni(f^1prdtc)(PPh_3)_2]ClO_4$ **(3)**, $[Zn(f^iprdtc)_2]$ **(4),** $[Zn(f^iprdtc)_2(1,10\text{-phen})]$ **(5)**, and $[Zn(f^iprdtc)_2(2,2'\text{-bipy})]$ **(6)** (where, f^1prdtc= N-furfuryl-N-isopropyldithiocarbamate, 1,10-phen= 1,10-phenanthroline, 2,2'-bipy= 2,2'-bipyridine) have been synthesized and characterization was done using elemental analysis, and electronic, IR, and NMR spectroscopy and single-crystal X-ray crystallography in case of compound **2** [75]. The compounds were screened against bacterial strains: S. aureus, E. coli, P. aeruginosa, and K. pneumonia, using disc diffusion assay at 200 and 400 µg L^{-1} concentrations [75]. The compounds showed antibacterial activity toward the test microbes [75].

2.5. Co, Cu, Mn, Hg, Pd, Pt dithiocarbamates

$Cu[S_2CN(C_6H_5)_2]$ (Figure 3b) [49] has been prepared, characterized and investigated for antifungal, antibacterial, and antioxidant potential. The compound showed considerable activity [49]. Ammonium phenyl dithiocarbamate complexes of

Cu(II), Co(II) and Hg(II) ions (Figure 7b) [69] were prepared, characterized and investigated for antibacterial potential. All the complexes showed prominent antibacterial activity towards E. coli, S. aureus, P. vulgaris, and P. aeruginosa [69]. Ajibade et al. synthesized four coordinated complexes of Cu(II), Pd(II), and Pt(II) ions with general formula [M(SD)(me-DTC)] and [M(SD)(et-DTC)] (where M= Co, Cu, Pd or Pt; SD= sulfadiazine; me-DTC= N-methyl-N-phenyl dithiocarbamate; et-DTC= N-ethyl-N-phenyl dithiocarbamate), characterized them using elemental analysis, conductivity measurements, and FT-IR and UV-visible spectroscopic techniques and screened against bacterial strains: S. aureus, S. faecalis, B. cereus, B. pumilus, E. coli, P. aeruginosa, P. vulgaris, and K. pneumonia using agar well diffusion method and determination of MIC and MIB [76]. The results showed varied antibacterial activities with the highest activity for [Co(SD)(et-DTC)] [76]. Similarly, Jayaraju et al. synthesized Cu(II) and Mn(II) dithiocarbamate complex: $[Cu(AMPDTC)_2Cl_2]$ and $[Mn(AMPDTC)_2Cl_2]$ respectively where, AMPDTC= 2-amino-2-methyl-1-propanol dithiocarbamate (Figure 9c) [77]. Characterization was done using elemental analysis, IR, ^1H NMR and ESR spectroscopic and TGA-DTA techniques [77]. The compounds were screened against four bacterial strains: S. aureus, B.subtilis, E. coli, and P. aeruginosa, using agar well diffusion technique [77]. The compounds exhibited selective activity against some of the test bacteria [77]. Mixed ligand complex, [M(mordtc)(1,10-phe)] (where M= Ni(II), Co(II), and Cu(II): mordtc= morpholinedithiocarbamate; 1,10-phe= 1,10-phenanthroline) have been synthesized, characterized, and investigated towards Gram-positive bacteria: S. pneumonia and S. aureus, and Gram-negative bacteria: K. subtilis and E. coli [50]. All compounds showed significant antibacterial activity against the test microbes [50]. Cu(II) mixed ligand complexes of pentamethylenedithiocarbamate (pmdtc) with amines such as ethylenediamine (en), diethylenetriamine (dien), and triethylenetetramine (trien) have been prepared, characterized and examined for antibacterial, antifungal and anticancer activities [56]. All the complexes have shown reasonable activity [56]. $[Co(L)_2(H_2O)_2]H_2O$ and $[Cu(L)_2(H_2O)_2]H_2O$ (where L= 5-cyano-3-formyl-1H-indole-1-carbothioate) were synthesized (Figure 9a) [63], characterized and their biological function was investigated by inhibition method towards one type of pathogenic fungal and two types of bacterial, one Gram-positive and other Gram-negative, strains [63]. The result elucidated potential of complexes as antimicrobial agent [63].

$(ATZDTC)_2Cu$, $(AECZDTC)_2Cu$, $(FMDTC)_2Cu$, $(AHMPYDTC)_2Cu$, $(AHPDTC)_2Cu$, $(AHPDTC)_2$ Pd, $(AHPDTC)_2Mn$, and $(AHPDTC)_2Co$ has been synthesized where, (ATZDTC) , (AHPDTC) , (AECZDTC) , (FMDTC), and (AHMPYDTC), are dithiocarbamates derived from 4-amino-1,2,4-Triazole, 2-amino-3-hydroxypyridine, 3-amino-9-ethylcarbazole, (Furon-2-yl)methanamine, and 2-amino-4-hydroxy-6-methylpyrimidine with CS_2 respectively, and characterized by NMR and FT-IR spectroscopy and elemental analysis [55]. The complexes were screened against E. coli, B. subtilis, and Klebsiella [55]. The results demonstrated that the complexes are better antibacterial agents than the ligand [55]. Heteroleptic complexes of Cu(II), Mn(II), and Co(II) ions with general formula $[MLL'].nH_2O$ (where L= N-methl-N-phenyldithiocarbamate and L'= benzoylacetone, n=0 for Co(II), Mn(II) and n=1 for Cu(II) complex) have been synthesized (Figure 9b) [54] and characterized using elemental analysis, electrical conductance, magnetic susceptibility and IR and UV-visible spectroscopy [54]. The complexes were screened towards Gram- positive bacteria: S. aureus and S. pneumonia, Gram- negative bacteria: E. coli and fungal strains: A. niger and A. candida and exhibited a broad spectrum of antimicrobial activities [54]. Nano-dithiocarbamate (DTC) complex, $[Co(pipdtc)_2(1,10\text{-phen})]$ (where phe= phenantroline; pipdtc= pentamethylene) was synthesized by the action of DTC on metal salt in the presence of ultrasound radiation and the structure was established using X-ray diffraction and scanning electron microscopy methods [78]. Antimicrobial activity was investigated towards C. albicans, A. flavous, A.niger, E. coli, K. pneumonia, S. aureua and B. subtilis [78]. The synthesized nanoparticles of DTC showed the potential for antibacterial and antifungal in comparison with their normal form [78]. Krishnan et. al. synthesized binuclear Co(II) complexes with general formula $[Co_2(pipdtc)(aa)_2(H_2O)_4]$, where pipdtc= piperazine dithiocarbamate (bridging ligand); (aa)= alanine(ala), phenylalanine(pheala), tyrosine(tyr), methionine(met), and glycine(gly) (deprotonated chelated anions) [79].

The compounds were characterized using elemental and thermal analysis, IR, UV-visible, and ESR spectroscopy and magnetic susceptibily determination techniques [79]. The complexes were screened against bacterial strains: S. aureus, E. coli, P. aeruginosa, A. hydropila and Vibrio spp. and fungal strains: C. albicans, A. niger, and Rizopus spp. [79]. The results of antibacterial and antifungal studies were encouraging [79]. The investigation of anticancer and antioxidant activities along with the DNA Cleavage studies was also carried out [79]. The results elucidated that the complexes are biologically significant [79].

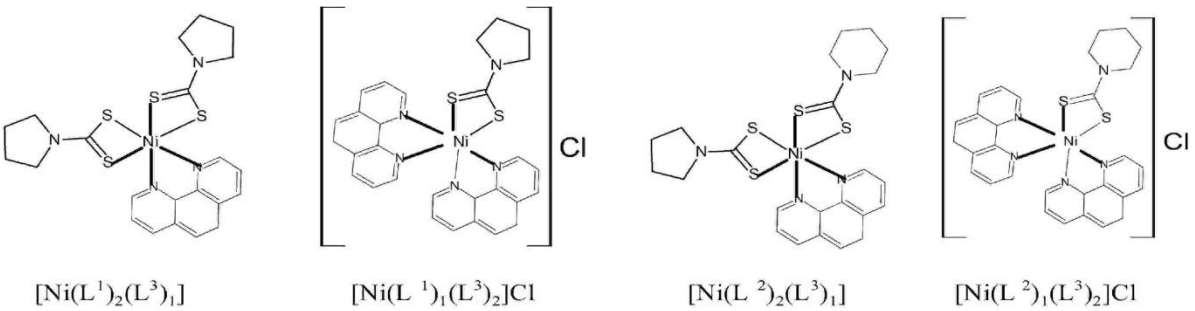


Figure 8. Molecular structure of the prepared Ni(II) compounds.

2.6. Ru dithiocarbamates

Nogueira et al. synthesized a series of ruthenium dithiocarbamate complexes: $[Ru_2(S_2CN(CH_3)_2)_5]$ (1), $[Ru_2(S_2CN(CH_2CH3)_2)_5]$ (2), $[Ru_2\{S_2CN(C(CH_3)_3)(H)\}_5]$ (3), $[Ru_2\{S_2CN(CH(CH_3)_2)(H)\}_5]$ (4), and $[Ru_2\{S_2CN(CH(CH_3)_2)_2\}_5]$ (5) [80]. The synthesized compounds were evaluated against A. clavatus, A. flavous, A. fumigates, A. niger, A. nomius, A. tamari, and A. terreus and exhibited antifungal activity toward some of the test microbes except A. nomius and A. terreus [80]. Low MIC value (4-8 µg mL^{-1}) was exhibited by the complexes 1 and 2 against A.clavatus and A. fumigates [80]. Complex 5 showed lowest MIC value towards A. niger [80]. Novel complexes of Au(II) and Ru(III) ions: $[AuCl_2(pipeDTC)]$ (1), $[Au(pipeDTC)_2]Cl$ (2), $[Ru(pipeDTC)_3]$ (3), and β-$[Ru_2(pipeDTC)_5]$ (4) (where, pipeDTC= piperidine dithiocarbamate) were prepared and characterized using several chemical analysis techniques [81].The compounds were screened against cancer cell lines: AGS (adenocarcinoma gastric cells) and HCT116 (human colon carcinoma cells) [81]. The compounds 1, 2, and 4 displayed significantly low IC_{50} value (in µM) as compared to cisplatin [81]. The complexes 1 and 4 drive different molecular mechanism. Compound 1 induced the protein level of the DNA damage response factor p53 and the autophagy protein p62, while compound 4 induced the ATF4 protein

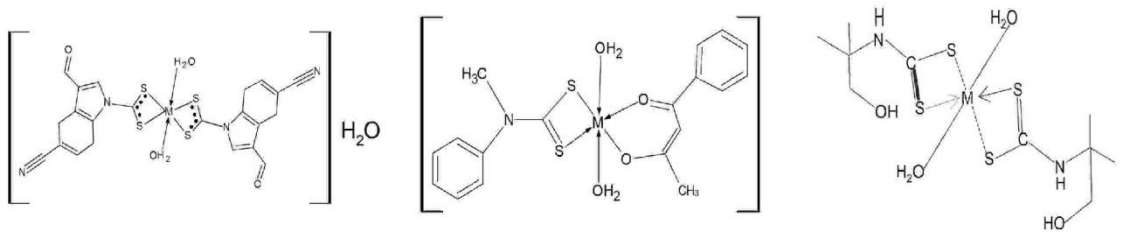


Figure 9. Molecular structure of (a) $[M(L)_2(H_2O)_2]H_2O$ (b) Cu, Co and Mn mixed ligand complexes. (c) $[Cu(AMPDTC)_2Cl_2]$ and $[Mn(AMPDTC)_2Cl_2]$

level, but depressed p62 [81]. Scintilla and coworkers prepared mono and di-nuclear Ru(III) complexes: $[Ru(PDT)_3]$ (1), β-$[Ru(PDT)_5]Cl$ (2), $[Ru(CDT)_3]$ (3), and α-$[Ru_2(CDT)_5]Cl$ (4) (where, PDT= pyrrolidine dithiocarbamate, CDT= carbazole dithiocarbamate) to compare their properties at chemical and antiproliferative levels to investigate structure- activity rationale [82]. The structures of the compounds were established by FT-IR, NMR, UV-visible, and ESI-MS spectroscopy, silica gel and thin layer chromatography, and elemental analysis techniques [82]. The in-vitro antiproliferative activity of the compounds was evaluated towards HeLa (cervix adenocarcinoma) and HCT116 (colon carcinoma) human tumor cell lines [82]. To overcome the scarce solubility of the compounds under physiological conditions, the biocompatible copolymer Plunoric® F127(water soluble micellar carriers) were used to encapsulate compounds [82]. Complex 2 exhibited in-vitro antiproliferative activity which increased with application of Plunoric® F127 [82]. On the other hand, complexes 3 and 4 showed no significant activity towards the test cancer cell lines [82].

Novel arene Ru(II) and cyclopentadienyl Ru(II) dithiocarbamate complexes (Figure 10a and Figure 10b respectively) have been prepared and characterized using NMR and EI-MS spectroscopic techniques [83]. The structures of compounds 1 and 3 were established by X-ray crystallography [83]. The in-vitro antitumor activity of the complexes was investigated towards human ovarian cancer (SKOV-3), human hepatoma carcinoma (HepG-2), human lung cancer (A549), rat pheochromocytoma (PC12) tumor cells and two murine cells: RAW246.7 and L6 by MTT method using cisplatin as standard [83]. Arene complexes were significantly less effective towards SKOV-3, PC12, and A549 cell lines than the standard [83]. Complex 5 exhibited strong

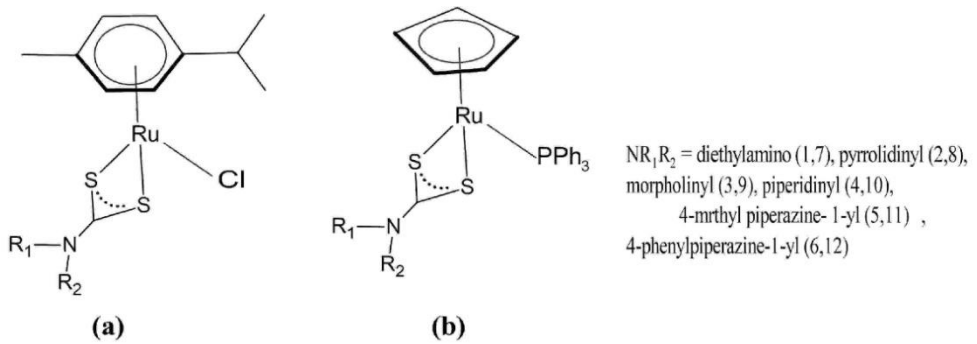


Figure 10. Molecular structures of (a) Arene ruthenium(II) dithiocarbamate complexes [1- 6] (b) Cyclopentadienyl ruthenium(II) complexes [7-12].

cytotoxicity towards HepG-2 cells and 6 and 8.3- fold higher IC_{50} values towards RAW246.7 and L6 cells, respectively, in comparison of cisplatin [83]. In cyclopentadienyl complexes only 7 and 8 showed high cytotoxic activity towards SKOV-3 cells as compared to other test cancer cells, with IC_{50} values of 6.8 and 8.7, respectively [83]. The selectivity of complexes 7 and 8 was less than complex 5 [83]. The overall result elucidated that the complex 5 possessed the highest cytotoxicity and selectivity towards tested cancer cell lines [83].

3. Conclusion

Duithiocarbamates are special class of organosulfur ligands that are able to form stable complexes with various metals. Dithiocarbamates have wide range of applications from pesticide to medicine. Dithiocarbamates and their metal derivatives possess various biological activities including modulation of key proteins participating in various biological processes, such as apoptosis, transcription, oxidative stress, and degradation, proteasome inhibition, and in-vitro cytotoxicity. They also have antibacterial, antifungal, antioxidant, antitumor and antileismanial activities. In some cases, it has been found that the investigated novel dithiocarbamate metal derivatives exhibited better activity than the current drugs used as standared during

the study. Thus, the facts described above including the recent studies and work done on the synthesis and applications of metal-dithiocarbamate complexes elucidated that the metal complexes of dithiocarbamates can be used as a potent antifungal, antibacterial and antitumor agents. They have been found other biological applications also. The discussed biological applications of dithiocarbamate complexes lead to the development and implementation of better medical agents. on the basis of overall discussion, it is also clear that there are many more metals that can be used to synthesize new metal dithiocarbamate compounds. Similarly, there is possibility to develop new dithiocarbamate ligands. Finally, we can say that there is a wide scope to synthesize novel metal dithiocarbamates and to find out ther applications in field of medicine.

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