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Research Article

VERSATILITY OF THERAPEUTIC BEHAVIOUR OF THIOSEMICARBAZONES AND ITS METAL COMPLEXES

Sonia Khanna

Department of Chemistry and Biochemistry, School of Basic Sciences and Research, Sharda University, Greater Noida (U.P), India

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A B S T R A C T

Thiosemicarbazone is a well known Schiff based ligand with versatile bonding modes and biological activities. Upon coordination to metal, thiosemicarbazones and its complexes have shown remarkable progress in the development of drugs for medical conditions owing to their antibacterial, antifungal, antiviral as well as antitumor properties. In this review article, the recent information about biological studies conducted on thiosemicarbazones and its complexes is summarized. Thiosemicarbazone complexes with transition metals hold several advantages over metal complexes because of their better acceptability and low toxicity in biological process. They have shown better performance than available therapeutic drugs like that of the antitumor drug *cis-platin.* This review will also provide latest updates on current advances in medical use of thiosemicarbazone complexes.

INTRODUCTION

Versatile biological properties of thiosemicarbazones (Figure 1) have received interest because of their bonding modes and biological properties such as antitumor, antiviral, antitubercular, antibacterial, antihypertensive and antimalarial activities (Lobana *et.al*., 2009; West *et al.* 1993; Suvarapu *et al.* 2012; West *et al.* 1993). They have also emerged as potential candidate for drugs for therapeutic diagnosis in various disease and development of novel generation of highly efficient drugs with minimal side effects and many have shown significant anti-proliferative effects, even stronger than for cisplatin. Many metal complexes showed better inhibitory effects than the parent ligands due to the increased lipophilic character of these complexes. It has been observed that the nature of metal ion in complex and substituent at N^4 of thiosemicarbazone ligand plays a significant role in deciding the action of complex. It has been observed that the presence of a bulky group attached to the terminal nitrogen of the thiosemicarbazone strongly enhances its pharmacological activity (West *et al.* 1993, Wang *et al.* 2009). The cytotoxic studies of thisoemicarbazone and its complexes has been reviewed (Khan *et. al.* 2015.) The anticancer properties of triapine (3-aminopyridine-2-carboxaldehyde thiosemicarbazone) is currently been examined on different types of cancer. In this review, the information about biological studies on thiosemicarbazone complexes with respect to the nature of metal ions and substituents is summarized. This information can be utilized in drug designing for various conditions.

Corresponding author:* **Sonia Khanna
Department of Chemistry and Biochemistry, School of Basic Sciences and Research, Sharda University, Greater Noida (U.P), India

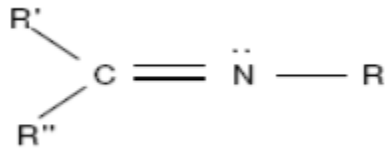

Figure 1 Thiosemicarbazone

Antimicrobial Studies

Thiosemicarbazone complexes possess a variety of antimicrobial activities such as antibacterial, antifungal, antimalarial activities etc. Antibacterial activity of compounds or agents, inhibit the growth and spread of bacteria, work either by stopping bacterial growth or by killing the bacteria. They inhibit the synthesis of peptidoglycan by altering the microbial cytoplasmic membrane and translation, inhibiting nucleic acid replication (by blocking topoisomerases) (Bakheet and Doig, 2010; Al-Amiery *et al.* 2012). Many thiosemicarbazone complexes of metals such as molybdenum, manganese, zinc, cadmium, silver etc. have shown effective antibacterial activity and are summarized below. The effect of substituent at N^4 atom of thiosemicarbazone is also highlighted.

Pyridine based Thiosemicarbazone and its complexes have shown considerable activity against various bacterial and fungal strains. Activity against gram positive bacteria

Staphylococcus aureus, gram negative bacteria *Escherichia Coli*, and fungus *Candida albicans* was shown by Nickel(II) and palladium(II) complexes of 2-acetylpyridine thiosemicarbazone and complexes of Chromium, Cobalt(II,III), Nickel(II) and copper(II) with 2, 6-pyridinedicarboxaldehyde thiosemicarbazone (Kovala-Demertzi *et al.* 2001; Ahmed and Mahammadynus, 2014). Bidentate complexes of copper (II) with thiosemicarbazones derived from pyridine based species like 2, 6-diacetylpyridine, 2-pyridine carboxaldehyde, pyridine-2-carboxaldehyde, showed antibacterial activity, while the ligands derived from 2, 6-diacetylpyridine had a greater effect against *E. coli* than the other bacteria (Prashanthi *et al.* 2010; Ispir *et al.* 2008). N^4 substituted analogues of this ligand with copper (II) showed moderate activity against bacteria MRSA and *B.Subtilis* (Abdalla *et al.* 2015). Tin (IV) complexes of 2-acetylpyridine-*N*(4) substituted thiosemicarbazone and 2-benzoylpyridine N(4) substituted thiosemicarbazone (N4-orthochlorophenyl, orthofluorophenyl, ortrhonitrophenyl) ligands showed similar minimum inhibitory concentration (MIC) values to that of fluconazole (Parrilha *et al*, 2013). Complexes of acetylpyrazine 3-azabicyclo-nonylthioisemicarbazone and acetylpyrazine 4N-methyl, 4N-dimethyl and 3-hexamethyleneiminyl thiosemicarbazone with copper(II) and nickel(II) showed higher antifungal activity against two human pathogenic fungi, *Aspergillus Niger* and *Paecilomyces variotii* (West *et al.* 1993).

A series of complexes with O, N, S donor ligand like salicylidene thiosemicarbazones were investigated against various bacterial strains and fungal species *in vitro* under liquid nutritive environment (2% of peptonate bullion (pH 7.0)). Copper complexes were found to be more active than those containing inner sphere amine (Pahontu *et al.* 2013). Copper(II) thiosemicarbazone complexes have also shown significant antimicrobial activity (Lobana *et al.* 2014; Ilies *et al.* 2014). Melha and Khlood reported significant *in vitro* antibacterial and antifungal activity of N(4)-(7'-chloroquinolin-4'-ylamino)-N(1)-(2-hydroxy-benzylidene) thiosemicarbazone against Gram + ve bacteria (*Staphylococcus aureus*), Gram - ve bacteria (*Escherichia coli*), fungi (*Candida albicans* and *Fusarium solani*) [Melha and Khlood. 2008). Khan *et al.*2014 reported the antibacterial activity of novel thiosemicarbazones and their Cu(II), Ni(II), and Co(II) complexes against bacterial species sub-cultured in BHI medium by the disk diffusion method (Khan *et al.* 2014). A set of aryl- and phenoxymethyl-thiosemicarbazones also showed activity against the larvae of *Aedes aegypti*, the vector responsible for diseases like Dengue and Yellow Fever (da Silva *et al.* 2015; Pahontu *et al.* 2015).

The transition metal complexes of 3-methyl butanalthiosemicarbazone were found to be good antibacterial agents against selected bacteria (such as *Escherichia coli*, *pseudomonas*, *Klebsiella* species) using agar-well diffusion method (Venkatesh *et al.* 2016). Complexes of Isatin-3-thiosemicarbazone when evaluated in vitro against the HM1: IMSS strain of *Entamoeba histolytica*, showed better anti-amoebic activity than the ligand. They also exhibited antibacterial and antifungal activities (Konstantinovic et al, 2008). Copper(II) complexes of 4[N-(benzalidene)amino] antipyrine thiosemicarbazone, 4[N-(4-methoxybenzalidene) amino] antipyrine thiosemicarbazone and standard drugs (ampicillin and teracycline) showed moderate antibacterial and antifungal activities by the agar-cup method in DMF solvent at a concentration of 50µg/mL (Agarwal, Singh and Sharma 2006). Similar antibacterial activity against gram-positive and gram-negative bacteria was also exhibited by antimony(III), Mn(II) complexes with 2-Butyl-4-chloro-5-formylimidazole thiosemicarbazone and Cr(III) complexes of anthraquinone N4benzylthiosemicarbazone. [Kasuga *et al.* 2006; Reddy *et al.* 2014; Chandraa *et al.*2013).

Antitrypanosomal and antimalarial Studies

A number of studies have been reported on the activity of thiosemicarbazone complexes on *trypanosoma species*. Ruthenium complexes Ru(II)-cyclopentadienyl Ru(η5-C_5H_5)(PPh_3)L] showed activity against *trypanosoma cruzi* (Dm28c strain), the infective form of *trypanosoma brucei* (strain 427), J774 murine macrophages and human-derived EA.hy926 endothelial cells, with IC_{50}values in the micromolar or submicromolar range, while m*anganese(II) complexes of N*4-methyl-4-nitrobenzaldehyde thiosemicarbazone, *N*4-methyl-4-nitroacetophenone thiosemicarbazone and *N*4-methyl-4-nitrobenzo-phenone thiosemicarbazone showed poor activity on their *in vitro* activity *in* bloodstream and intracellular forms of *Trypanosoma Cruzi* (Fernandez *et al.* 2015; Batista *et al.* 2010). Platinum (II) complexes with 3-(5-nitrofuryl) acroleine thiosemicarbazone, displayed IC50 values in the micromolar range against two different strains of *Trypanosoma cruzi* causative agent of Chagas disease (American Trypanosomiasis). Platinum (II) complexes with 5-nitrofuryl thiosemicarbazones were found to be as active as the anti-trypanosomal drug nifurtimox (Vieties *et al.* 2009). Antimony (III) complexes of 2-acetylpyridine and 2-benzoylpyridine based thiosemicarbazones were found to be excellent inhibitors of *Trypanosoma cruzi* growth (Parrilha *et al.* 2013). A series of Pd(II) and Pt(II) complexes with 1-indanones derived thiosemicarbazones showed significantly higher activity against *T. cruzi* than the corresponding free ligands (Santos *et al.* 2012).

The gold(I) thiosemicarbazone complexes displayed their activity against malaria parasite *Plasmodium falciparum* and *cysteine protease falcipain*-2 (Khanye *et al.* 2010). A series of both mono- and dinuclear gold(I) phosphine complexes containing monoanionic seleno- and thiosemicarbazones exhibited activity similar to that of chloroquine, while the selenium derivatives displayed only moderate anti-malaria activity (Molter *et al.* 2011). Palladium complexes with aryl based thiosemicarbazones showed antimalarial activity against two *Plasmodium falciparum* strains-3D7 (chloroquine sensitive) and K1 (chloroquine and pyrimethamine resistant) and by 2-benzoyl pyridine thiosemicarbazone and its N4-Phenyl derivative with IC50of 10-7 to < 10-6 M (Chellan *et al.* 2010; Pingaew *et al.* 2010). Copper (II), nickel(II), iron(III) and manganese (II) complexes of 2-acetylpyridine thiosemicarbazone showed reduced antimalarial activity in mice infected with *Plasmodium bergei* (Scovill *et al.* 1982). Cobalt (III) complexes derived from 2-acetylpyridine N(4)-R thiosemicarbazone (Hatc-R, R = alkyl, aryl) showed satisfactory antitubercular activity with minimal inhibitory concentration value under 10 µmol L^{-1} and one presented quite low cytotoxicity against VERO and J774A.1 cells (IC_{50}), resulting in high selectivity index (SI > 10) (Oliviera *et al.* 2014).

Cytotoxic Studies

A great deal of work has been done on the antitumor property of thiosemicarbazone ligands and its complexes.

Thiosemicarbazones are potent inhibitors of the enzyme ribonucleotide reductase (RR) and are capable of interrupting DNA synthesis and repair resulting in alteration or enhancement of their biological activity on incorporation into metal centre (Kovala-Demertzi *et al.* 2002). They have been actively developed in their use against cancer and are very much dependent on the typology of tumor cells. This property has been exhibited by various transition metal complexes of thiosemicarbazone with metals like copper, iron, nickel, palladium, platinum etc (Table 1). Thiosemicarbazone complexes have been found to inhibit the enzyme ribonucleotide reductase essential for DNA synthesis. Current section discusses current advances of thiosemicarbazones and its complexes as potent anticancer agents, describing recent insights into their mechanism of action.

A number of important anticancer activities have been exhibited by copper-thiosemicarbazone complexes especially with chelating ligands like di-2-pyridylketone thiosemicarbazones (Park *et al.* 2006). Thirty two Cu(II), Ni(II) and Zn(II) complexes with a series of salicylidene thiosemicarbazones were tested for their antimicrobial activity as well as antiproliferative activity against HL-60 cells using three concentrations: 0.1, 1.0 and 10 μmol/L. The ligands and metal complexes showed non-significant inhibitor activity at 0.1 and 1.0 μmol/L, but at10 μmol/L, salicylidene-4-phenylthiosemicarbazone, 5-Br-salicylidene-4-phenyl thiosemicarbazone and 5-NO2-salicyliden-4-phenyl thiosemicarbazone inhibited the cell proliferation (90, 75 and 70%, respectively) (Melha *et al.* 2008).

Table 1 Metal complexes and their studies on various cancerous cell lines

S. No	Ligand	Metal	Activity on-	Reference
1.	3-methyl-5-oxo-1-phenyl-3-pyrazolin-4-carboxaldehyde thiosemicarbazone; 5-oxo-3-phenyl-3-pyrazolin-4-carboxaldehyde thiosemicarbazone	Copper(II)	HL60, REH, C6, L929 and B16 cancer cell lines	Leovac *et al.* 2011
2.	salicylidene-4-phenylthiosemicarbazone, 5-Br-salicylidene-4-phenylthiosemicarbazone and 5-NO2-salicyliden-4-phenyl thiosemicarbazone	Cu(II), Ni(II) and Zn(II) complexes	HL-60 cancer cells	Pahontu *et al.* 2013
3.	Aqua(pyridoxal thiosemicarbazone)	Copper(II)	retroviruses HIV-I and HIV-1/2	Pelosi *et al.* 2010
4.	4-hydroxy-3-methyl-1,2-naphthoquinone-1-thiosemicarbazone	Cu(II)	MCF-7	Saha et al, 2002
5.	N(4)-phenyl-2-benzoylpyridine thiosemicarbazone	Tin (IV)	MCF-7, TK-10 and UACC-62 human tumor cell lines	Perez-Rebolledo *et al.* 2005
6.	3-hydroxypyridine-2-carbaldehyde thiosemicarbazone	Organotin	MCF-7 (human breast cancer cell line), T-24 (bladder cancer cell line), A-549 (nonsmall cell lung carcinoma) and a mouse L-929	Wiecek *et al.* 2010.
7.	1-phenyl-3-methyl-4-benzoyl-5-pyrazolone 4-ethyl thiosemicarbazone	Copper(II)	HL-60	Pahontu *et al.* 2015
8.	pyridine-2-carbaldehyde thiosemicarbazone; (1*E*)-1-pyridin-2-ylethan-1-one thiosemicarbazone	Zinc(II)	MCF-7 (human breast cancer cell line), T24 (bladder cancer cell line) and a mouse fibroblast L-929 cell line	Kovala-Demertzi *et al.* 2006
9.	cyclohexanone thiosemicarbazone and cyclohexanone N(4)-phenyl thiosemicarbazone	Zinc(II)	calf thymus DNA (CT-DNA) and bovine serum albumin (BSA)	Vikneswaran *et al.* 2016
10.	pyridine-2-carbaldehyde thiosemicarbazone and (1E)-1-pyridin-2-ylethan-1-one thiosemicarbazone	Zinc(II)	human breast cancer cell line MCF-) and bladder cancer cell line T24	Kovala-Demertzi *et al.* 2006
11.	3, 5-diacetyl-1,2,4-triazol bis (4N-substituted thiosemicarbazone	Pd(II)	renal LLC-PK1 cells	Matesanz *et al.* 2011
12.	2-formylpyridine-4-N-ethyl-thiosemicarbazone	Pd(II)	MCF-7 (human breast cancer cell line), T24, A-549 cell lines and a mouse L-929 cell line	Kovala-Demertzi *et al.* 2013
13.	methyl-3-formyl pyrazole-N(4)- dimethyl thiosemicarbazone and 5-methyl-3-formylpyrazoleN(4)-diethyl thiosemicarbazone	Iron (III)	cervical carcinoma cells HeLa	Saha *et al.*, 2012
14.	4-R benzaldehyde thiosemicarbazone	Pt(II)	human leukemia cell line (HL-60) and human lymphoma cell line (U-937	Halder *et al.* 2012
15.	quinoline-2-carboxaldehyde thiosemicarbazone	Copper(II) and Nickel (II)	lymphoma cell line U937	Bisceglie *et al.* 2015
16.	*N*(4)-phenyl 2-benzoylpyridine thiosemicarbazone	Gold(I)	Jurkat, HL-60, MCF-7 and HCT-116	Lessa *et al.* 2011
17.	aminopyridine-2-carboxaldehyde thiosemicarbazone		Pam-*ras* cells	Popović-Bijelić *et al.* 2011
18.	chalcone-derived 3-phenyl-1-pyridin-2-ylprop-2-en-1-one thiosemicarbazone, 3-(4-chlorophenyl)-1-pyridin-2-ylprop-2-en-1-one thiosemicarbazone, 3-(4-bromophenyl)-1-pyridin-2-ylprop-2-en-1-one thiosemicarbazone and 3-(4-nitrophenyl-1-pyridin-2-ylprop-2-en-1-one thiosemicarbazone	Copper(II)	HL60 (wild type human promyelocytic leukemia), Jurkat (human immortalized line of T lymphocyte), MDA-MB 231 (human breast carcinoma) and HCT-116 (human colorectal carcinoma) tumor cell lines	da Silva *et al.* 2013.
19.	2-acetylpyridine thiosemicarbazone, its *N*(4)-methyl and *N*(4)-phenyl derivatives; *N*(4)-phenyl 2-benzoylpyridine thiosemicarbazone	Gold (I)	Jurkat (immortalized line of T lymphocyte), HL-60 (acute myeloid leukemia), MCF-7 (human breast adenocarcinoma) and HCT-116 (colorectal carcinoma) tumor cell lines.	Lessa *et al.* 2011

Copper (II) complex with pyridoxal thiosemicarbazone also showed potent anti HIV activity (Pelosi *et al.* 2010). Copper (II) complexes showed higher antiproliferation activity against human breast adenocarcinoma cancer cell lines MDA-MB-231 and MCF-7 (Low *et al.* 2016). Coordination to copper (II) complexes with chalcone based thiosemicarbazones showed a significant increase in cytotoxicity in Jurkat, MDA-MB 231 and HCT-116 cells and also induced DNA fragmentation in solid tumor cells indicating their pro-apoptotic potential (da-Silva *et al* 2013). The copper(II) complexes of 4-hydroxy-3-methyl-1,2-naphthoquinone-1-thiosemicarbazone, showed cytotoxic properties when tested *in vitro* against human breast cancer cell line MCF-7 (Saha *et al.* 2002). Similar cytotoxic activity was also observed by copper (II) thiosemicarbazone complexes against several cell lines (human leukemia cell lines K562 and U937) (Leovac *et al.* 2011; Ferrari *et al.* 2002).

Tin(IV) complexes of N(4)-phenyl-2-benzoylpyridine thiosemicarbazone (H2Bz4Ph) were active against the MCF-7, TK-10 and UACC-62 human tumor cell lines and were proved to be better as cytotoxic agent than the clinically used drug etoposide (Perez-Rebolledo *et al*. 2005). Diorganotin complexes with 3-hydroxypyridine-2-carbaldehyde thiosemicarbazone showed high cytotoxicity compared to cis-platin against various cancer cell lines (Agarwal *et al.* 2006; Wiecek *et al.* 2010). Pahontu *et al* 2015 reported higher *in vitro* antibacterial and antifungal activity of the copper (II) complexes with 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone 4-ethyl thiosemicarbazone and reported antiproliferative activity against HL-60 leukaemia cells (Pahontu *et al.* 2015). Zinc (II) complexes with pyridine-2-carbaldehyde thiosemicarbazone and (1*E*)-1-pyridin-2-ylethan-1-one thiosemicarbazone showed IC50 values in a μM range similar to or better than that of the antitumor drug *cis-platin*, making them as potential antitumor activity candidates for further stages of screening in vitro and/or in vivo (Kovala-Demertzi *et al.* 2006). Likewise, zinc(II) complexes with cyclohexanone thiosemicarbazone and cyclohexanone N(4)-phenyl thiosemicarbazone gave GI50 values lower than 5 μg/mL were reported to be advantageous as anticancer agents (Vikneswaran *et al.* 2016). The tin (IV) complex with meclofenamic acid was found to be a promising anti-mycobacterial lead compound, displaying high activity against *M. tuberculosis* H37R with -formyl and 2- acetyl pyridine and hexamethyleneiminyl ring incorporated at N(4) position of thiosemicarbazones against human cancer cell lines, such as MCF-7, T24 and A-549 (non-small cell lung carcinoma) (Kovala-Demertzi *et al.* 2009).

2-Acetylpyridine thiosemicarbazones and their substituted compounds showed excellent cytotoxic activity against RT2 (expressing p53 protein) and T98 (expressing mutant p53 protein) glioma cells (Lessa *et al.* 2010). The cytotoxic and antimalarial activities of 2-benzoylpyridine thiosemicarbazone and its N4 substituted derivatives exhibited the potent activity against HuCCA-1, HepG2, A549 and MOLT-3 cancer cell lines with IC50 values of 0.03, 4.75, 0.04 and 0.004 μg/mL, respectively (Pingaew *et al.* 2010). Iron (III) complexes of methyl-3-formyl pyrazole-N(4)- dimethyl thiosemicarbazone and 5-methyl-3-formylpyrazoleN(4)-diethyl thiosemicarbazone were found to be more cytotoxic against cervical carcinoma cells (HeLa) than their parent ligands (Saha *et al.* 2012).The cytotoxic activity of Pd(II) and Pt(II) complexes were reported with 5-substituted thiophene -2-carboxaldehyde against human cervix carcinoma (Karakucuk *et al.* 2011). Platinum (II) complexes of 4-R benzaldehyde thiosemicarbazones when tested on the human leukemia cell line (HL-60) and human lymphoma cell line (U-937), showed potential cytotoxic nature on the tested cells (Halder *et al.* 2012). Antiproliferative behaviour of palladium (II) and platinum (II) complexes with 2,6-diacetylpyridine bis(4*N*-tolyl thiosemicarbazone (L) showed important antitumor properties on their in vitro activity against various human cancer cell lines (Matesanz *et al.* 2013). The palladium (II) and platinum (II) complexes derived from α-diphenyl ethanedione bis (thiosemicarbazone) and α-diphenyl ethanedione bis (4-ethylthiosemicarbazone) showed IC50 values for ligands and platinum complex higher than that of cisplatin but the maximum antiproliferative activity was similar (Matesanz *et al.* 2007).

The copper(II) and nickel(II) complexes of a series of quinoline-2-carboxaldehyde thiosemicarbazones, *trans*-cinnamaldehyde thiosemicarbazone and cuminaldehyde thiosemicarbazone showed antiproliferative properties on lymphoma cell line U937 (Bisceglie *et al.* 2014, 2015). Manganese (II) complexes derived from 2-acetylpyridine-N(4)-R-thiosemicarbazones, when investigated for anti-*Mycobacterium tuberculosis* activity by in vitro cytotoxicity on VERO and J774A.1 cells, showed promising anti-*M. tuberculosis* properties, with SI values comparable or better than some commercial drugs available for the *tuberculosis* treatment (Oliveira *et al.* 2014).

Gold (I) complexes of 2-acetylpyridine thiosemicarbazone induced DNA fragmentation in HL-60 and Jurkat cells indicating their pro-apoptotic potential [60]. Kalyani *et al* 2016 investigated the curcumin thiosemicarbozone (curTSC) derivatives of gold (III)complexes, for the nuclease activity on pBR 322 plasmid DNA by agarose gel electrophoresis in the presence of H_2O_2. At micro molar concentration, the ligands exhibited no significant activity. The nuclease activity was greatly enhanced by incorporation of metal ions in the ligands (Kalyani *et al.* 2016)**.** Nickel(II) thiosemicarbazone complexes containing 4-chromone *N*(4)-substituted thiosemicarbazone ligands showed good anticancer activity against MCF-7 cancer cell line due to the terminal substituted thiosemicarbazones (Selvamurugan *et al.* 2016). Afrasiabi *et al* 2005 reported the antiproliferative activity of Ni(II) complexes of *ortho*-naphthaquinone thiosemicarbazone on MCF-7 human breast cancer cells than the thiosemicarbazone analogues (Afrasiabi *et al.* 2005). Palladium(II) complexes with 2 formyl pyridine-4-N-ethyl-thiosemicarbazone displayed IC50 values in a μM range better than that of the antitumor drug *cis-platin* against MCF-7 and T-24 cell lines and can be considered as agent with potential antitumor activity candidates and thus used for further investigation *in vitro* and/or *in vivo (Kovala-demetrzi et al. 2013)*. Ferraz *et al* 2011 reported the cytotoxic activity behaviour of the palladium (II) and platinum(II) complexes of *N*(4)-*ortho*, *N*(4)-*meta* and *N*(4)-*para*-(H2Bz4pT) tolyl-2-benzoylpyridine-derived thiosemicarbazones showed moderate anti-proliferative activity against HepG2 (hepatoma) and UACC-62 (melanoma) cancer cell lines, but showed high anti-proliferative effect against A431, suggesting the potential of these complexes as chemotherapeutic drug candidates (Ferraz *et al.* 2011). 3-aminopyridine-2 carboxaldehyde thiosemicarbazone is reported to show anticancer properties. Popović-Bijelić *et al* 2011 reported the cytotoxic activity of this ligand and and its iron (III), gallium(III), zinc(II) and copper(II) complexes (Popovic-Beijelic *et al.* 2011).

CONCLUSION

The survey of the literature has revealed the ability of thiosemicarbazone and its complexes as a versatile compound for designing potential bioactive agents. Its derivatives have been reported to possess broad spectrum biological activities. Many of the thiosemicarbazone ligands and their complexes showed better performance than available drugs like nutriflox, cisplatin etc and many such complexes have also been recognised as potential drugs for therapeutic intervention in various diseases. For instance, acetylpyridine N(4) substituted thiosemicarbazone and its complexes have shown activity against malignant gliomas. Such information can be used by biotechnologists and pharmacologists for designing drugs in such a way that they can be useful in treatment of different diseases. Research is still continuous and can be used for further formulation of drugs. It can be concluded that many other derivatives of thiosemicarbazone can be synthesized which will exhibit potent pharmacological activities.

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Compliance with ethical standards

Conflict of interest: The author declares that there is no conflict of interest.

Ethical approval This review does not contain any studies with human participants or animal performed by author

Reference

Al-Amiery, A.A., Al-Majedy, Y. K., Ibrahim, H. H., Al-Tamimi, A. A. Antioxidant, antimicrobial, and theoretical studies of the thiosemicarbazone derivative Schiff base 2-(2-imino-1-methylimidazolidin-4-ylidene) hydrazinecarbothioamide (IMHC), Organic and Medicinal Chemistry Letters 2 (2012) 4. doi: 10.1186/2191-2858-2-4.

Ahmed, M. F. A., Mahammadyunus, V. Microwave Synthesis and Antimicrobial Activity of some Copper (II), Cobalt (II), Nickel (II) and Chromium (III) Complexes with Schiff Base 2, 6-Pyridinedi carboxaldehyde-Thiosemicarbazone Orient. J. Chem., 30(1) (2014)111-117. ISSN: 0970-020 X.

Abdalla, O., Farina, Y., Ibrahim N.. Synthesis, Characterization and Antibacterial study of copper (II) complexes of thiosemicarbazones, *Malaysian Journal of Analytical Sciences*, 6(2015) 1171 - 1178.

Agarwal, R.K., Singh, D.K.Sharma. Synthesis, Spectral, and Biological Properties of Copper(II) Complexes of Thiosemicarbazones of Schiff Bases Derived from 4-Aminoantipyrine and Aromatic Aldehydes, Bioinorganic Chemistry and Applications , 1-10, (2006) Article ID 59509.

Afrasiabi, Z., Sinn, E., Lin, W., Ma, Y., Campana, C., Padhye, S. Nickel (II) complexes of naphthaquinone thiosemicarbazone and semicarbazone: Synthesis, structure, spectroscopy, and biological activity J. Inorg. Biochem. 99 (2005) 1526-1531. doi: 10.1016/j. jinorgbio.2005.04.012

Bakheet, T. M. and Doig, A. J. Properties and identification of antibiotic drug targets, BMC Bioinformatics. 11(2010)195-204.

Batista, D.G.J., da Silva, P. B., Lachter, D. R., Silva, R. S., Aucelio, R. Q., Louro, S. R. W., Beraldo, H., de Nazaré, M., Soeiro, C., Teixeira, L. R.. Manganese(II) complexes with N4-methyl-4-nitrobenzaldehyde, N4-methyl-4-nitroacetofenone, and N4-methyl-4-nitrobenzophenone thiosemicarbazone: Investigation of in vitro activity against Trypanosoma cruzi Polyhedron, 29(2010) 2232-2238. doi.org/10.1016/j.poly.2010.04. 023

Bisceglie, F., Pinelli, S., Alinovi, R., Goldoni, M., Mutti, A., Camerini, A., Piola, L., Tarasconi, P., Pelosi, G. Cinnamaldehyde and cuminaldehyde thiosemicarbazones and their copper (II) and nickel(II) complexes: A study to understand their biological activity *J. Inorg. Biochem*. 140(2014) 111-125.

Bisceglie, F., Musiari, A., Pinelli, S., Alinovi, R., Menozzi, I., Polverini, Tarasconi, P., Tavone, M., Pelosi, G. Quinoline-2-carboxaldehyde thiosemicarbazones and their Cu(II) and Ni(II) complexes as topoisomerase IIa inhibitors J. Inorg. Biochem. 152(2015) 10-19. doi.org/10.1016/j.jinorgbio.2015.08.008.

Chandraa, J.S.,.Kumaria, Y.A.S.J.P, Rania, P.N.V.V.L.P., Sunandamma, Y. Anthraquinone Benzylthiosemicarbazone Cr (III) Complex as a Potential AntiCancer Drug-Characterization and Activity, *Indian Journal of Advances in Chemical Science*, 2(2013) 32-37.

Chellan, P., Nasser, S., Vivas, L., Chibale, K., Smith, G.S. Cyclopalladated complexes containing tridentate thiosemicarbazone ligands of biological significance: Synthesis, structure and antimalarial activity, J. Organomet. Chem., 695 (19-20), (2010) 2225-2232. doi: 10.1016/j.jorganchem.2010.06.010

Da Silva, J. B.P, A.F. Navarro DM do, A.G. da Silva, G.K.N.Santos, K.A.Dutra, D.R.Moreira, M.N. Ramos, J. Wanderlan, P. Espíndola, A. D. T. de Oliveira, D. J. Brondani, A. C. L. Leite, M. Z. Hernandes, V.R.A. Pereira, L.F.da Rocha, M.C.A.B. de Castro, B.C. de Oliveira, Q. Lan, K.M. Merz. Thiosemicarbazones as Aedes aegypti larvicidal, *Eur. J. Med. Chem*. 100(2015) 162-175. doi.org/10.1016/j.ejmech.2015.04.061

Da Silva, J. G., Despaigne, A. A. R., Louro, S. R. W., Bandeira, C. C., Souza-Fagundes, E. M., Beraldo, H. Cytotoxic activity, albumin and DNA binding of new copper(II) complexes with chalcone-derived thiosemicarbazones European Journal of Medicinal Chemistry, 65(2013) 415-426 doi.org/10.1016/j.ej mech.2013.04.036.

Fernández, M., Arce, E.R., Sarniguet, C., Morais, T.S., Tomaz, A.I., Azar, C.O., Figueroa, R., Maya, J.D., Medeiros, A., Comini, M., Garcia, M.H., Otero, L., Gambino, D. Novel ruthenium(II) cyclopentadienyl thiosemicarbazone compounds with antiproliferative activity on pathogenic trypanosomatid parasites, *J. Inorg. Biochem*. 153 (2015) 306-314. .doi.org/10. 1016/j.jinorgbio.2015.06.018.

Ferrari, M. B., Bisceglie, F., Fava, G. G., Pelosi, G., Tarasconi, P., Albertini, R., Pinelli, S. Synthesis, characterization and biological activity of two new polymeric copper(II) complexes with α-ketoglutaric acid thiosemicarbazone *J. Inorg. Biochem* 89 (2002) 36-44.

Ferraz, K. O. S., Cardoso, G. M.M., Bertollo, C. M., Souza-Fagundes, E. M., Speziali, N., Zani, C. L., Mendes, I.

C., Gomes, M. A., Beraldo, H. N(4)-tolyl-2-benzoylpyridine-derived thiosemicarbazones and their palladium(II) and platinum(II) complexes: Cytotoxicity against human solid tumor cells Polyhedron, 30(2011) 315-321. doi.org/10.1016/j.poly.2010.10.014

Garcia-Tojal, J., Garcia-Orad, A., Serra, J. L., Pizarro, J. L., Lezamma, L., Arriortua, M. I., Rojo, T. Synthesis and spectroscopic properties of copper(II) complexes derived from thiophene-2-carbaldehyde thiosemicarbazone. Structure and biological activity of [Cu(C6H6N3S2)2] *J. Inorg. Biochem*. 75(1999) 45-54. doi.org/10.1016/S0162-0134 (99)00031-8.

Halder, S., Paul, P., Peng, S. M., Lee, G. H., Mukherjee, A., Dutta, S., Sanyal, U., Bhattacharya, S.. Benzaldehyde thiosemicarbazone complexes of platinum: Syntheses, structures and cytotoxic properties. Polyhedron, 45(2012) 177-184. doi.org/10.1016/j.poly.2012.07.037

Ispir, E., Toroglu, S., Kayraldiz, A.. Syntheses, characterization, antimicrobial and genotoxic activities of new Schiff bases and their complexes. Trans. Met. Chem., 33(2008) 953-960. doi: 10.1007/s11243-008-9135-2.

Ilies, J.C., Pahontu, E., Shova, S., Georgescu, R., Stanica, N., Olar, R., Gulea, A., Rosu, T.. Synthesis, characterization, crystal structure and antimicrobial activity of copper(II) complexes with a thiosemicarbazone derived from 3-formyl-6-methylchromone Polyhedron 81 (2014) 123-131. doi.org/10.1016/j.poly.2014.05.074

Kalyani, P., Naidu, P. V. S., Prakash, K. M.M.S.. Synthesis, structure and biological activity of novel curcumin thiosemicarbozone gold(iii) complex: potential anticancer drug, Eur. J. Pharm.and Med. Res., 2 3(6) (2016) 325-329.

Karakucuk-iyidogan, A., Tasdemir, D., Oruc-Emre, E. E., Balzarini, J. Novel Platinum(II) and Palladium(II) Complexes of Thiosemicarbazones Derived from 5-Substitutedthiophene-2-carboxaldehydes and Their Antiviral and Cytotoxic Activities. Eur. J. Med. Chem. 46(2011) 5616-5624. doi.org/10.1016/j.ejmech.2011.09.031

Kasuga, N.C., Onodera, K., Hayashi K.N., Nomiya, K.. Syntheses, crystal structures and antimicrobial activities of 6-coordinate antimony(III) complexes with tridentate 2-acetylpyridine thiosemicarbazone, bis(thiosemicarbazone) and semicarbazone ligands, J. Inorg.Biochem. 100 (2006) 1176-1186. .doi.org/10.1016/j.jinorgbio.2006.01.037

Khan, S.A., Asiri, A.M., Al-Amry, K.., Malik, M.A. Synthesis, Characterization, Electrochemical Studies, and In Vitro Antibacterial Activity of Novel Thiosemicarbazone and Its Cu(II), Ni(II), and Co(II) Complexes, (2014) The Scientific World Journal, Article ID 592375.

Khanye, S.D., Smith, G.S., Lategan, C., Smith, P.J., Gut, J., Rosenthal, P.J., Chibale, K. Synthesis and in vitro evaluation of gold(I) thiosemicarbazone complexes for antimalarial activity J. Inorg.Biochem.,104(2010) 1079-1083. doi.org/10.1016/j.jinorgbio.2010.06.005.

Kovala-Demertzi, D., Demertzi, A. M., Miller, J.R., Papadopoulou, C., Dodorou, C. and Filousis, G. Platinum(II) complexes with 2-acetylpyridine thiosemicarbazone" Synthesis, crystal structure, spectral properties, antimicrobial and antitumour activity, J. Inorg. Biochem., 86(2001) 555-563.

Kovala-Demertzi, D., Demertzis, M. A., Miller, J. R., Frampton, C. S., Jasinski, J. P., West, D. X.. Structure of bis(2-acetylpyridine 3-hexamethyleneiminylthiosemicarbazonato) palladium(II), a potential antitumor complex, J. Inorg. Biochem. 92(2002) 137-140. doi.org/10.1016/S0162-0134(02)00493-2.

Kovala-Demertzi, D., Yadav, P. N., Wiecek, J., Skoulika, S., Varadinova, T., Demertzis, M. A. Zinc(II) complexes derived from pyridine-2-carbaldehyde thiosemicarbazone and (1E)-1-pyridin-2-ylethan-1-one thiosemicarbazone. Synthesis, crystal structures and antiproliferative activity of zinc(II) complexes, J. Inorg. Biochem., 100 (2006) 1558-1567. doi.org/10.1016/j.jinorgbio.2006.05.006.

Kovala-Demertzi, D., Galani, D. A., Miller, J.R., Frampton, C. S., Demertzis, M. A.. Synthesis, structure, spectroscopic studies and cytotoxic effect of novel palladium(II) complexes with 2-formylpyridine-4-Nethyl-thiosemicarbazone: Potential antitumour agents Polyhedron 52(2013) 1096-1102. doi.org/10.1016/j.poly.2012.06.068

Kovala-Demertzi, D., Papageorgiou, A., Papathanasis, L., Alexandratos, A., Daleziz, P., Miller, J.R., Demertzis, M.A.. In vitro and in vivo antitumor activity of platinum(II) complexes with thiosemicarbazones derived from 2-formyl and 2-acetyl pyridine and containing ring incorporated at N(4)-position: Synthesis, spectroscopic study and crystal structure of platinum(II) complexes with thiosemicarbazones, potential anticancer agents, Eur. J. Med. Chem. 44(2009) 1296-1302. doi.org/10.1016/j.ejmech.2008.08.007

Konstantinović, S.S., Radovanović, B.C., Sovilj, S.P., Stanojević, S. Antimicrobial activity of some isatin-3--thiosemicarbazone complexes, J. Serb. Chem. Soc. 73(2008) 7-13. doi: 10.2298/JSC0801007K

Leovac, V. M., Bogdanović, G. A., Jovanović, L. S., Joksović, L., Marković, V., Joksović, M. D., Denčić, S. M., Isaković, A., Marković, I., Heinemann, F. W., Trifunović, S., Đalović, I. Synthesis, characterization and antitumor activity of polymeric Synthesis, characterization and antitumor activity of polymeric copper(II) complexes with thiosemicarbazones of 3-methyl-5-oxo-1-phenyl-3-pyrazolin-4-carboxaldehyde and 5-oxo-3-phenyl-3-pyrazolin-4-carboxaldehyde, J. Inorg. Biochem. 105(11) (2011) 1413-1421. doi.org/10.1016/j.jinorgbio.2011.07.021

Lessa, J. A., Mendes, I. C., da Silva, P. R. O., Soares, M. A., dos Santos, R. G., Speziali, N. L., Romeiro, N. C., Barreiro, E. J., Beraldo, H.. 2-Acetylpyridine thiosemicarbazones: Cytotoxic activity in nanomolar doses against malignant gliomas, *Eur. J. Med. Chem*. 45(2010) 5671-56777. doi.org/10.1016/j.ejmech.2010. 09.021

Lessa, J.A., Guerra, J.C., de Miranda, L.F., Romeiro, C. F. D., Da Silva, J. G., Mendes, I. C., Speziali, N.L., Souza-Fagundes, E. M., Beraldo, H.. Gold(I) complexes with thiosemicarbazones: Cytotoxicity against human tumor cell lines and inhibition of thioredoxin reductase activity, J.Inorg. Biochem. 105(12) (2011) 1729-1739. doi: 10.1016/j.jinorgbio.2011.09.008.

Lobana, T.S., Indoria, S., Jassal, A.K., Kaur, H., Arora, D. S., Jasinski, J.P. Synthesis, structures, spectroscopy and antiomicrobial properties of complexes of copper(II) with salicylaldehyde N-substituted thiosemicarbazomnes and 2,2'-bipyridine or 1,10-phenanthroline. Eur. J.Med. Chem. 76((2014) 145-154. doi.org/10.1016/j.ejmech.2014. 02.009

Low, M. L., Maigre, L., Tahir, M. I. M., Tiekink, E. R. T., Dorlet, P., Guillot, R., Begum, T., Ravoof, L., Rosli, R.,. Pagès, J. M., Policar, C., Delsuc, N., Crouse, K. A.. New insight into the structural, electrochemical and biological aspects of macroacyclic Cu(II) complexes derived from S-substituted dithiocarbazate schiff bases, *Eur.J.Med. Chem*. 120(2016) 1-12. doi: 10.1016/j.ejmech.2016.04.027

Matesanz, A. I., Leitao, I., Souza, P.. Palladium(II) and platinum(II) bis(thiosemicarbazone) complexes of the 2,6-diacetylpyridine series with high cytotoxic activity in cisplatin resistant A2780cisR tumor cells and reduced toxicity, *J. Inorg. Biochem*. 125(2013) 26-31. doi.org/10.1016/j.jinorgbio.2013.04.005

Matesanz, A. I., Souza, P.. Novel cyclopalladated and coordination palladium and platinum complexes derived from α-diphenyl ethanedione bis(thiosemicarbazones): Structural studies and cytotoxic activity against human A2780 and A2780cisR carcinoma cells, J.Inorg. Biochem. 101(10) (2007) 1354-1361. doi.org/10.1016/j.jinorgbio.2007.05.013

Melha, A., Khlood, S. In-vitro antibacterial, antifungal activity of some transition metal complexes of thiosemicarbazone Schiff base (HL) derived from N4-(7′-chloroquinolin-4′-ylamino) thiosemicarbazide, J Enzyme Inhib Med Chem. 23(4) (2008)493-503. doi.org/10.1080/14756360701631850.

Molter, A., Rust, J., Lehmann, C. W., Deepa, G., Chiba, P., Mohr, F.. Synthesis, structures and anti-malaria activity of some gold(I) phosphine complexes containing seleno- and thiosemicarbazonato ligands., Dalton trans., 40(38)(2011): 9810-9820. doi:10.1039/c1dt10885a

Oliveira, C.G., da S. Maia, P.I., Miyata, M., Pavan, F.R., Leite, C.Q.F., de Almeida, E.T., Deflon, V. M.. Cobalt(III) complexes with thiosemicarbazones as potential anti-Mycobacterium tuberculosis agents, J. Braz. Chem. Soc. 25 (2014). doi.org/10.5935/0103-5053.20140149

Pahontu, E., Fala, V., Gulea, A., Poirier, D., Papcob, V. and Rosu, T..Synthesis and characterization of Some New Cu (II), Ni(II) and Zn(II) complexes with Salicyclidene Thiosemicarbazones: Antibacterial, Antifungal and in Vitro Antileukemia Activity. Molecules, 18 (2013) 8812-8836. doi: 10.3390/molecules18088812.

Pahontu, E., Julea, F., Rosu, T., Purcarea, V., Chumakov, Y., Petrenco, P., Gulea, A. (2015). Antibacterial, antifungal and invitro antileukaemia activity of metal complexes with thiosemicarbazones, J. Cell. Mol. Med., 19(4) (2015) 865-878. doi:10.1111/jcmm.12508

Parrilha, G.L., Dias, R.P., Rocha, W.R., Isolda, C., Benítez, D., Varela, J., Cerecetto, H., González, M. Melo, C.M.L., Neves, J.K.A.L., Pereira, V.R.A., Beraldo H. 2-Acetylpyridine- and 2-benzoylpyridine-derived thiosemicarbazones and their antimony(III) complexes exhibit high anti-trypanosomal activity. Polyhedron, 31(1) (2013) 614-621. doi.org/10.1016/j.poly.2011.10.018.

Park, K. C., Fouani, L., Jansson, P.J.,. Wood, D, Sahni, S., Lane, D. J. R., Palanimuthu, D., Lok, H. C., Kovačević, Z., Huang, M. L. H., Kalinowski, D. S., Richardson, D.. Copper and conquer: copper complexes of di-2-pyridylketone thiosemicarbazones as novel anti-cancer therapeutics, Metallomics, (2006) doi: 10.1039/C6MT00105J.

Pingaew, R., Prachayasittikul, S., Ruchirawat, S. Synthesis, Cytotoxic and Antimalarial Activities of Benzoyl Thiosemicarbazone Analogs of Isoquinoline and Related Compounds, Molecules, 15(2010) 988-996. doi:10.3390/molecules15020988

Pelosi, G., Bisceglie, F., Bignami, F., Ronzi, P., Schiavone Re, M.C., Casoli, C. L., Pilotti, E.. Antiretroviral Activity of Thiosemicarbazone Metal Complexes *J. Med. Chem*., 53 (24) (2010) 8765-8769.

Perez-Rebolledo, A., Ayala, J. D., de Lima, G. M., Marchini, N., Bombieri, G., Zani, C. L., Souza-Fagundes, E. M., Beraldo, H.. Structural studies and cytotoxic activity of N(4)-phenyl-2-benzoylpyridine thiosemicarbazone Sn(IV) complexes, *Eur. J. Med. Chem*. 40(5) (2005) 467-472. doi.org/10.1016/j.ejmech. 2005.01.006

Popović-Bijelić, A., Kowol, C. R., Lind, M.E. S., Luo, J., Himo, F., Enyedy, E. A., Arion, V. B., Gräslund, A. Ribonucleotide reductase inhibition by metal complexes of Triapine (3-aminopyridine-2-carboxaldehyde thiosemicarbazone): A combined experimental and theoretical study *J. Inorg. Biochem*., 105(11) (2011) 1422-1431. doi: 10.1016/j.jinorgbio.2011.07.003

Prashanthi, Y., Raj, S.. Synthesis and Characterization of Transition Metal Complexes with N, O; N-Nand S-N donor Schiff Base Ligands, *J. Sci. Res*., 2 (1) (2010) 114-126. doi: 10.3329/jsr.v2i1.2732.

Reddy, A.S., Reddy, M.S., Kotakadi V.S., Chalapathi, P., Reddy, A.V.. Synthesis, spectroscopic characterization and antimicrobial activity studies of 2-Butyl-4-chloro-5-formylimidazole thiosemicarbazone and its manganese (II) complex. *J App Pharm Sci*. 4(2014)95-101. doi:10.7324/JAPS.2014.41217.

Santos, D., Parajón-Costa, B., Rossi, M., Caruso, F., Benítez, D., Varela, J., Cerecetto, H., González, M., Gómez, N., Caputto, M.E., Moglioni, A.G., Moltrasio, G.Y., Finkielsztein, L.M., Gambino, D. Activity on Trypanosoma cruzi, erythrocytes lysis and biologically relevant physicochemical properties of Pd(II) and Pt(II) complexes of thiosemicarbazones derived from 1-indanones *J. of Inorg. Biochem*., 117(2012) 270-276. doi.org/10.1016/j.jinorgbio.2012.08.024.

Saha, D. K., Padhye, S., Sinn, E., Newton, C.. Synthesis, structure, spectroscopy and antitumor activity of hydroxyl naphoquinone thiosemuicarbazone and its metal complexes against MCF-7 human breast cancer line. Indian journal of Chemistry Sect A: Inorganic, physical, theoretical & analytical, 41(2002) 279-283.

Saha N. C., Biswas, C., Ghorai, A., Ghosh, U., Seth, S. K., Kar, T. Synthesis, structural characterisation and cytotoxicity of new iron(III) complexes with pyrazolyl thiosemicabazones. Polyhedron, 34(2012)1-12 doi.org/10.1016/j.poly.2011.10.033

Selvamurugan, S., Ramachandran, R., Vijayan, P., Manikandan, R., Prakash, G., Viswanathamurthi, P., Velmurugan, K., Nandhakumar, R., Endo, A.

Synthesis, crystal structure and biological evaluation of Ni(II) complexes containing 4-chromone-N(4)-substituted thiosemicarbazone ligands Polyhedron, 107(2016)57-67. doi.org/10.1016/j.poly.2016.01.011.

L. R. Suvarapu, A. R. Somala, J. R. Koduru, S. O. Baek, V. R. Ammireddy. A Critical Review on Analytical and Biological Applications of Thio-and Phenylthiosemicarbazones, *Asian Journal of Chemistry*, 24 (2012) 1889-1898 AJC-10786

Venkatesh, K., Rayam, P., Shekhar, K.B.C., Mukkanti, K. Synthesis, characterization and biological activity of some new thiosemicarbazide derivatives and their transition metal complexes. *International journal of applied biology and pharmaceutical technology* 1(2016) 258-266.

Vieites, V, Otero, L., Santos, D., Olea-Azar, C., Norambuena, E., Aguirre, G., Cerecetto, H., González, M., Kemmerling, U., Morello, A., Maya, J.D., Gambino, D. Platinum-based complexes of bioactive 3-(5-nitrofuryl)acroleine thiosemicarbazones showing anti-Trypanosoma cruziactivity, *J. Inorg. Biochem*., 103(2009) 411-418. doi.org/10.1016/j.jinorgbio.2008. 12.004.

Vikneswaran, R., Eltayeb, N. E., Ramesh, S., Yahya, R. New alicyclic thiosemicarbazone chelated zinc (II) antitumor complexes: Interactions with DNA/protein, nuclease activity and inhibition of topoisomerase-I Polyhedron, 105(2016) 89-95. doi.org/10.1016/j.poly. 2015.12.012

West, D. X., Liberta, A. E., Padhye, S. B., Chikate, R. C., Sonawane, P. B., Kumbhar, A. S., Yerande, R. G. Thiosemicarbazone complexes of copper(II): Structural and biological studies, Coord. Chem. Rev. 123(1993) 49-71. doi: 10.1016/0010-8545(93)85052-6.

Wiecek, J., Kovala-Demertzi, D., Ciunik, Z., Zervou, M., Demertzis, M. A. Diorganotin Complexes of a Thiosemicarbazone, Synthesis: Properties, X-Ray Crystal Structure, and Antiproliferative Activity of Diorganotin Complexes Bioinorg. Chem. and Applications, (2010) doi:10.1155/2010/867195

Wang, B. D., Yang, Z. Y., Lü, M.H., Hai, J., Wang, Q., Chen, Z. N. Synthesis, characterization, cytotoxic activity and DNA binding Ni(II) complex with the 6-hydroxy chromone-3-carbaldehyde thiosemicarbazone. *Journal of Organomet*. Chem. 694(2009) 4069-4075. doi.org/10.1016/j.jorganchem.2009.08.024

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