



REVIEW

A Critical Review on Analytical and Biological Applications of Thio- and Phenylthiosemicarbazones

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In present study, we summarized the analytical applications of thio- and phenylthiosemicarbazones in metal ions separation and determination from various samples by using spectrophotometer. We reviewed the analytical applications of thio and phenylthiosemicarbazones from 1991 to 2011. This two decades survey is very useful to the analytical chemists working on separation and determination of metal ions and biological activities of their complexes. In this article first we summarized the basic introduction and structural information of thio- and phenylthiosemicarbazones and then we reviewed their analytical applications in the separation and determination of metal ions from real samples, synthetic samples and alloy samples. Finally we discussed their biological activities. The literature survey reveals that the thio and phenyl thiosemicarbazones are promising chelating agents for the separation and determination of transitional metal ions. In addition to this the complexes formed by thio and phenylthiosemicarbazones with transitional metal ions are having biological activities.

Key Words: Thiosemicarbazones, Phenylthiosemicarbazones, Spectrophotometry, Separation and Determination of metal ions, Biological activities of metal complexes.

INTRODUCTION

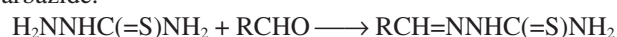
In the last few years, much interest has been directed towards the use of chelating ligands containing sulphur and nitrogen in analytical studies, such as separation, purification and estimation of metal ions as well as in structural studies of metal complexes^{1,2}. By the wide application and rapid growth in the popularity of sulphur ligands is due to their remarkable property as potential donors to form stable as well as characterized complexes in which the back bonding from the metal ion is possible under favourable conditions. In addition, the presence of nitrogen along with sulphur tends to lower the solubility of the complexes, making the isolation of these complexes easier. Further, the sulphur containing ligands are known for the biocidal activities, owing to their ability to chelate with the soft acidic metal ions in tracer level.

Among various organic reagents containing S and N as donor atoms thiosemicarbazones and their aromatic derivatives occupy a unique place. Thiosemicarbazones are a group of compounds obtained by condensing thiosemicarbazide with

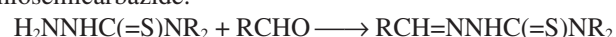
carbonyl compounds in the presence of a few drops of glacial acetic acid. These reagents function as good chelating agents and form complexes with several metal ions by bonding through thionate sulphur atom and hydrazino nitrogen atom. In a few cases, they behave as tridentate ligands and form a bond through additional coordinating groups depending on the nature of the metal ions.

Several authors critically reviewed the utility of thiosemicarbazones as analytical reagents^{3,4}. The thiosemicarbazones are classified into four types, based on the participating aldehyde and ketone in the condensation process as shown below:

(1) Aldehydes or substituted aldehydes with thiosemicarbazide.



(2) Aldehydes or substituted aldehydes with substituted thiosemicarbazide.



(3) Ketones or substituted ketones with thiosemicarbazide and



(4) Ketones or substituted ketones with substituted thiosemicarbazide.



Depending on the type of parent aldehyde or ketone used for condensation they can act as unidentate, bidentate or multidentate chelating agents during complexation with metal ions. Besides their interesting coordination chemistry, thiosemicarbazones have attracted considerable interest because of their potentially beneficial biological activities such as antiviral⁵, antitumour⁶, antimalarial⁷, antifungal⁸ and antibacterial⁹. The medicinal properties of metal-thiosemicarbazone complexes are believed to be due to their high power of chelation with tracer of metal ions present in biological systems.

Thiosemicarbazones also find application in fluorimetric analysis. Among several thiosemicarbazones available, only 2-hydroxy-1-naphthaldehyde thiosemicarbazone¹⁰ and 2-hydroxybenzaldehydethiosemicarbazone¹¹ are used for fluorimetric determination of gallium(II) and indium(II) respectively.

The literature survey has revealed that a good number of thiosemicarbazones are available for the spectrophotometric and extractive spectrophotometric determination of metal ions. In the present paper, we reviewed the applications of thio and phenyl thiosemicarbazones in spectrophotometry as analytical reagents. In this point of view some reviews are already available but they are very old, the latest review⁴ was published on 1991. Because of ease of synthesis and biological activity of metal complexes still the thio- and phenyl thiosemicarbazones play a vital role in the determination of metal ions. This forces us to review the analytical potentialities of the thio and phenylthiosemicarbazones since 1991. In this paper, we discussed the analytical applications of the thio- and phenylthiosemicarbazones from last two decades. We believe that this review article is very useful for analytical chemists particularly focusing on separation and determination of metal ions with spectrophotometer.

Structures of thiosemicarbazones

Nature of metal ligand linkage: Thiosemicarbazones form a class of mixed hard-soft oxygen/nitrogen-sulphur chelating ligands that show a variety of coordination modes in metal complexes. The thiosemicarbazones can act as a monodentate ligand that binds to the metal ion through the sulphur atom¹² or as a bidentate ligand that coordinates to the metal ion through the sulphur atom and one of the nitrogen atoms of the hydrazine moiety to form four or five membered chelate rings¹³. The coordination capacity of thiosemicarbazones can be increased due to the presence of aldehydes or ketones containing additional functional group(s) in position(s) suitable for chelation¹⁴.

Monothiosemicarbazones: The chelation of monothiosemicarbazone with the metal ion occurs through the sulphur and the hydrazine nitrogen atom (marked with an asterisk) as shown in Fig. 1. However, a different situation exists when there is a hydroxyl group in the ortho position in compounds such as *o*-hydroxyacetophenonethiosemicarbazone, 2,4-dihydroxyacetophenonethiosemicarbazone (Fig. 2) and so on.

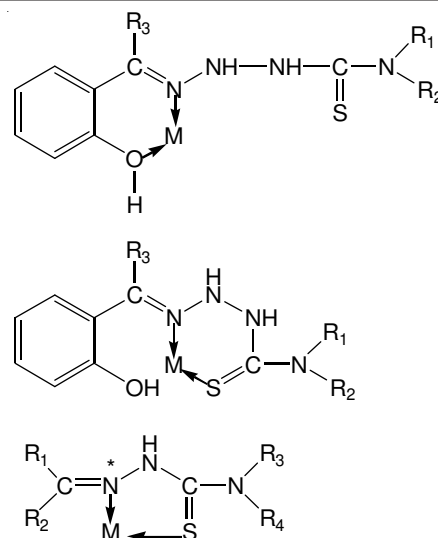


Fig. 1. Structure of monothiosemicarbazones

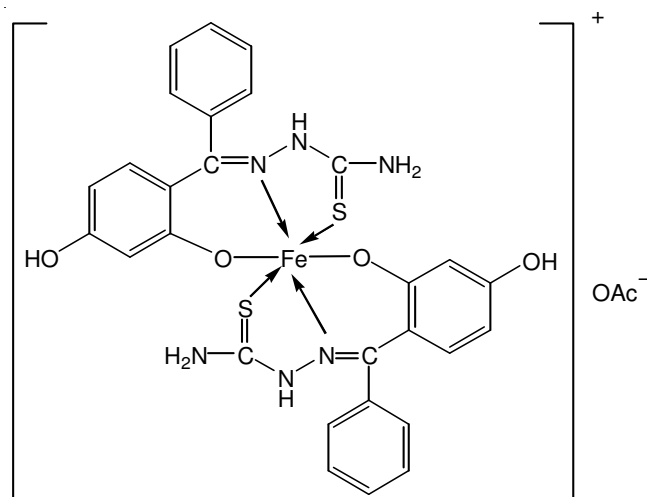


Fig. 2. Structures of monothiosemicarbazones with hydroxyl group on *ortho*-position

Dithiosemicarbazones: The probable structures of 1:1 and 1:2 metal to ligand complexes of dithiosemicarbazones as explained by Krishna *et al.*¹⁵ are shown in Fig. 3.

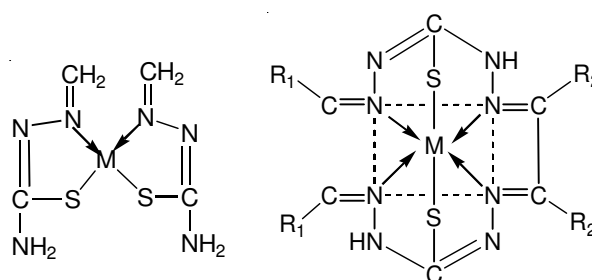


Fig. 3. Structures of dithiosemicarbazones

Analytical applications of thiosemicarbazones: The use of thiosemicarbazones in inorganic analysis has been reviewed in detail by Singh *et al.*¹⁶ and also briefly by Asuero and Ganzalez¹⁷. The literature survey revealed that various thiosemicarbazones are employed in the detection and determination of various cations and anions. The quantitative determination of ions is often carried out by spectrophotometry

or extractive spectrophotometry, though other techniques such as gravimetry, fluorimetry and titrimetry are also employed. Among these, spectrophotometric methods are preferred because they are cost saving and easier to handle, with comparable sensitivity and accuracy.

Separation and determination of metal ions with thio and phenylthiosemicarbazones using spectrophotometry:

The applications of thio- and phenylthiosemicarbazones in the separation and determination of metal ions by using spectrophotometer are presented in Table-1. For every reagent (thio- and phenylthiosemicarbazone) the established conditions for the separation and determination of the corresponding metal ion(s) such as λ_{\max} , pH, validity of Beer's law, molar absorptivity (ϵ), metal to reagent composition (M:L), extractant (solvent) are summarized in Table-1¹⁸⁻¹¹⁵. This summary clearly indicates that thio- and phenyl thiosemicarbazones are promising chelating agents for the analytical chemists working on the separation and determination of metal ions.

Determination of metal ions in real and synthetic alloy samples with thio- and phenylthiosemicarbazones:

Thio- and phenylthiosemicarbazones were applied as analytical reagents for the determination of various metal ions in different environmental samples (soil, water, human blood, etc.), food samples (leafy vegetables, medicinal leaves, etc.), pharmaceutical samples, synthetic mixtures and standard alloy samples. The applications of the thio- and phenylthiosemicarbazones in the determination of metal ions in real samples are summarized in Table-2. Based on this we conclude that the thio- and phenylthiosemicarbazones plays a vital role in the determination of metal ions at trace levels in real samples (environmental, pharmaceutical and medicinal leafy samples).

Biological application of thio- and phenylthiosemicarbazones: Besides their interesting coordination chemistry, thiosemicarbazones have attracted considerable interest because of their potentially beneficial biological activities¹¹⁶⁻¹¹⁸.

A good number of reports are available on the biological activity of transition metal complexes of thiosemicarbazones¹¹⁹⁻¹²². The mechanism of biological activity of thiosemicarbazones is due to their ability to inhibit the biosynthesis of DNA, possibly by blocking the enzyme ribonucleotide diphosphate reductase; binding to the nitrogen bases of DNA, hindering or blocking base replication; creation of lesions in DNA stands by oxidative rupture^{123,124}. In some cases the activity is associated with a metal atom. Recently several authors have been reported antitumor activity¹²⁵⁻¹²⁹ of palladium(II) and platinum(II) thiosemicarbazone complexes. Collins *et al.*¹³⁰ have been reported the correlation between structure and antibacterial activity in a series of 2-acetyl pyridine thiosemicarbazone. In many cases, by coordination to different transition metal ions that can be found in biological systems, it is possible to obtain complexes that are more efficient drugs than the corresponding free ligands¹³¹⁻¹³⁴.

Some of the important thiosemicarbazones with antibacterial activity reported earlier are discussed here under.

Kovala-Demertzi *et al.*¹³⁵ have reported the anti-tumor activity of 2-acetyl pyridine-4N-ethylthiosemicarbazone and its platinum(II) and palladium(II) complexes. Elena Bermejo *et al.*¹³⁶ have reported the biological activities of complexes of zinc(II), cadmium(II), mercury(II), palladium(II) and

platinum(II) with 2-acetylpyridine-4-methyl-thiosemicarbazone and its metal complexes assayed *in vitro* for antifungal activity against the pathogens *Aspergillus niger* and *Paecilomyces variotii*. Among the above mentioned transition metal complexes only zinc(II) complex shows some activity at a concentration of 600 $\mu\text{g mL}^{-1}$. The minimum inhibition zone for zinc(II) complex was found as 9.5 mm. Dimitra Kovala-Demertzi *et al.*¹³⁷ have been reported the antibacterial and antifungal activities of nickel(II) and palladium(II) complexes of 2-acetylpyridinethiosemicarbazone. Antibacterial activities were evaluated against gram positive bacteria *Staphylococcus aureus* and gram negative bacteria *Escherichia coli*. Antifungal activity was evaluated against *Candida albicans*.

The antimicrobial activities of copper(II) and nickel(II) complexes with benzil *bis*thiosemicarbazone against the gram positive bacteria (*Bacillus macerans*) and gram negative bacteria (*Pseudomonas striata*) have been reported by Chandra *et al.*¹³⁸. The authors reported that the metal chelates exhibit more inhibitory effects than the parent ligand. Sathisha *et al.*¹³⁹ have reported the antibacterial and antifungal activities of the *bis*-isatinthiosemicarbazone complexes of copper(II), cobalt(II), nickel(II) and zinc(II) ions. The authors have evaluated the antibacterial activity against the bacteria *Bacillus cirroflagellosus* and antifungal activities against *Aspergillus niger* and *Candida albicans* by cup-plate method.

The antibacterial activities of complexes of nickel(II), copper(II) and cobalt(II) with a series of thiosemicarbazone derivatives of 2-hydroxy-8-R-tricyclo-tridecane-13-one (R = H, CH₃, C₆H₅) was reported by Rosu *et al.*¹⁴⁰. Antibacterial activities are evaluated against five bacterial strains *i.e.* *Acinetobacter boumanii*, *Klebsiella pneumonia*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas auriginosa*.

Agarwal *et al.*¹⁴¹ have reported the biological properties of copper(II) complex of 4[N-benzilidene]amino]antipyridinethiosemicarbazone (BAAPTS) and 4[N-(4'-methoxybenzilidene)amino]antipyridinethiosemicarbazone (MBAAPTS). The authors were evaluated the antibacterial activities of copper(II) complexes of BAAPTS, MBAAPTS and compared with the standard drugs (ampicillin and tetracycline) by agar-cup method in dimethylformamide (DMF) solvent at a concentration of 50 $\mu\text{g mL}^{-1}$. The antibacterial activities were evaluated against gram positive bacteria, *Bacillus subtilis* and *Staphylococcus aureus* and gram negative bacteria, *Escherichia coli* and *Staphylococcus typhi*. Kuniaki *et al.*¹⁴² have reported the synthesis of a tetrameric silver(I) cluster, [Ag(mtsc)₄] from N-morpholy-2-acetylpyridinethio-semicarabacarbazone (mtsc) and silver(I) sources containing Ag-O bonds. The authors have reported that the chloroform solution of tetrameric complex shows moderate activities against bacteria like *Bacillus subtilis*, *Staphylococcus aureus* and *Pseudomonas aeuruginosa* and effective activity against the yeast like *Candida albicans* and *Saccharomyces cerevisiae*. But it did not inhibit the growth of any selected microorganism in a water-suspension system. The lack of activity in water-suspension system can be attributed to the extraordinary stability or the low solubility of this complex. Noriko Chikaraishi Kasuga *et al.*¹⁴³ have reported the synthesis and antibacterial activity of twelve zinc(II) complexes of semi- and thiosemicarbazones.

TABLE-1
 APPLICATIONS OF THIO- AND PHENYLTHIOSEMICARBAZONES IN DETERMINATION OF
 METAL IONS AS ANALYTICAL REAGENTS IN SPECTROPHOTOMETRY

Reagent	Metal ion(s)	λ_{max} (nm)	pH	Beer's law (ppm)	$\epsilon \times 10^4$	M:L	Solvent	Ref.
Acetophenone <i>p</i> -chlorophenyl-thiosemicarbazone	Cu(II)	600	4.0-9.0	0.25-6.35	1.30	1:2	-	18
2-Acetylthiophene-4-phenyl-3-thiosemicarbazone	Cu(II)	385	4.5	0.10-0.51	2.92	1:1	-	19
2-Acetylthiophenethiosemicarbazone	Cu(II)	370	5.0-7.0	0.20-6.00	1.83	1:1	-	20
Benzaldehyde-4-(2-hydroxy-5-sulpho phenyl)-3-thiosemicarbazone	Cu(II)	325	4.5	0.0-7.62	0.74	1:2	-	21
[{(2-Benzaldehyde)oxoethyl} amine]-thiosemicarbazone	Ag(I)	-	-	-	-	3:1	-	22
Benzildithiosemicabazone	Ni(II)	410	9.0	0.10-1.60	3.62	1:1	Chloroform	23
	Co(II)	387	6.5	1.00-8.00	0.73	1:2	Chloroform	24
	Ag(I)	375	5.0	0.30-5.50	2.70	1:1	Chloroform	25
	Cu(II)	380	4.0	0.50-4.00	1.63	1:1	Chloroform	26
	Zn(II)	405	9.5	1.00-18.00	0.42	1:1	Chloroform	27
	Pd(II)	395	2.5	0.25-3.50	3.02	1:1	Methylisobutyl ketone (MIBK)	28
Benzil- α -monoximethiosemicarbazone	Cd(II)	365	10.5	1.00-6.00	0.19	1:1	Isoamylalcohol	29
	Cu(II)	355	-	-	2.20	-	-	30
2- <i>H</i> -Benzopyran-2-one-3-acetyl thiosemicarbazone	Cu(II)	410	8.8-9.2	2.00-25.00	0.07	1:2	MIBK	31
2-Benzoylpyridine-4-phenyl-3-thio semicarbazone	Zn(II)	401	5.7	-	3.41	-	-	32
	Ni(II)	388	5.7	-	4.32	-	-	
	Cu(II)	404	9.6	-	2.25	-	-	
	Co(II)	406	9.6	-	2.35	-	-	
Benzylxybenzaldehydethiosemi-carbazone	Pd(II)	365	5.0	5.00-60.00	0.40	1:1	Cyclohexanol	33
	Cu(II)	370	5.0	0.50-5.20	1.50	1:1	<i>n</i> -Butanol	34
Bipyridylglyoxalbis(4-phenyl-3-thiosemicarbazone)	Ga(III)	390-448	2.5	0.20-20.00	0.18-4.60	-	-	35
5-Bromosalicylaldehyde-4-phenyl-3-thiosemicarbazone	Pd(II)	412	-	0.00-8.00	1.42	-	-	36
5-Bromosalicylaldehydethiosemi-carbazone	Fe(II)	385	5.0-6.0	0.28-5.60	1.72	-	-	37
5-Bromosalicylaldehydethiosemicarbazone	Cu(II)	390	Acidic	0.31-6.35	1.08	-	-	38
4-Chloroisnitrosoacetophenone thiosemicarbazone	Cu(II)	400	7.5-8.5	0.20-20.00	0.25	1:2	-	39
	Zn(II)	-	-	-	-	-	-	40
1,3-Cyclohexanedione thiosemicarbazone	Zn(II)	570	6.3	-	1.42	-	-	41
1,2-Cyclohexanedionethio semicarbazone	Cu(I)	-	-	0.10-10.00	-	-	-	42
Diacetylmonoxime(<i>p</i> -anisyl) thiosemicarbazone	Tl(III)	460	-	0.25-2.60	5.60	1:2	-	43
2,6-Diacetylpyridinebis-4-phenyl-3-thiosemicarbazone	Co(II)	400	4.0	0.60-60.00	2.20	1:1	Isoamyl alcohol	44
	Cu(II)	370	3.0	0.63-6.30	0.85	1:1	-	45
	Mo(VI)	500	3.5	0.90-9.00	1.21	1:1	<i>n</i> -butanol	46
3,5-Dibromosalicylaldehyde-4-phenyl-3-thiosemicarbazone	Cu(II)	400	2.8-7.5	0.20-50.00 ng/mL	2.06	1:1	Chloroform	47
2,7-Dichloroquinoline-3-carbaldehyde thiosemicarbazone	Cu(II)	406	6.0	0.00-0.03	0.18	-	-	48
N,N-(Diethylamino)benzaldehyde thiosemicarbazone	Pd(II)	408	3.0	0.00-3.60	3.33	1:2	-	49
2,4-Dihydroxyacetophenone thiosemicarbazone	Pd(II)	-	3.5	0.70-12.00	1.30	1:2	-	50
3,4-Dihydroxybenzaldehyde thiosemicarbazone	Mo(VI)	365	3.0-5.0	0.19-1.34 mg/mL	3.85	1:1	-	51
2,2-Dihydroxybenzophenone thiosemicarbazone	Mo(VI)	500	-	-	0.33	1:1	-	52
2,4-Dihydroxy-5-bromoacetophenone thiosemicarbazone	Cu(II)	420	6.0	0.00-12.7	0.14	1:1	-	53
	Fe(III)	380	4.0	0.00-9.41	0.60	1:2	-	
2,3-Dihydro-1 <i>H</i> -naphtho[2,1, β] pyrane-1-one semicarbazone	Pd(II)	415	8.2-8.6	-	0.15	1;1	<i>n</i> -Butanol	54
4-(Dimethylamino)benzaldehyde thiosemicarbazone	Pd(II)	405	2.2-3.6	0.00-2.30	4.59	1:2	-	55

Reagent	Metal ion(s)	λ_{\max} (nm)	pH	Beer's law (ppm)	$\epsilon \times 10^4$	M:L	Solvent	Ref.
4-[N,N-(Dimethyl)amino] benzaldehyde thiosemicarbazone	Cu(II)	420	4.4-5.4	0.00-4.70	1.72	1:2	Chloroform	56
5,5-Dimethyl-1,3-cyclohexanedione dithiosemicarbazone	Cr(VI)	360	0.5-2.5	0.16-1.49	1.63	-	-	57
5,5-Dimethyl-1,2,3-cyclohexanetrione thiosemicarbazone	Cu(II)	383	-	0.00-11.20	0.46	1:3	-	58
N-Ethyl-3-carbazolecarboxaldehyde-3-thiosemicarbazone	Zn(II)	420	6.0	0.40-6.00	1.55	1:1	Benzene	59
	Cu(II)	380	3.0	0.40-3.60	2.24	1:1	<i>n</i> -Butanol	60
	Pd(II)	410	4.0	0.00-6.60	1.64	1:1	<i>n</i> -Butanol	61
	Ni(II)	400	6.0	1.20-5.60	1.11	1;1	<i>n</i> -Butanol	62
9-Ethyl-3-carbazolecarboxaldehyde-4-phenyl-3-thiosemicarbazone	Cu(II)	400	8.8	-	4.16	Thermodynamic studies		63
	Co(II)	400	8.8	-	4.37	-	Co(II)	
	Cd(II)	401	8.8	-	3.62	-	Cd(II)	
	Zn(II)	410	8.8	-	2.62	-	Zn(II)	
9-Ethyl-3-carbazolecarboxaldehyde-3-thiosemicarbazone	Cu(II)	393	-	0.20-1.90	-	-	-	64
2-Hydroxyacetophenone N(3)-propyl thiosemicarbazone	Pd(II)	-	-	-	-	-	-	65
2-Hydroxyacetophenonethiosemicarbazone	Cd(II)		5.0	Solid phase extraction studies				66
	Cu(II)							
	Ni(II)							
4-Hydroxyacetophenone thiosemicarbazone	Co(II)	-	-	-	-	-	-	67
2-Hydroxy-1-acetonaphthone thiosemicarbazone	Pt(IV)	346	5.5	-	6.47	2:3	-	68
3-Hydroxybenzaldehyde thiosemicarbazone	Cu(II)	-	5.5	-	0.87	-	-	69
	Pd(II)		2.5		1.25			
4-Hydroxybenzaldehyde thiosemicarbazone	Pd(II)	-	-	-	-	-	-	70
2-Hydroxy-4-isopropoxyaceto phenone thiosemicarbazone	Ni(II)	400	9.0	0.00-16.44	0.08	1:2	90 % EtOH	71
2-Hydroxy-3-methoxybenzaldehyde thiosemicarbazone	Pd(II)	445	3.0	0.21-12.78	-	-	-	72
	Ru(III)	385		0.25-13.42				
	Co(II)	390	6.0	0.06-2.35	2.74	1:2	-	73
2-Hydroxy-3-methoxybenzaldehyde thiosemicarbazone	Ni(II)	410	4.0-8.0	0.06-2.35	2.05	1:1	-	74
	Mo(VI)	385	1.0-2.0	0.24-4.32	2.30	1:1	-	75
	Co(II)	468.5	6.0	0.06-3.30	Simultaneous determination			76
	Ni(II)	474.5		0.06-3.26				
2-Hydroxy-3-methoxybenzaldehyde thiosemicarbazone	V(V)	380	6.0	0.05-2.04	2.75	1:2	-	77
	Pd(II)	380	1-7	0.43-4.26	2.20	2:3	-	78
1-(2-Hydroxy-4-methoxy benzophenone -4-phenyl-3-thiosemicarbazone	V(IV)	560	1.5	0.00-10 ⁻⁴ M	0.40	1:1	-	79
2-Hydroxy-1-naphthaldehyde-4-phenyl-3-semicarbazone	Pd(II)	437	-	0.00-8.00	1.41	-	-	80
Isatin- β -thiosemicarbazone	Co(II)	415	-	-	0.04	1:2	-	81
	Ni(II)	455			0.12	1:2		
	Cu(II)	450	-	-	0.06	1:1	-	
	Zn(II)	402			0.03	1:1		
	Pd(II)	378	-	-	0.03	1:1	-	
	Hg(II)	398			0.04	1:1		
Isonitrosopropiophenone thiosemicarbazone	Cu(II)	390	10.0	0.50-6.00	0.58	1:2	-	82
Isovanilline thiosemicarbazone	Ni(II)	400	9.0	-	0.64	1:2	<i>n</i> -Butanol	83
	Co(II)	440	8.4	-	0.01	1:2	Ethylacetate	84
7-Methoxy-2-chloroquinoline-3-carbaldehydethiosemicarbazone	Cu(II)	400	4.0	0.00-5.00	0.003	-	-	85
8-Methoxy-2-chloroquinoline-3-carbaldehydethiosemicarbazone	Cu(II)	410	5.0	0.00-3.00	0.003	1:1	-	86
Nicotinaldehyde-4-phenyl-3-thiosemicarbazone	Pd(II)	365	3.0	0.50-8.00	2.81	1:1	-	87
<i>o</i> -Hydroxyacetophenone thiosemicarbazone	Pd(II)	370	6.0	0.42-10.06	0.90	1:1	-	88
						1:2		
2- <i>o</i> -Vanillinethiosemicarbazone	Cu(II)	-	2.5-4.0	Solid phase preconcentration				89
	Zn(II)		5.5-6.5					
	Pb(II)		6.0-7.5					
<i>p</i> -Anisaldehydethiosemicarbazone	Pd(II)	370	2.7-4.3	0.06-3.30	2.16	1:1	-	90
Phenanthraquinone monophenyl thiosemicarbazone	Cd(II)	520	6.0	0.01-0.34	2.40	1:2	-	91
	Cu(II)	545	3.0-3.5	3.00-4.00	2.30	1:1	-	92
		517	6.0	ppb	4.80	1:2		
	Zn(II)	526	4.5-7.5	0.05-1.0 mg/l	18.30	1:2	-	93

Reagent	Metal ion(s)	λ_{\max} (nm)	pH	Beer's law (ppm)	$\epsilon \times 10^4$	M:L	Solvent	Ref.
Phenanthraquinone monophenyl thiosemicarbazone	Pb(II)	520	9.0	0.00-40.00	2.40	-	Chloroform	94
1-Phenyl-1,2-propanedione-2-oxime thiosemicarbazone	Cu(II)	465	3.0-8.0	0.38-7.63	0.56	1 : 2	-	95
	Ni(II)	395	3.0-6.0	0.42-3.76	1.01	1 : 2	-	
1-Phenyl-1,2-propanedione-2-oxime thiosemicarbazone	Cu(II)	401	5.8	-	-	-	-	96
	Au(III)	282	-	-	-	-	-	97
	Cu(II)	278	-	-	-	-	-	
	Cu(II)	500	3.0-8.0	-	0.57	1 : 2	-	98
	Ni(II)	467.5	-	-	1.20	-	-	
Phthalaldehydic acid thiosemicarbazone	Pd(II)	355	4.0	0.10-2.00	5.10	-	MIBK	99
Piconaldehyde-4-phenyl-3-thiosemicarbazone	V, Co, Fe	415	3.0	-	-	-	-	100
	Cd	-	-	-	-	-	-	101
Piperenolthiosemicarbazone	Pd(II)	363	-	0.50-2.45	3.80	1 : 2	-	102
	Pt(IV)	360	0.033	0.00-6.50	3.24	-	-	103
			H ₂ SO ₄					
Pyridine-2-carbaldehyde thiosemicarbazone	Mn(II)	259	-	-	0.57	1 : 1	-	104
	Zn(II)	244	-	-	0.33	1 : 1	-	
Pyridoxal-4-phenylthiosemicarbazone	Co(II)	292.0	Simultaneous determination					105
	Cu(II)	420.4						
Pyridoxal-4-phenyl-3-thiosemicarbazone	Co(II)	450	5.0	0.50-6.00	1.40	1 : 1	<i>n</i> -Butanol	106
	Cu(II)	440	3.0-5.5	0.20-5.00	2.16	1 : 1	<i>n</i> -Butanol	107
	Zn(II)	430	5.0-6.0	0.00-6.00	1.60	1 : 1	<i>n</i> -Butanol	108
	Pd(II)	460	3.0	0.40-6.40	2.20	1 : 1	Benzene	109
	Ni(II)	430	4.0-6.0	0.50-5.00	1.92	1 : 1	<i>n</i> -Butanol	110
Pyruvaldehyde(N,N'-dibutyl)bis-thiosemicarbazone	Cu(II)	375	6.5-7.5	0.50-6.00	0.92	1:1	-	111
Thiophenylaldehyde-4-phenyl-3-thiosemicarbazone	Co(II)	254	-	-	-	-	-	112
	Cu(II)							
	Fe(II)							
	Pd(II)	-	-	0.40-6.00	-	-	Chloroform	113
Thiosemicarbazone of citrol	Cu(II)	-	5.6	-	0.87	-	-	114
	Ni(II)	-	2.6	-	1.25	-	-	
3,4,5-Trimethoxybenzaldehyde thiosemicarbazone	Se(IV)	-	3.0	-	-	-	-	115

TABLE-2
DETERMINATION OF METAL IONS IN REAL AND SYNTHETIC ALLOY
SAMPLES WITH THIO- AND PHENYLTHIOSEMICARBAZONES

Reagents	Analyzed samples	Metal ion(s)	Ref
Acetophenone <i>p</i> -chlorophenylthiosemicarbazone	Water, vitamin and certified steel samples	Cu(II)	18
2-Acetylthiophene-4-phenyl-3-thiosemicarbazone	Edible oils and seeds	Cu(II)	19
2-Acetylthiophenethiosemicarbazone	Alloys and edible oils	Cu(II)	20
Benzildithiosemicarbazone	Nichrome wire and certified steel samples	Ni(II)	23
	Medicinal leaves and beer samples	Co(II)	24
	Photofilm waste water	Ag(I)	25
	Pharmaceutical, industrial effluents and standard alloy samples	Cu(II)	26
	Milk, chillies, industrial effluents and certified alloy samples	Zn(II)	27
	Synthetic mixtures and hydrogen catalysts	Pd(II)	28
	Soil, medicinal leaves, leafy vegetables and water samples	Cd(II)	29
Benzil- α -monoximethiosemicarbazone	Edible oils and seeds	Cu(II)	30
2- <i>H</i> -Benzopyran-2-one-3-acetyl thiosemicarbazone	Synthetic samples	Cu(II)	31
Benzoyloxybenzaldehydethiosemicarbazone	Water samples and synthetic mixtures	Pd(II)	33
Benzoyloxybenzaldehydethiosemicarbazone	Water samples (river, sea) and food samples	Cu(II)	34
Bipyridylglyoxalbis(4-phenyl-3-thiosemicarbazone)	Semiconductor and medicinal drugs	Ga(III)	35
5-Bromosalicylaldehydethiosemicarbazone	Grape leaves, multivitamin capsules and human blood	Fe(II)	37
	Grape leaves and aluminum based alloys	Cu(II)	38
4-Chloroisoinitrosoacetophenone thiosemicarbazone	Alloy and pharmaceutical samples	Cu(II)	39
	Alloys, pharmaceutical samples and synthetic mixtures	Zn(II)	40
1,3-Cyclohexanedione thiosemicarbazone	Pharmaceutical samples	Zn(II)	41
1,2-Cyclohexanedionethio semicarbazone	Catalysts and alloy samples	Cu(I)	42
Diacetylmonoxime(<i>p</i> -anisyl)thiosemicarbazone	Minerals, alloys, human urine, soil and water samples	Tl(III)	43
2,6-Diacetylpyridinebis-4-phenyl-3-thiosemicarbazone	Soil, water, vegetables and standard alloys	Co(II)	44
2,6-Diacetylpyridinebis-4-phenyl-3-thiosemicarbazone	Food samples, leafy vegetables and milk samples	Cu(II)	45
	Food samples and water samples	Mo(VI)	46

Reagents	Analyzed samples	Metal ion(s)	Ref
N,N-(Diethylamino)benzaldehyde thiosemicarbazone	Alloys, catalysts, complexes and model mixtures	Pd(II)	49
2,4-Dihydroxyacetophenone thiosemicarbazone	Synthetic mixtures	Pd(II)	50
3,4-Dihydroxybenzaldehyde thiosemicarbazone	Alloys, steel, Pharmaceutical, human hair and waste water	Mo(VI)	51
2,2-Dihydroxybenzophenone thiosemicarbazone	Agriculture plants	Mo(VI)	52
2,4-Dihydroxy-5-bromoacetophenone thiosemicarbazone	Brass Pharmaceutical samples	Cu(II) Fe(III)	53
2,3-Dihydro-1H-naphtho[2,1,β]pyrane-1-one-semicarbazone	Palladium catalysts, binary mixtures	Pd(II)	54
4-(Dimethylamino)enzaldehyde thiosemicarbazone	Artificial palladium mixtures	Pd(II)	55
4-[N,N-(Dimethyl)amino]benzaldehyde thiosemicarbazone	Water, alloys and pharmaceutical samples	Cu(II)	56
5,5-Dimethyl-1,3-cyclohexanedione dithiosemicarbazone	Alloy steels and industrial effluents	Cr(VI)	57
N-Ethyl-3-carbazolecarboxaldehyde-3-thiosemicarbazone	Chilies, leafy vegetables and milk samples Soil, industrial effluents, pharmaceutical and standard alloy samples	Zn(II) Cu(II)	59 60
	Water, synthetic mixtures and hydrogen catalysts	Pd(II)	61
	Soil, industrial effluents and standard alloy samples	Ni(II)	62
2-Hydroxyacetophenone thiosemicarbazone	Leafy vegetables and medicinal plants	Cd(II), Cu(II), Ni(II)	66
2-Hydroxy-3-methoxybenzaldehyde thiosemicarbazone	Hydrogen catalysts Water samples Alloy steel, vitamin B ₁₂ , tea leaves and vehicle exhaust Aluminium based steel, drinking water, plant samples and vegetable oils Food stuffs and alloy samples Tea leaves and eligiloy alloy Plant leaves Milk, alloy steel, pharmaceutical, water, soil and human urine Alloy samples and hydrogen catalysts	Pd(II) Ru(III) Co(II) Ni(II) Mo(VI) Co(II) Ni(II) V(V) Pd(II)	72 73 74 75 76 77 78 79
1-(2-Hydroxy-4-methoxybenzophenone-4-phenyl-3-thiosemicarbazone	Synthetic mixtures, wastes of power stations, simulated samples and real ores	V(IV)	79
Isovanilline thiosemicarbazone	Synthetic and real samples	Co(II)	84
Nicotinaldehyde-4-phenyl-3-thiosemicarbazone	Real samples	Pd(II)	87
2-ortho-Vanillinethiosemicarbazone	River water samples	Cu(II) Zn(II) Pb(II)	89
Phenanthraquinone monophenyl thiosemicarbazone	Human hair and natural water samples Natural water, serum blood and drug samples	Cd(II) Cu(II)	91 92
Phenanthraquinone monophenyl thiosemicarbazone	Pharmaceutical, natural water and spiked samples Certified reference materials, human blood and natural water samples	Zn(II) Pb(II)	93 94
1-Phenyl-1,2-propanedione-2-oxime thiosemicarbazone	Edible oils, seeds and synthetic samples Water and alloy samples Mineral residuals, minerals and natural waters	Cu(II) Ni(II) Cu(II) Au(III) Cu(II)	95 96 97
Phthalaldehydicacid thiosemicarbazone	Synthetic mixtures and pd-activated charcoal	Pd(II)	99
Piconaldehyde-4-phenyl-3-thiosemicarbazone	Crude oil and water samples	V, Co, Fe	100
Piperenolthiosemicarbazone	Palladium complexes and synthetic mixtures Hydrogen catalysts and platinum complexes	Pd(II) Pt(IV)	102 103
Pyridoxal-4-phenylthiosemicarbazone	Steel samples	Co(II) Cu(II)	105
Pyridoxal-4-phenyl-3-thiosemicarbazone	Soil, pharmaceutical, standard alloys and food samples Leafy vegetables, pharmaceutical and standard alloy samples Leafy vegetables, chilies milk and certified reference materials	Co(II) Cu(II) Zn(II)	106 107 108
Pyridoxal-4-phenyl-3-thiosemicarbazone	Synthetic mixtures and hydrogen catalysts Medicinal leaves, soil, industrial effluents and standard alloy samples	Pd(II) Ni(II)	109 110
Thiophenylaldehyde-4-phenyl-3-thiosemicarbazone	Pharmaceutical samples	Co(II) Cu(II) Fe(II)	112
	Brazing filler metals	Pd(II)	113
3,4,5-Trimethoxybenzaldehydethiosemicarbazone	Fire-reined copper	Se(IV)	115

Antibacterial activities of these complexes are evaluated by minimum inhibition concentration (MIC) against two gram positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*), two gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), two yeast (*Candida albicans* and *Saccharomyces cerevisiae*) and two molds (*Aspergillus niger* and *Penicillium citrinum*). The antibacterial activities suggest that the zinc(II) complexes which can form intermolecular hydrogen bonding with a counter anion or hydrated water molecules are modest to effective towards antimicrobial activities. Kizilcikli *et al.*¹⁴⁴ have reported antimicrobial activity of a series of thiosemicarbazones and S-alkylthiosemicarbazones. MIC values of the compounds were determined by the disc diffusion method against *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Shigella flexneri*, *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Candida albicans*. The thiosemicarbazones show antibacterial and antifungal effects with free ligand and metal complex forms. S-Alkylthiosemicarbazones did not effect the tested microorganisms but their zinc(II) complexes show selective activity.

Conclusion

From the survey we reveal that thio- and phenylthiosemicarbazones are good chromogenic reagents for the separation and determination of metal ions due to strong chelating ability of the hydrazine nitrogen (C=N) and thioketonic (C=S) group. The present survey concludes that the thio and phenylthiosemicarbazones were employed for the separation and determination of the metal ions such as Cu(II), Pd(II), Co(II), Ni(II), Zn(II), Cd(II), Mo(VI), Fe(III), Pb(II), V(V), V(IV), Ru(III), Pt(IV), Ag(I), Ga(III), Tl(III), Cr(VI), Hg(I), Cu(I), Hg(II), Au(III) and Mn(II) from various sources.

Most of the reagents were employed for the determination of Cu(II) (30 %) followed by Pd(II) (18 %), Co(II) (11 %), Ni(II) (10 %), Zn (9.5 %), Cd (4 %) and Mo(VI) (3 %) (Fig. 4). But the metal ions such as Ga(III), Tl(III), Cr(VI), Cu(I), Hg(II), Au(III) and Mn(II) which needs more attention. This survey has the complete information regarding the separation and determination of metal ions with thio and phenylthiosemicarbazones by using spectrophotometer in last two decades. We strongly believe that it is useful to the analytical chemists who are working on this area of interest.

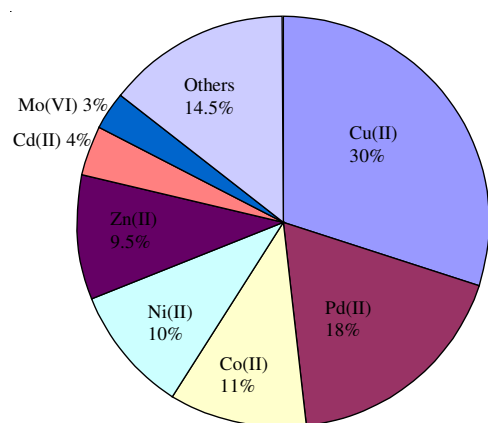


Fig. 4. Percentage of metal ions determined with thio- and phenylthiosemicarbazones

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