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Dithiocarbamates as hazardous remediation agent: A critical review on progress in environmental chemistry for inorganic species studies of 20th century

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Review

Abstract This article provides a critical review and a wide range of applications of dithiocarbamates (DTCs) in environmental samples. The characteristics of DTCs are reviewed with particular emphasis on inorganic speciation studies using state-of-the-art analytical instrumentation coupled with computational methods of analysis.

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1. Introduction

Dithiocarbamates (DTCs), a group of small organic molecules with a strong chelating ability toward inorganic species have extensively been used in the agricultural industry for more than 80 years. In recent years their applications have not only become apparent as pesticides and fungicides, but also widely used as vulcanization accelerators in the rubber industry. Moreover, DTCs are also of biological importance due to their antibacterial, antituberculosis and antifungal properties. Their anti-oxidant properties make them even more valuable compounds, among them are disodium ethylenebisdithiocarbamate (commercially known as Nabam), its zinc and manganese complexes

(Zineb and Maneb) and the zinc and iron complexes of dimethyldithiocarbamic acid (Ziram and Ferbam). The insolubility of metal salts (with the exception of sodium and other alkali and alkaline earth metals) and the capacity of the DTCs to form stable metal-complexes are mainly responsible for the extensive use of this class of compounds as superior ligands. Therefore, DTCs exhibit strong binding properties with a number of transition metal ions resulting in stable colored complexes.

Most of these reagents have been employed in the determination of toxic heavy metal ions at trace and ultra-trace levels. The quantitative determination is often carried out by spectroscopy, although other techniques such as gravimetry, fluorimetry, titrimetry, neutron activation analysis (NAA), turbidimetry, voltammetry and chromatography are less widely used.

Today, yearly consumption of DTCs is between 25,000 and 35,000 metric tonnes, and most of the DTCs applied as fungicides are classified by the World Health Organization (WHO) as being hazardous (WHO, 1988 & 2005). Existing reviews merely highlighted an array of analytical methods for the analysis of DTCs and their potential degradation products in

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Table 1 Structures of DTCs and their physical properties reported in the literature.

DTCs	Structures	Physical properties	Citation
Diethyldithiocarbamate		Molecular weight: 171.26 melting point: 93–95 °C solubility: water	Liu et al. (2000), Cesur (2003), Sarang et al. (2012), Arfana et al. (2012)
Piperazinedithiocarbamate		Molecular weight: 179.05 boiling point: 149.3 °C solubility: water	Cesur et al. (2000)
Ammonium Pyrrolidine dithiocarbamate		Molecular weight: 164.3 melting point: 153–155 °C solubility: water	Gordeeva et al. (2002), Laghari et al. (2010), Ramesh et al. (2002)
Phenylpiperazine dithiocarbamate		Molecular weight: 235.15 melting point: 158–160 °C solubility: water	Cesur et al. (2000)
Pentamethylene dithiocarbamate		Molecular weight: 254.45 melting point: 423.14 solubility: water	Arain et al. (2002)
Ammonium piperidine-1-carbodithioate		Molecular weight: 178.38 melting point: 196–199 °C solubility: water	Venkatasubba Naidu et al. (2011b), Kanchi et al. (2011, 2012, 2013)
Ammonium morpholine dithiocarbamate		Molecular weight: 198.29 melting point: 182–185 °C solubility: water	Venkatasubba Naidu et al. (2011a), Kanchi et al. (2011, 2012, 2013)

environmental samples, pharmaceutical and in foodstuff (Szo-lar, 2007) Accordingly, this review article aims to provide an extensive overview of the inorganic speciation studies of DTCs related to environmental chemistry using a variety of state-of-the-art analytical techniques including the application of computational chemistry to better understand the DTC–metal complexation as a strong remediation agent.

2. Chemistry of DTCs

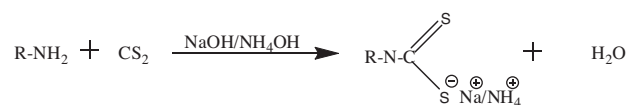
For ease of reference, some of the DTC structures and their physical properties reported in the literature are tabulated in Table 1.

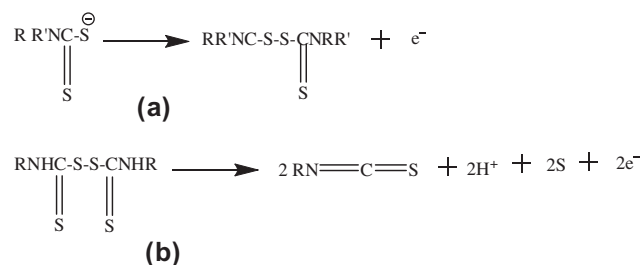
2.1. Synthesis of DTCs

DTCs are formed by the exothermic reaction between carbon disulfide and either ammonium or a primary/secondary amine in the presence of sodium hydroxide or excess amine. *N*-substituted dithiocarbamic acids are generally prepared as their

substituted ammonium or sodium salts by the reaction of carbondisulfide (CS₂) with a primary/secondary amine in alcoholic (Hester and Rohm, 1953) or aqueous solution (Martin, 1959).

In order to conserve the more valuable amine, it is a common practice to use an alkali metal hydroxide to form the salt. Ammonium dithiocarbamate was prepared (Thorn and Ludwig, 1962) by the reaction of ammonia and carbon disulfide as shown in Scheme 1. The free dithiocarbamic acid can be obtained by treatment of ammonium dithiocarbamate with cold acid and decomposes to thiocyanic acid and hydrogen sulfide. Monoalkyldithiocarbamates are formed from the exothermic reaction between carbon disulfide and a monoalkylamine; which after a while decomposes, in alkali solution and more

**Scheme 1** General synthesis reaction of DTCs.



Scheme 2 (a) Oxidation of dialkyldithiocarbamate to thiuram disulfides (b) monoalkyldithiocarbamates to isothiocyanate and elemental sulfur.

complicated amino-compounds has been described (Kanchi et al., 2011a, 2012a, 2013; Thorn and Ludwig, 1962; Reid, 1962). The sodium salts are extremely soluble in water and in ethanol, but relatively insoluble in non-polar solvents such as ether and chloroform. Most of the sodium salts are hydrated.

2.2. Stability of DTCs in different environments (acidic and basic solutions)

The free acids formed from DTCs in acid, are generally unstable; diphenyldithiocarbamic acid was, however, said to be stable (Halls, 1969). The decomposition of DTCs at constant pH was first order and the rate was proportional to the hydrogen ion concentration. The half-life of diethyldithiocarbamate at pH 2 (0.3 s) describes the extreme instability of this compound at low pH. Other DTCs, such as pyrrolidinedithiocarbamate and dibenzylidithiocarbamate, are far more stable at low pH.

Monoalkyldithiocarbamates are more stable than dialkyldithiocarbamates in acidic solutions, but at low pH the rate of decomposition of most dialkyldithiocarbamates is too high to permit any measurement. This can be explained by the steric influence of the second alkyl group causing a higher strain on the C–N bond. The monoalkyl dithiocarbamates show lower pK_a values than the corresponding dialkyldithiocarbamates. The inductive effect of the second alkyl group increases the electron density on the nitrogen atom which stabilizes the ammonium ion formed which influences the polarity of the S–H bond.

2.3. Oxidation of DTCs

Dialkyldithiocarbamates form thiuram disulfides on oxidation with iodine, bromine, potassium ferricyanide, iron(III) chloride or hydrogen peroxide as shown in Scheme 2. These thiuram disulfides are insoluble in aqueous solvents. In scheme 2, it was also reported (Halls, 1969) that the oxidation of monoalkyldithiocarbamates goes further to form the isothiocyanate and elemental sulfur.

2.4. Metal complexation ability of DTCs

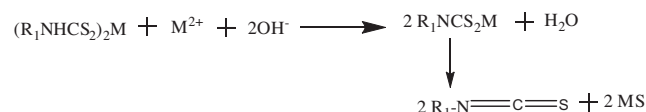
The complexes of DTCs with heavy metals are prepared by adding a solution of the heavy metal to a solution of ammonium or alkali metal–DTC. These complexes are sparingly soluble in water but more soluble in non-polar organic solvents such as chloroform, carbon tetrachloride and ether. Pb(II), Zn(II), and Hg(II) salts are colorless, in contrast to Cu(II),

Ni(II), Co(II) and Fe(II)/(III) complexes which are intensely colored. These DTC complexes have a general formula $(R_1R_2NCS_2)_2M$ where 'M' represents a divalent metal, such as dialkyldithiocarbamates. However, at high pH the monoalkyldithiocarbamates form a further transient complex of the type $(R_1NCS_2)M$, which subsequently decomposes to the metal sulfide and isothiocyanate (Halls, 1969) as illustrated in Scheme 3.

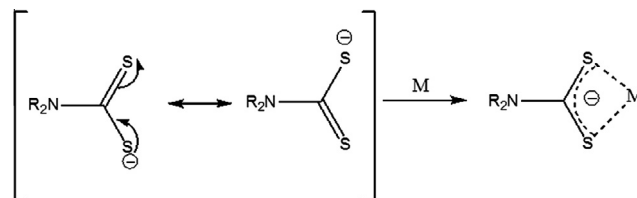
Scheme 4 shows several canonical forms of the structure of the DTC group in their metal salts $M(S_2CNR_2)_n$, where all forms equally contribute to the structures of *N,N*-dialkyldithiocarbamic acid derivatives. However, the canonical form (see scheme 4) arises from the mesomeric electron releasing tendency of the R_2N- group. This electron drift into sulfur atoms increases their electron donor capacity, thus permitting the formation of stronger complexes with the heavy metals, with reducing tendency to form dative Π -bonds from the metal-sulfur atoms.

2.5. Catalytic hydrogen current properties of DTCs

Generally DTCs with oxygen, nitrogen and sulfur atoms exhibit catalytic hydrogen currents after complexation with metal ions. A distinctive property of organic sulfur containing catalysts is the sharp increase in their catalytic activity on addition of transition metal salts, which are applied mostly for ultra-trace analysis of metal ions. These currents are more sensitive and stable than simple catalytic, diffusion and kinetic currents. Although a large number of investigations have dealt with the catalytic waves of organic sulfur containing compounds, several aspects of the mechanism of this process have not yet been fully explored. However, all the literature reviews suggest two common steps, (a) complexation of ligand through metal with +2 oxidation state and (b) adsorption of metal ion complex on mercury electrode/drop or stabilization of zero valent metal ions on mercury electrode/drop through adsorbed product of ligand. Literature studies reveal that catalytically active species are always in a zero valent state of metal ion in its complex $[M^0RS]$. The zero valent metal thiolate complex has a tendency to get protonated because of its increased basicity and subsequently get reduced to give catalytic hydrogen currents



Scheme 3 Metal complexation ability of DTCs.



Scheme 4 Resonance hybrid of metal-DTCs.

Table 2 Summary of developed techniques for the analysis of inorganic species with various DTCs.

DTCs	Analytes	Technique/method	Instrument	Matrix	Detection limits	Citation
Hexamethylene dithiocarbamic acid hexamethylene ammonium salt	Cu(II), Ni(II), Fe(III), Cd(II), Pb(II), Co(II)	Preconcentration/co-precipitation	FAAS	Waste water, sediment, metallic zinc	5.9 $\mu\text{g L}^{-1}$ [Cd(II)] 61.0 $\mu\text{g L}^{-1}$ [Pb(II)]	Elci et al. (2003)
Ni(II)-diethyldithiocarbamate	Cu(II), Cd(II), Fe(III)	Flow injection/co-precipitation	FAAS	Mussel (GBW-08571), soil (ESS-4, ESS-1, GSS-1), human hair (GBW-09107)	0.5 $\mu\text{g L}^{-1}$ [Cu(II)] 2.7 $\mu\text{g L}^{-1}$ [Pb(II)] 0.2 $\mu\text{g L}^{-1}$ [Cd(II)] 2.5 $\mu\text{g L}^{-1}$ [Fe(III)]	Liu et al. (2000)
Zn(II)-piperazinedithiocarbamate	Cu(II), Ni(II), Cd(II)	Preconcentration /solid phase extraction	FAAS	Standard metal alloys, natural water	15.7 ng L^{-1} [Cu(II)] 23.5 ng L^{-1} [Ni(II)] 11.8 ng L^{-1} [Cd(II)]	Cesur et al. (2000)
Pyrrolidine dithiocarbamate	Zn(II), Mg(II), Mn(II), Cr(III), Cu(II), Fe(III), Ca(II)	Preconcentration/solid phase extraction	FAAS	Yogurts, human milk	0.02–0.03 mg L^{-1} [Zn(II)] 1.10–9.47 mg L^{-1} [Mg(II)] 0.05–0.11 mg L^{-1} [Mn(II)] 0.02–3.08 mg L^{-1} [Cr(III)] 0.01–0.87 mg L^{-1} [Cu(II)] 0.47–18.08 mg L^{-1} [Fe(III)] < 0.01–278 mg L^{-1} [Ca(II)]	Nwosu et al. (2003)
Phenylpiperazine dithiocarbamate	Mn(II), Cu(II), Cd(II), Pb(II)	Preconcentration/solid phase extraction	FAAS	Water, standard alloys	17 ng mL^{-1} [Mn(II)] 15 ng mL^{-1} [Cu(II)] 11 ng mL^{-1} [Cd(II)] 56 ng mL^{-1} [Pb(II)]	Cesur (2003)
Hexamethylenammonium hexamethylene dithiocarbamate	Cu(II), Pb(II), Ni(II), Cd(II), Mn(II), Fe(III)	Preconcentration/solid phase extraction	FAAS	Sea water, waste water	0.006 $\mu\text{g mL}^{-1}$ [Cu(II)] 0.9999 $\mu\text{g mL}^{-1}$ [Pb(II), Cu(II)] 1.0000 $\mu\text{g mL}^{-1}$ [Mn(II)] 0.9998 $\mu\text{g mL}^{-1}$ [Fe(III)]	Tokahoglu et al. (2002)
Bi(III)4-methylpiperidine dithiocarbamate	Cd(II), Cu(II), Pb(II)	Preconcentration/co-precipitation	FAAS	Water	0.18–0.50 $\mu\text{g L}^{-1}$	Efendioglu et al. (2007)
Pb(II)-methylpiperidine dithiocarbamate	Cu(II)	Preconcentration/solid phase extraction	FAAS	Water	0.27–0.90 $\mu\text{g L}^{-1}$	Cesur and Bati (2000)
Metal-diethyldithiocarbamate	Mn(II), Zn(II), Cd(II), Fe(III), Co(II), Cu(II), Ni(II), Pb(II), Hg(II)	Preconcentration/solid phase extraction	FAAS	Water, standard alloy	0.05–5 $\mu\text{g mL}^{-1}$	Cesur (2003)
Emetine-dithiocarbamate	Mercury, methy, ethyl, phenyl mercury	Reverse phase extraction	HPLC	Water, biological	30 ng L^{-1} (Mercury) 17 ng L^{-1} (Methyl Mercury) 21 ng L^{-1} (Ethyl Mercury) 22 ng L^{-1} (Phenyl Mercury)	Kodamatani et al. (2012)
Sodiumdiethyl dithiocarbamate	Pb(II), Hg(II), Cd(II), Zn(II), Co(II), Ni(II), Cu(II), Fe(III), UO_2^{2+} , VO^{2+} , Bi(III)	Solid phase extraction	TLC	–	–	Sarang et al. (2012)
Pyrrolidine dithiocarbamate	Cu(II), Ni(II), Fe(III)	Solvent extraction	GC, AAS	Coins, sewage water	–	Laghari et al. (2010)
Pentamethylene dithiocarbamate	Fe(III), Cr(III), Mn(II), Cu(II), Ni(II), Co(II)	Solvent extraction	HPLC, AAS	Water	14.2–542 $\mu\text{g L}^{-1}$	Arain et al. (2009)
Pentamethylene dithiocarbamate	Cu(II), Ni(II), Co(II), Fe(III), Mn(II), Cr(III)	Solvent extraction	GC, HPLC, AAS	Water	2–6 $\mu\text{g mL}^{-1}$	Arain et al. (2002)

Diethyldithiocarbamate	Mo(VI), Cr(VI), Ni(II), Pd(II), Co(II)	Micellar electrokinetic chromatography (MEKC)	CE	Potatoes, almonds, vegetable oils, pharmaceuticals	0.005–0.0167 $\mu\text{g mL}^{-1}$	Arfana et al. (2012)
Emetine dithiocarbamate metal complexes	Cu(II), Ni(II), Co(II)	Capillary zone electrophoresis	CE	–	50 nM	Tsukagoshi et al. (2002)
Metal bis(carboxymethyl)-dithiocarbamate complexes	Cd(II), Ni(II), Pb(II), Hg(II), Cu(II)	Capillary zone electrophoresis/solid phase extraction	CE	Standard metal alloys	1.6–45 $\mu\text{g L}^{-1}$	Ructnev et al. (2000)
Ammonium piperidine-1-carbodithioate	Se(IV), Co(II)	Capillary zone electrophoresis/Pre-capillary complexation	CE	Fresh water prawns and their feeding materials	3.0 $\mu\text{g mL}^{-1}$ [Se(IV)]	Kanchi et al. (2012)
<i>N</i> -methylethylxanthocarbamate	Cd(II)	Solid phase extraction	DPP	Standard alloys, biological, environmental	5.0 $\mu\text{g mL}^{-1}$ [Co(II)] 0.05 ppm	Hussain et al. (2002)
Ammonium piperidine and morpholine dithiocarbamates	Cr(III)	Catalytic hydrogen wave	DC polarography, DPP	Water, industrial effluents, vegetables	0.05 ppm	Kanchi et al. (2011)
Ammonium pyrrolidine dithiocarbamate	Pb(II)	Preconcentration	Square wave adsorptive stripping voltammetry	Water	0.89 ppb	Morsi et al. (2011)
Ammonium piperidine and morpholine dithiocarbamates	Co(II)	Catalytic hydrogen wave	DC polarography, DPP	Water, agricultural materials, pharmaceuticals	0.001 ppm	Kanchi et al. (2011)
Ammonium piperidine dithiocarbamate	Cu(II)	Catalytic hydrogen wave	DC polarography, DPP	Water, vegetables, alloys	0.05 ppm	Venkatasubba Naidu et al. (2011a)
Ammonium piperidine & morpholine dithiocarbamates	Cu(II)	Direct current-catalytic hydrogen wave	DC polarography, DPP	Leafy vegetables, milk, blood	0.001 ppm	Kanchi et al. (2013)
Ammonium piperidine and morpholine dithiocarbamates	Mn(II)	Catalytic hydrogen wave	DC polarography, DPP	Leafy vegetables, medicinal plants	0.001 ppm	Kanchi et al. (2012)
Ammonium morpholine dithiocarbamates	Ni(II)	Catalytic hydrogen wave	DC polarography, DPP	Water, agricultural materials	0.05 ppm	Venkatasubba Naidu et al. (2011b)
Lead diethyl dithiocarbamate	Cu(II)	Precipitation/solid phase extraction		Spectrophotometry	Alloys, water	0.2 mg dm^{-3}
Cesur (2007)						
Sodium diethyldithiocarbamate and piperidine dithiocarbamate	Bi(III)	Preconcentration/solid phase extraction	ICP-AES	Natural water, sea water	0.9–1.2 $\mu\text{g L}^{-1}$	Gadupudi et al. (2006)
Ammonium pyrrolidine dithiocarbamate and piperidine dithiocarbamate	Cd(II), Cu(II), Mn(II), Ni(II), Pb(II), Zn(II)	Preconcentration/solid phase extraction	ICP-AES	Saline water	0.1–0.6 $\mu\text{g L}^{-1}$	Ramesh et al. (2002)
Pyrrolidine dithiocarbamate	Co(II), Cu(II), Fe(III), Ni(II), Pb(II), V(VI), Zn(II)	Solvent extraction	X-ray fluorescence	Sea water	0.1–0.3 $\mu\text{g L}^{-1}$	Gordeeva et al. (2002)

(Kanchi et al., 2011b, 2012a, 2013; Venkatasubba Naidu et al., 2011a) as shown in Eqs. (1)–(3) below:



M = metal ion, RS = dithiocarbamate.

3. Dithiocarbamates as hazardous remediation agent

DTCs have been employed in more selective techniques for inorganic speciation studies (See Table 2) from different environmental matrices. The characteristic properties of DTCs combined with their insolubility of the metal salts (with the exception of those of sodium and other alkali and alkaline earth metals) and the capacity of the molecules to form complexes, are mainly responsible for the extensive use of these

compounds as analytical reagents in various matrices of environmental importance (see Fig. 1).

3.1. Atomic absorption spectrometric methods

One of the most reliable techniques for trace metal analysis is flame atomic absorption spectrometry (FAAS), but the detection limit is usually insufficient for $\mu\text{g L}^{-1}$ concentration levels of metal ions.

For this purpose, the preconcentration technique was developed (Elci et al., 2003) to improve its detection limit and selectivity for the determination of Cu(II), Ni(II), Fe(II), Cd(II), Pb(II), and Co(II) with the co-precipitation method in wastewater, sediment and metallic zinc samples using hexamethylene-dithiocarbamic acid hexamethylene ammonium salt (HMDTC-HMA). Several parameters including pH, amount of carrier, and volume of sample solution governing the efficiency and throughput of the procedure were evaluated. The influences of matrix ions of the real samples on analyte

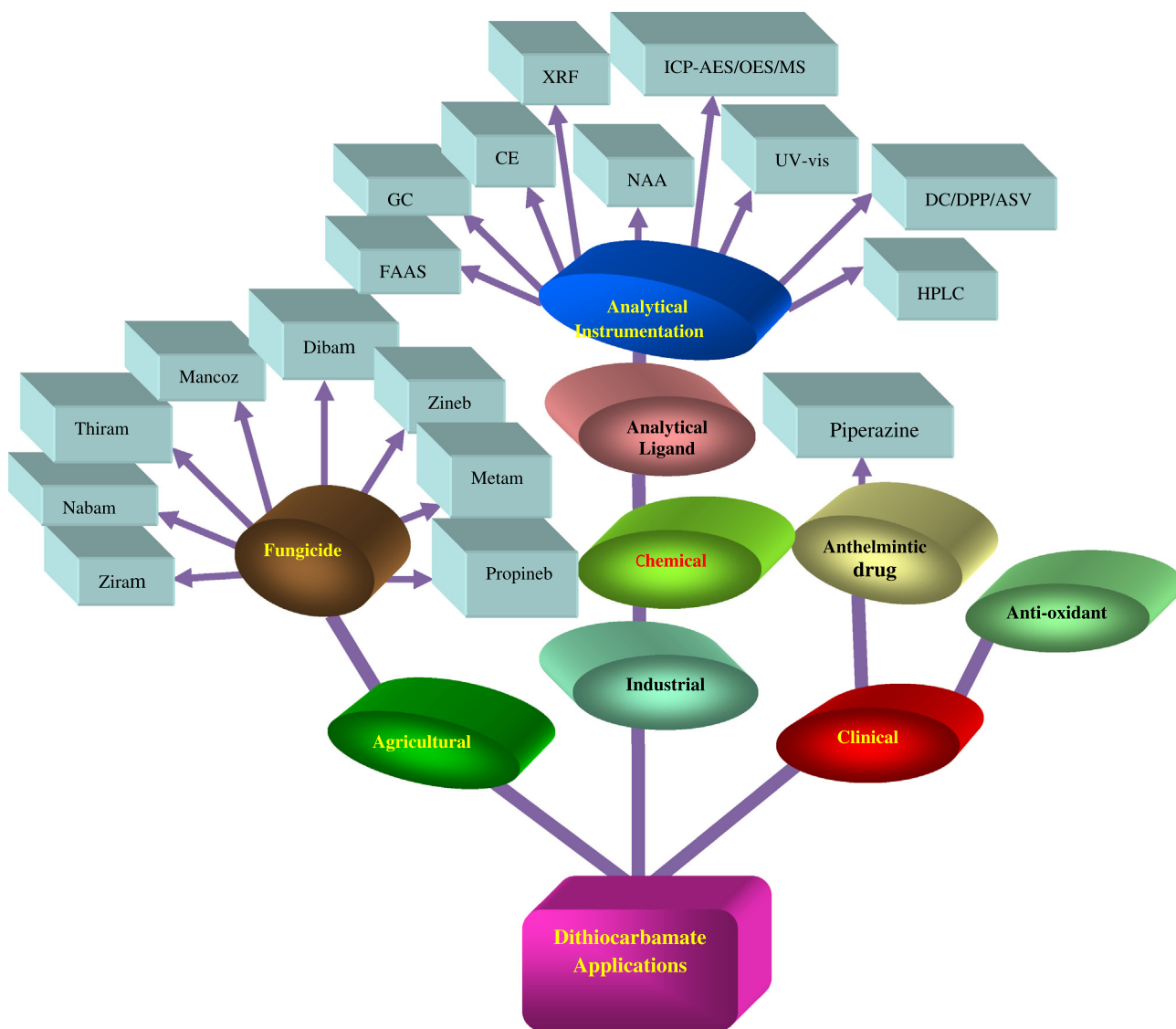


Figure 1 Flow chart representation of versatility of DTC applications.

recoveries were also investigated with detection limits of 5.9 and 61.0 $\mu\text{g L}^{-1}$ for Pb(II) for Cd(II), respectively and recoveries > 95% and RSD < 10%.

On-line flow injection co-precipitation system with diethyldithiocarbamate (DDTC)–Ni(II) system was used as a carrier for the trace determination of Cu(II), Pb(II), Cd(II), and Fe(II) in different environmental and biological systems by employing FAAS. In this study the metal ions were co-precipitated on-line with DDTC–Ni(II) in 0.3 M nitric acid, and the precipitate was collected in a knotted reactor. The precipitate was then dissolved in isobutyl methyl ketone (IBMK) and transported directly into the nebulizer system of a FAAS. Enhancement factors of 60, 58, 65, and 59 of this system were obtained for Cu(II), Pb(II), Cd(II), and Fe(II), respectively at the sampling frequency of 60 h^{-1} and detection limits of 0.5, 2.7, 0.2, and 2.5 $\mu\text{g L}^{-1}$, and relative standard deviations ($n = 10$) of 3.0% for 40 $\mu\text{g L}^{-1}$, 2.0% for 80 $\mu\text{g L}^{-1}$, 3.5% for 10 $\mu\text{g L}^{-1}$, 2.8% for 60 $\mu\text{g L}^{-1}$ were obtained for Cu(II), Pb(II), Cd(II), and Fe(II), respectively. This method was applied in the determination of the metals in waters and environmental reference material of soil, and biological reference materials of mussel and human hair (Liu et al., 2000). A method was developed (Cesur et al., 2000) for the preconcentration of Cu(II), Ni(II), and Cd(II) in various water systems and standard metal alloy samples prior to their determination by FAAS, using the Zn(II)–piperazine dithiocarbamates complex [Zn(II)–PDC] loaded onto activated carbon. In this methodology Cu(II), Ni(II), and Cd(II) in the liquid phase quantitatively replaced Zn(II) on a Zn(II)–PDC-activated carbon solid phase. Thereafter, the metals on the solid phase were easily eluted by Hg(II) solution into the aqueous phase, and were quantified by FAAS. Optimum experimental parameters such as pH, sample volume, and effect of matrix ions for the preconcentration of the metals were investigated to increase the selectivity and to avoid the interference effects. The range of linearity 0–6, 0–5, 0–3 $\mu\text{g mL}^{-1}$, correlation coefficient 0.998, 0.996, 0.999, detection limits 15.7, 23.5, and 11.8 $\mu\text{g mL}^{-1}$ and determination limits 136, 179, and 98 $\mu\text{g mL}^{-1}$ in final Hg(II) solution were obtained for Cu(II), Ni(II), and Cd(II), respectively.

Comparison preconcentration coupled with solid phase extraction studies were carried out on five samples of yogurts and human milk to analyze Zn(II), Mg(II), Mn(II), Cr(III), Cu(II), Fe(III), and Ca(II) with 1% 8-hydroxyquinoline, 1% ammonium pyrrolidinedithiocarbamate (APDC) extracted with methyl-isobutylketone (MIBK) onto activated carbon in HNO_3 and the metal ions were quantified using FAAS. In the case of the yogurt samples, the powdered activated carbon in HNO_3 exhibited the highest complexing ability with values ranging from 0.04–0.17, 335–476, 1.52–3.82, 0.08–0.27, 0.09–0.28, 1.31–8.78, and 888–12693 mg L^{-1} concentration for Zn(II), Mg(II), Mn(II), Cr(III), Cu(II), Fe(III), and Ca(II), respectively. The concentrations of Zn(II), Mg(II), Mn(II), Cr(III), Cu(II), Fe(III), and Ca(II) were determined to be in the range of 0.02–0.03, 1.10–9.47, 0.05–0.11, 0.02–3.08, 0.01–0.87, 0.47–18.08, <0.01–278 mg L^{-1} respectively, for the APDC/MIBK extraction method. The complexing ability of APDC/MIBK appeared to be lower (Nwosu et al., 2003) in 1% 8-hydroxyquinoline/MIBK. The solid-phase extraction preconcentration technique for the analysis of Mn(II), Cu(II), Cd(II), and Pb(II) in water samples and their determination by

FAAS using phenylpiperazine dithiocarbamate as a novel DTC (Cesur, 2003a) was discussed. The obtained recoveries ranged from 90 to 100%, while the enrichment factor was 400 for metal -spiked sample solutions. Cu(II), Pb(II), Ni(II), Cd(II), Mn(II), and Fe(III) metal ions were also determined using FAAS after preconcentration on Amberlite XAD-16 resin with hexamethylenammonium–hexamethylenedithiocarbamate (HMA–HMDTC) as a chelating agent in $\text{NH}_3/\text{NH}_4\text{Cl}$ medium at pH 9.0. The RSD and LOD were in the range of 0.8–2.9% and 0.006–0.277 $\mu\text{g mL}^{-1}$ respectively. Recoveries obtained by the column method were quantified (>95%) at optimum conditions and was applied for the determination of metal ions in seawater and waste water samples (Tokahoglu et al., 2002).

Co-precipitation and preconcentration protocols were explained in the literature to analyze trace amounts of Cd(II), Cu(II), and Pb(II) in water samples by FAAS using potassium 4-methylpiperidinedithiocarbamate (K4-MPDC) as a hazardous remediation agent and Bi(III) as a carrier element (Efen-dioglu et al., 2007). The method was based on the preparation of Cd(II), Cu(II), and Pb(II) precipitates with Bi(III)4–MPDC. This precipitation solution was filtered onto a cellulose nitrate membrane and the precipitates together with the membrane filter were dissolved in concentrated nitric acid. Several parameters including pH of sample solution, amount of carrier element and reagent, standing time, sample volume for precipitation and the effects of diverse ions were examined. The accuracy of the method was tested with standard reference material (MBH, C31XB20, and CRM BCR-32) and Cd(II), Cu(II), and Pb(II) added samples and also in sea water, river water and tap water samples. The obtained recoveries were found to be >95% with relative standard deviations of 10%.

Metal–DTC complexes loaded onto an adsorbent have been used for the preconcentration of some metal ions in aqueous systems. It was reported that from the point of selective extraction of the metal ions and the stability in acid solutions, metal–DTCs were more useful than ammonium or alkali metal salt of dithiocarbamic acids (Cesur et al., 2000; Cesur and Bati, 2000). Novel solid phase extraction procedures were established using freshly precipitated metal–diethyl dithiocarbamate (DDTC) complexes such as Mn(DDTC)₂, Zn(DDTC)₂, Cd(DDTC)₂, Fe(DDTC)₃, Co(DDTC)₂, Cu(DDTC)₂, Ni(DDTC)₂, Pb(DDTC)₂, and Hg(DDTC)₂ as reagents, for the selective extraction of Mn(II), Zn(II), Cd(II), Fe(III), Co(II), Cu(II), Ni(II), Pb(II), and Hg(II) ions in aqueous system. These reagents showed excellent selectivity for the extraction of metal ions with higher conditional stability constants (or extraction constants). Freshly precipitated Ni(II)–(DDTC)₂ were used as an example of the preconcentration of Cu(II) in aqueous system prior to its determination by FAAS (Cesur 2003b).

3.2. Chromatographic methods

Mercury ion, methyl mercury, ethyl mercury, and phenyl mercury, were determined using high performance liquid chromatography (HPLC) after complexation with emetine-dithiocarbamate (emetine- CS_2), and their subsequent injection into an instrument coupled with a tris(2,2'-bipyridine)ruthenium(III) chemiluminescence detection system. The emetine- CS_2 complexing agent was effectively used to measure the concentration of analytes in addition to serving as a separation

and detection reagent. The limit of detection for (emetine- CS_2) $_2$ Hg, emetine- CS_2 -methyl mercury, emetine- CS_2 -ethyl mercury, and emetine- CS_2 -phenyl mercury was 30, 17, 21, and 22 ng L⁻¹ respectively. Furthermore, the method was applied to biological samples in combination with acid leaching and liquid-liquid extraction using emetine- CS_2 as an extraction reagent (Kodamatani et al., 2012).

Thin layer chromatography (TLC), a very convenient and rapid method for the separation and identification of inorganic ions. Therefore, many attempts to improve TLC for this application seem to be of interest for chromatographers. Various heavy metal ions and several binary mixtures were separated on thin layer cellulose plates and paper chromatographic strips impregnated with sodium diethyldithiocarbamate (Rathore and Sing, 2002), and chromatographic behavior of various dithiocarbamate fungicides (Sarang et al., 2012) was studied on cellulose plates. Different heavy metal ions such as Pb^{2+} , Hg^{2+} , Cd^{2+} , Zn^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Fe^{3+} , UO_2^{2+} , VO_2^{2+} and Bi^{3+} have been chromatographed on thin layer of carbamide-formaldehyde polymer impregnated with sodium diethyl-dithiocarbamate. Common solvents namely acetone, benzene, carbon tetrachloride, methanol and ethanol have been used as a mobile phase. Semi-quantitative determination of Hg^{2+} , Bi^{3+} and Ni^{2+} by visual comparison of color intensities on the TLC plates as well as by measurement of spot area has also been attempted (Sarang et al., 2012).

DTCs have been extensively studied and reported as complexing reagents for a large number of metal ions for the solvent extraction, spectrophotometric and HPLC determination of metal ions. They form co-ordinatively saturated, neutral metal chelates, which are easily extractable in organic solvents. They also provide adequate shielding to the metal ions to enable them to elute from a GC column. Gas chromatography (GC) analysis of metal chelates of diethyl dithiocarbamate, di(trifluoroethyl)dithiocarbamate and pentamethylenedithiocarbamate from packed and capillary columns have been reported. Pyrrolidinedithiocarbamate (PDTC) has advantages as an analytical reagent for metal analyses because of its complexation in acidic media. A number of studies have been made for HPLC determination of metal ions using PDTC, but the GC is characterized by its increased resolving power with respect to HPLC and GC involves less running cost than HPLC. The selective conversion of the analyte to a volatile product, could possibly remove a number of matrix effects. The goals of the authors in this work were to extend the range of complexing reagents for GC separation and to analyze metal ions. For this purpose pyrrolidinedithiocarbamate (PDTC) chelates of Cu(II), Ni(II), Fe(III), and Mn(II) were extracted in MIBK and subjected to capillary gas chromatography (Laghari et al., 2010).

HPLC methodology (Arain et al., 2009) has been developed for the simultaneous determination of Fe(III), Cr(III), Mn(II), Cu(II), Ni(II), and Co(II) from fresh river water samples collected from river Indus at Ghulam Muhammad barrage. In this preconcentration technique, using pentamethylene dithiocarbamates (PMDTC) as a derivatizing reagent and the subsequent solvent extraction are fairly discussed to quantify Fe(III), Cr(III), Mn(II), Cu(II), Ni(II), and Co(II). The average levels ($n = 12$) of metal ions ranged from 14.2 to 542 $\mu\text{g L}^{-1}$.

Pentamethylene dithiocarbamate was used for the separation and analysis of Cu(II), Ni(II), Co(III), Fe(III), Mn(II), and

Cr(III) with GC and HPLC. Pentamethylene dithiocarbamate chelates with metal ions in slightly acidic media (pH 5) were extracted into MIBK or chloroform. Capillary GC elution and separation were carried out on methylsilicone DB-1 column (25 and 30.2 mm i.d.) with film thickness of 0.25 mm with an electron-capture detector. Elution was carried out at an initial column temperature of 200 °C with an increment at a rate of 5 °C min⁻¹ up to 250 °C and a maximum temperature maintained for 10 min. Symmetrical peaks with a baseline separation were obtained for the metal chelates investigated with a linear calibration ranging from 5 to 25 $\mu\text{g mL}^{-1}$ for each metal ion and detection limits in the range of 0.5–6.0 $\mu\text{g mL}^{-1}$ corresponding to 27–333 pico-gram level of metal ion reaching the detector. HPLC separation was carried out from Li-Chrosorb ODS, 5 mm column and complexes eluted with methanol-water–1 mM sodium acetate (70:28:2, v/v) with a flow-rate of 1.2 mL min⁻¹ at 260 nm using UV detector. The detection limits obtained were in the range of 2–6 $\mu\text{g mL}^{-1}$. This method was applied to the determination of metal ions in canal water and coal samples with RSD values within 4.15% (Arain et al., 2002).

3.3. Electrophoretic methods

Micellar electrokinetic chromatography (MEKC) was described for the separation and determination of Mo(VI), Cr(VI), Ni(II), Pd(II), and Co(III) as diethyl dithiocarbamate (DDTC) chelates. The separation was achieved from fused silica capillary (52 cm \times 75 μm i.d.) with an effective length of 40 cm, background electrolyte (BGE) borate buffer pH 9.1 (25 mM), cetyltrimethylammoniumbromide (CTAB) 30% (100 mM) and 1% butanol in methanol (70:30:5 v/v/v) with negative applied voltage of 10 kV using reverse polarity. The maximum wavelength (λ_{max} 225 nm) was achieved using a photodiode array detector. The linear calibration for each element was obtained within 0.16–10 $\mu\text{g mL}^{-1}$ with a limit of detection (LOD) 0.005–0.0167 $\mu\text{g mL}^{-1}$. The separation and determination were repeatable with relative standard deviation (RSD) within 2.4–3.3% ($n = 4$) in terms of migration time and peak height/peak area. The method was applied for the determination of Mo(VI) from potatoes and almonds, Ni(II) from hydrogenated vegetable oil, and Co(III) from pharmaceutical preparations (Arfana et al., 2012).

Emetine dithiocarbamate metal complexes, were prepared from emetine, carbon disulfide, and metal(II), indicated large chemiluminescence intensities on tris(2,9-bipyridine)-Ru(II). Capillary electrophoresis with chemiluminescence detection was developed for the analysis of emetine and the metal complexes. After the optimization of various analytical conditions, the mixture of the Cu(II), Ni(II), and Co(II) complexes as a model sample was injected into the capillary electrophoresis system with chemiluminescence detection. They were successfully separated and detected with a detection limit of 50 nM (Tsukagoshi et al., 2002).

Lowest detection in CE is often a challenge for the determination of trace metal analysis. This limitation has however been addressed by the development of an enrichment procedure combining the formation of water soluble, metal-bis(carboxymethyl) dithiocarbamate complexes, at basic pH and sparingly soluble in an acidic environment with solid-phase extraction. Appropriate conditions were developed for a solid-phase extraction step compatible with subsequent capillary

electrophoretic separation in terms of the composition of electrophoresis and eluting buffers. At pH below 4.0 when the ligand carboxyl groups are non-ionized, metal ion complexes have no apparent charge and are efficiently retained on a conventional C₁₆ cartridge. Application of a basic eluent, a borate buffer at pH 9.0, causes the complexes to be ionized and eluted rapidly and quantitatively. Parameters affecting the retention/recovery behavior, such as the pH and ligand concentration of the loading solution, flow-rate, eluting buffer pH and concentration, were examined to attain the best possible enrichment factors for trace metal analysis. As a result, an increase in sensitivity over two orders of magnitude results in the lowering of detection limits to levels of $\mu\text{g L}^{-1}$ for Cu(II), Pb(II), Cd(II), Ni(II), and Hg(II) (Ructnev et al., 2000).

A simple, sensitive and rapid method was developed for the separation and identification of Se(IV) and Co(II) in *Macrobrachium lamarrei*, fresh water prawn samples and their feeding materials after pre-capillary complexation with ammonium piperidine-1-carbodithioate (APC) using CE (Kanchi et al., 2012b). Microwave assisted procedure was adapted to analyze Se(IV) and Co(II) in prawn samples which are eco-friendly to the environment. Optimized parameters such as pH, complexing agent concentration, buffer nature, applied voltage and interferences by other metal ions were also investigated. Authors calculated and correlated their results with the FAAS method in terms of Student's "t"-test and Variance ratio "f"-test to make this discussion statistically sound. The method was applied for the analysis of Se(IV) and Co(II) in various *M. lamarrei*, fresh water prawn samples and their feeding materials (Kanchi et al., 2012b).

3.4. Voltammetric methods

Polarographic methods enabled the direct determination of metals after the extraction of their metal complexes into organic solvents but with poor sensitivity and reproducibility, due to the low dielectric constant of the organic solvent and partial evaporation of these solvents during the removal of dissolved oxygen. Although, adsorptive and stripping voltammetric methods are fairly sensitive, they are more time consuming and also depend on the rigorous control of experimental conditions. Various reagents may be used for the determination of metal ions but *N*-methylethylxanthocarbamate is relatively cheap, sensitive and does not interfere with the polarographic determination of metal ions. *N*-methylethylxantho carbamate has been used as an analytical reagent for the determination of trace amounts of Cd(II) in standard alloys, biological, and environmental samples. This reagent forms a water insoluble complex with Cd(II) and quantitatively adsorbs over microcrystalline naphthalene in the pH range of 2.5–12.0. The metal complex was desorbed with HCl and Cd(II) determined by differential pulse polarography (DPP). The detection limit was 0.05 ppm (signal-to-noise ratio = 2) and the linearity concentration range of 0.2–25 $\mu\text{g mL}^{-1}$, with a correlation coefficient of 0.9995 and a relative standard deviation of ~0.81%. Characterization of the electro-active process included an examination of the degree of reversibility. Various parameters such as pH, reagent concentration, amount of naphthalene, volume of aqueous phase, and the interference of metal ions on the determination of Cd(II), have been extensively studied to optimize the conditions for its determination in various complex

materials (Hussain et al., 2002). Novel sensitive catalytic hydrogen direct current polarographic method was developed for the determination of Cr(VI) with ammonium piperidine dithiocarbamates (Amm Pip-DTC) and ammonium morpholine dithiocarbamates (Amm Mor-DTC) in various water systems and vegetables. This method was based on the catalytic hydrogen wave of Amm Pip/Mor-DTC-Cr(VI) complexes in the presence of NH₄Cl–NH₄OH at pH 7.5 and 9.6 producing catalytic hydrogen waves at –1.59 and –1.65 V vs. SCE, respectively. Different optimum parameters such as pH, concentration effects of NH₄Cl–NH₄OH and Amm Pip/Mor-DTC on peak heights were also discussed to enhance the sensitivity, selectivity and detection limits of this method in comparison with the DPP method (Kanchi et al., 2011a).

Ammonium pyrrolidine dithiocarbamate (APDC) was used as a preconcentrating agent for the determination of Pb(II) using the hanging mercury drop electrode (HMDE) in acetate buffer media, using square wave anodic stripping voltammetry (SWASV). The optimized experimental conditions included pH, APDC concentration, accumulation time, accumulation potential, scan rate, pulse amplitude and square wave frequency. A linear relationship between the peak current and Pb(II) concentration was obtained over the range (5–40 ppb) with a correlation co-efficient of 0.99911, detection limits of 0.89 ppb and a standard deviation of 0.03706. The formation of a complex formed between Pb(II) and APDC was investigated using both SWASV and cyclic voltammetry (CV). These two techniques have been utilized to elucidate and confirm the possible complexation reactions between Pb(II) and APDC. Two prominent peaks were observed in SWASV, one corresponding to a reduction process of free (labile) Pb²⁺ at $E_p = -0.36$ V, this peak current decreased and shifted to a more negative potential with the addition of APDC. On the other hand, a new peak corresponding to the reduction process was formed at more positive potential ($E_p = -0.29$ V) and its height increased with the addition of the ligand. Cyclic voltammetric studies showed oxidation and reduction peaks for APDC at –0.53 and –0.34 V, respectively which disappear upon the addition of the metal. Pb²⁺ showed reduction and oxidation peaks at –0.40 and –0.35 V, respectively which decrease by the addition of a ligand. Two peaks appeared at –0.134 and –0.146 V at pH 3.5 in 0.1 M acetate buffer solution, where the Pb(II)–APDC complex formed as new species (Morsi et al., 2011). Amm Pip-DTC/Amm Mor-DTC was synthesized and applied for the development of rapid and cost effective catalytic hydrogen current technique to analyze Co(II) in the presence of NH₄Cl–NH₄OH at pH 7.8 and 8.4. These ligands produced catalytic hydrogen current with Co(II) at peak potentials –1.24 and –1.44 V vs. SCE, respectively prior to the determination by direct current polarography. Quantitative experimental conditions were developed by studying effects of pH, supporting electrolyte (NH₄Cl), ligand and metal ion concentrations and the effects of adverse ions on peak height to improve the sensitivity, selectivity and detection limits of the catalytic hydrogen current methodology. This method was applied to environmentally important matrices such as drinking waters, pharmaceuticals and agricultural materials. Following an extensive investigation, the authors reported the order of recovery percentage of the Co(II) from these matrices as follows: Pharmaceuticals > agricultural materials, Agricultural materials > drinking water samples,

Pharmaceuticals > drinking water samples (Kanchi et al., 2011b). Consequently this resulted in an economical, novel, eco-friendly and robust method developed for the quantification of Co(II) in various waters, leafy vegetables, milk and blood samples using the direct current catalytic hydrogen wave (DC-CHW) technique. The Amm Pip/Mor-DTCs complexed with Cu(II) in the presence of $\text{NH}_4\text{Cl-NH}_4\text{OH}$ medium at $\text{pH } 6.5 \pm 1$ produced CHW's at -0.35 ± 1 V vs. SCE. Specifically, optimal parameters such as preparation medium, effect of pH, ligand concentration, metal ion concentration effects on peak heights were optimized to enhance the sensitivity and selectivity. More recently, the interaction of Amm Pip/Mor-DTCs with Cu(II) was confirmed with CV and supported by computational calculations using Density Functional Theory (DFT) methods (Venkatasubba Naidu et al., 2011b; Kanchi et al., 2013). Catalytic hydrogen nature of Amm Mor-DTC-Ni(II) complex was investigated on dropping mercury electrode in the presence of $\text{NH}_4\text{Cl-NH}_4\text{OH}$ as a supporting electrolyte at $\text{pH } 6.0$ using direct current polarography at -1.30 V vs. SCE. The efficiency of this technique was evaluated using environmental samples (Venkatasubba Naidu et al., 2011a).

Cost-effective, rapid, sensitive and novel catalytic hydrogen wave technique (CHW) was developed for the analysis of Mn(II) in $\text{NH}_4\text{Cl-NH}_4\text{OH}$ medium at $\text{pH } 6.2$ and produced CHWs at -0.60 and -0.56 V vs. SCE with Amm Pip-DTC and Amm Mor-DTC respectively. In this study various leafy vegetables and medicinal plants were collected around Tirupati and Chittoor District in Andhra Pradesh, a famous pilgrimage center in India (Kanchi et al., 2012ab). This CHW technique was novel, spontaneous, reliable and highly sensitive for the determination of Mn(II) in Indian traditional leafy vegetables and medicinal plants. The limit of detection of the developed method was superior in comparison to the methods reported in the literature (Divrikli et al., 2003, 2006; Soyak and Unsal, 2010).

3.5. Spectrophotometric methods

UV-VIS spectrophotometry is a versatile, widespread and more economical technique compared to AAS and ICP-AES protocols. On the other hand, its selectivity is lower and the interfering effects are considerably higher. For this purpose the authors developed a new solid-phase extraction for the selective extraction of Cu(II) in an aqueous system using freshly precipitated Pb(II)diethyldithiocarbamate [Pb(II)-(DDTC)_2] as a reagent. The method was based on the quantitative replacement of Pb(II) ions in the solid Pb(II)-(DDTC)_2 phase by Cu(II) ions present in the aqueous phase, and the resulting solution was dissolved in chloroform. Beer's law was obeyed at 435 nm over a concentration range of 0.2 – 5 mg L^{-1} . The molar absorptivity and Sandell's sensitivity coefficients of the solutions were 1.0689×10^4 $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ and 0.0060 $\mu\text{g cm}^{-2}$ respectively. The optimum conditions for each parameter were experimentally determined and possible interferences of various salts were also studied. However, the sorption of Cu(II) in the aqueous phase using Pb(II)-(DDTC)_2 was more selective than the alkali salts of dithiocarbamic acids. Additionally, Pb(II)-(DDTC)_2 was more stable in acidic aqueous media and freshly precipitated Pb(II)-(DDTC)_2 could selectively sorb Cu(II) ions without the help of any other adsorbents (Cesur 2007).

3.6. Inductively coupled plasma-atomic emission spectrometric methods

A column solid-phase extraction procedure for the separation and preconcentration of Bi(III) in natural water samples using sodium diethyldithiocarbamate (Na-DTTC) or piperidine dithiocarbamate (pip-DTC)-coated Amberlite XAD-7 resin prior to their determination by inductively coupled plasma atomic emission spectrometry (ICP-AES) was discussed. The results showed that solution pH and flow rate affected the sorption of Bi(III) eluted with 4 M HNO_3 . The extractor system with good sorption capacity values of 9.82 mg g^{-1} of Bi(III) coated on Na-DTTC resin and 9.56 mg g^{-1} of Bi(III) coated on pip-DTC resin. The preconcentration factors were 150 and 170 for pip-DTC-coated resin and Na-DTTC-coated resin, respectively. The detection limits were 0.9 and 1.2 mg L^{-1} for the resin coated with Na-DTTC and pip-DTC respectively. These results revealed that the resin coated with Na-DTTC performed slightly better in the recovery of bismuth than those coated with pip-DTC. The accuracy of the proposed method was investigated by determining the bismuth in spiked water samples. The relative standard deviations of the determination of bismuth were below 5% (Gadupudi et al., 2006).

Preconcentration of Cd(II), Cu(II), Mn(II), Ni(II), Pb(II) and Zn(II) in saline matrices on Amberlite XAD-4 resins coated with ammonium pyrrolidine dithiocarbamate (APDC) and piperidine dithiocarbamate (pip-DTC) and subsequent determination by inductively coupled plasma atomic emission spectrometry were studied. Parameters such as effect of pH, and effect of HNO_3 concentration on the elution of metals from resin were discussed. The results showed that Amberlite XAD-4 coated with APDC was more efficient in the recovery of metal ions compared with Amberlite XAD-4 coated with pip-DTC, in the concentration range of 0.1 – 200 $\mu\text{g L}^{-1}$, for 1.0 g of Amberlite XAD-4 coated resin. For resin coated with APDC the detection limits are 0.1 , 0.4 , 0.3 , 0.4 , 0.6 , and 0.5 $\mu\text{g L}^{-1}$ for Cd(II), Cu(II), Mn(II), Ni(II), Pb(II), and Zn(II) respectively. While, for resin coated with pip-DTC the corresponding detection limits for the divalent metals were 0.7 , 1.0 , 0.8 , 0.9 , 1.7 , and 1.2 $\mu\text{g L}^{-1}$ respectively. This method was applied to trace metal analysis in artificial sea and natural water samples (Ramesh et al., 2002).

3.7. X-ray fluorescence methods

Small amounts of toxic heavy metals in environmental samples, raw food materials, and foodstuffs are frequently determined by combined methods including preconcentration. An efficient technique is a dynamic sorption preconcentration; it is technologically convenient and makes it possible to automate preconcentration and the whole analysis cycle as well (Venitsianov et al., 1998). A promising technique is the combination of dynamic sorption preconcentration and multi-element determination of elements by X-ray fluorescence spectrometry. The performance characteristics of the X-ray fluorescence determination of elements are largely governed by the macro composition of the sample and the quality of its surface. Thus, a high sensitivity of the determination is attained with the use of thin-layer organic matrices, because the fluorescence of elements incorporated in these matrices (C, N, H, and O) is beyond the recorded spectrum and the small

thickness and low density of these materials minimize the absorption and scattering of primary and fluorescence radiation. However, it is difficult to obtain thin-layer sorbents with high dynamic capacity with respect to different forms of elements. Pyrrolidine dithiocarbamate (PDTC) complexes of Co(II), Cu(II), Fe(III), Ni(II), Pb(II), V(IV), and Zn(II) were obtained after mixing solutions of the reagent and the sample. The recoveries were calculated by the calibration plot. In the case of the concentration of elements in reference samples, filter concentrates were dissolved in 6–7 M HNO₃ with the addition of H₂O₂, while the concentration of elements in the resulting solutions was determined by inductively-coupled plasma atomic-emission spectrometry. Conditions of the quantitative extraction of Co(II), Cu(II), Fe(III), Ni(II), Pb(II), V(IV), and Zn(II) were obtained from solutions on cellulose filters in the form of pyrrolidinedithiocarbamates. The respective elements were determined on filters by X-ray fluorescence spectrometry, with detection limits ranging from 0.1, 1.2, 0.4, 0.2, 0.2, 0.4, and 0.3 mg on the filter. The relative standard deviation of the results was not higher than 8% for the amount of elements on the filter ranging from 5 to 50 mg. The accuracy

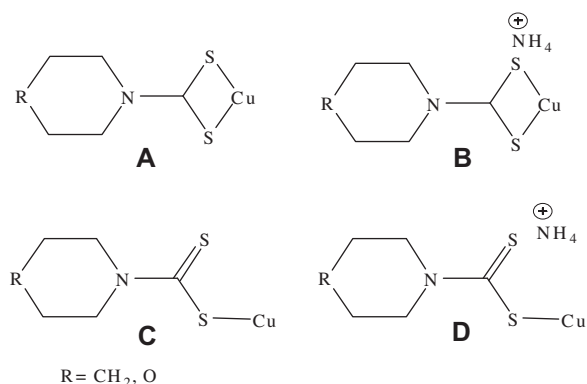


Figure 2 Possible coordination for both single and double coordination of sulfur atoms with Cu(II) in the presence/absence of ammonium ions of ammonium salt of Pip/Mor-DTCs (reproduced with permission from Intern. J. Electrochem. Sci., Kanchi et al., 2013).

of the determination of elements by the proposed sorption–X-ray fluorescence method in river and sea water including soil extract was verified by the added–found method (Gordeeva et al., 2002).

4. Significant role of computational chemistry in metal-DTC complexes

Over the years, computational calculations have been extensively used to understand the mechanisms, thermodynamics and kinetics of the reactions, drug-receptor interactions and metal–metal coordination in the complexes. Recently, we performed the DFT calculations to determine the possible coordination of Amm Pip/Mor-DTCs with the Cu(II) (see Fig. 2) in the presence/absence of ammonium ions. All starting structures (A–D, Fig. 2) were fully optimized at the B3LYP level using the 6–31G*/lanl2dz mixed basis sets. All calculations were performed using the Gaussian 03 computer program (Frisch et al., 2003). The optimized geometries pictorially represented in Fig. 3a,b and Fig. 4a,b were verified by the second derivative frequency calculations to obtain their true ground state minima. Clearly, in the absence of ammonium ion (NH₄⁺), both structures A and C (Fig. 2) irrespective of the starting coordination/amines, were optimized to similar geometries with the Cu(II) centrally coordinated by both sulfur atoms of the Amm Pip/Mor-DTCs (Fig. 3a,b). The optimized energies of the complexes of morpholine (Fig. 3a) and piperidine (Fig. 3b) with Cu(II) were found to be –541.6596833 and –505.7721889 Hartrees respectively. The bond distances between the copper and sulfur atoms were found to be 2.38 Å in both dithiocarbamates (Fig. 3a,b). The presence of NH₄⁺ ion in the complexes B and D (Fig. 2) shifted the coordination *via* a single sulfur atom present in amine DTCs with a bond distance of 2.41 Å, between the bonded sulfur and Cu(II) depicted in Fig. 4a,b, with energies of –598.7700982 and –562.8998656 Hartrees respectively. Hence, it is believed that the Mor/Pip-DTCs coordinate preferably *via* a single sulfur atom with the Cu(II), and is probably due to the decreased electron density of the sulfur atom in the vicinity of the NH₄⁺ ion. However, in the absence of NH₄⁺ ion, both sulfur atoms are equally available for coordination due to their uniform electron density distribution (Kanchi et al., 2013).

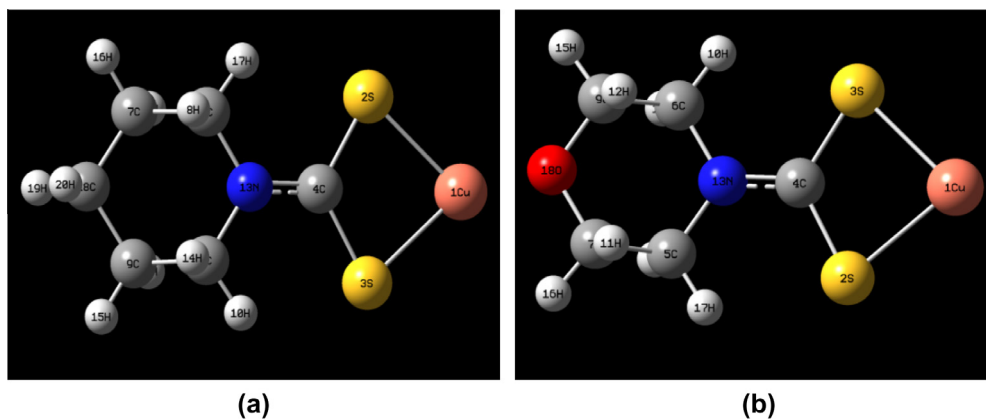


Figure 3 Optimized complexes of Cu(II) with (a) Mor-DTC and (b) Pip-DTC in the absence of ammonium ion (reproduced with permission from Intern. J. Electrochem. Sci., Kanchi et al., 2013).

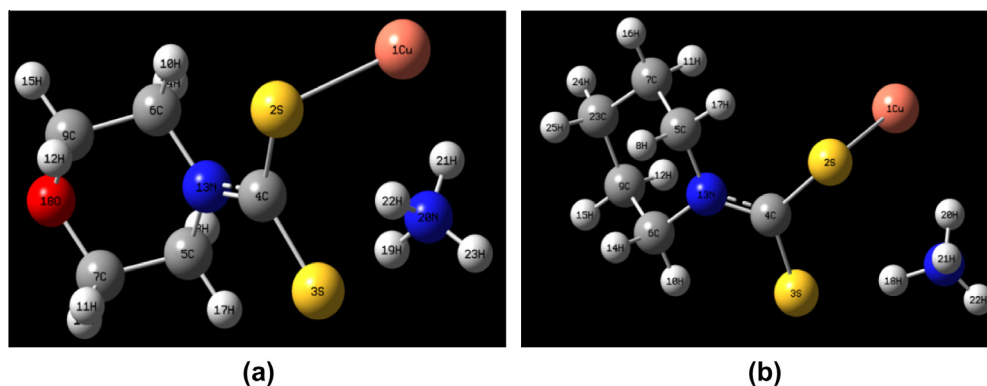


Figure 4 Optimized complexes of Cu(II) with (a) Mor-DTC and (b) Pip-DTC in the presence of ammonium (NH_4^+) ion (reproduced with permission from Intern. J. Electrochem. Sci., Kanchi et al., 2013).

5. Other significant applications of DTCs

5.1. Environmental applications of DTCs as pesticide

Besides the applicability of dithiocarbamates as strong analytical and electro-analytical chelating agents, some of the dithiocarbamates like [ethylenebis-dithiocarbamates (EB-DTC) such as Nabam, Mancozeb, Maneb, Zineb], [propylenebis-dithiocarbamates (PB-DTC) such as Propineb], [methylthiocarbamates (M-DTC) such as Metam], DMDTC [dimethyl-dithiocarbamates (DM-DTC) such as Dibam, Ferbam, Ziram], and [tetramethylthiuram disulfide (TMTDS), Thiram] have also been used as pesticides worldwide. Analytical methods for trace analysis of dithiocarbamates in food and different environmental matrices have been developed due to their toxicological (neuropathological, thyroid, CNS developmental, and cholinesterase activity) behavior (Mulkey, 2001).

Chromatographic technique such as Ion-pair chromatography (IPC) was productively employed for the separation of Metam-sodium, Ziram, Mancozeb/Zineb, and Propineb (Van Lishaut and Schwack, 2000) and analyzed in fruits and vegetables using UV-visible spectrometry at 286 nm and electrochemical detection at 600 mV. At basic medium (pH 10–11), Thiram undergoes degradation to produce DMDTC, sulfenates and sulfinates with 10 mM phosphate/tetrabutylammonium hydrogen sulfate buffer and methanol using isocratic and gradient mode during the extraction step. This problem could be solved by the addition of sulfite resulting in the formation of equal amounts of a sulfite addition product and DMDTC. Cysteine was used as a stabilizing agent for the determination of Ziram, however, simultaneous analysis of Ziram and Thiram was found to be a challenging task, which requires various calibrations and buffers for extraction. Another mode of the determination method was developed using the EDTA to chelate the metal ions present in the pesticide molecules prior to their analysis by transferring dithiocarbamates as soluble sodium salts into the aqueous medium. The developed method was evaluated with known concentrations of spiked samples of Ziram, Zineb and Propineb ranging 0.2, 1.0, and 3.0 ppm (w/w) in different crops and their recoveries were found to be 93–120%. In case of Thiram analysis, a low recovery (78.5–91.2%) was observed due to interference of Ziram in the same range of concentration values.

Thiram, Disulfiram, Dazomet (3,5-dimethyl-1,3,5-thiadiazinane-2-thione), ethylenethiourea (ETU), and propylenethiourea (PTU) were analyzed by reverse phase high performance liquid chromatography coupled with mass spectrometry and atmospheric pressure chemical ionization (APCI) and electrospray ionization (ESI) in various fruits and vegetables using a methanol/water gradient on a C_8 separation column (Blasco et al., 2004). In this investigation two extraction protocols, matrix solid phase dispersion (MSPD) and solid phase extraction (SPE) have been reported. According to the obtained results, MSPD was more selective than SPE due to high recovery values. APCI was found to be superior over ESI showing significantly higher sensitivity for ETU and PTU. Furthermore, APCI was more robust and showed reproducible spectra of compounds without adduct formation. The capillary electrophoretic method was used for the separation and quantification of ziram and zineb with LODs of ~ 0.6 – 0.7 ppm (w/v) using UV detector in spiked wheat samples. Simple borate buffer system was used as a back ground electrolyte solution (Kumar Malik and Faubel, 2000).

5.2. Pharmaceutical applications of DTCs

For more than 50 years Disulfiram [Tetraethylthiuram disulfide (TETDS)] has been used in the treatment of alcohol abuse. Consequently, several analytical methods mainly in the field of chromatography were developed for the analysis of this drug in quality control laboratories in pharmaceutical industries.

Automated pre-column derivatization method was developed using Co(II) by RP-HPLC with UV detection for the analysis of PDTC. In this study, several heavy metals such as Co(II), Cr(III), Ni(II), Zn(II), Mn(II), and Ag(I) etc., were tested as complexing reagent. Ni(II) and Mn(II) formed precipitation on the guard column due to its instability, whereas no complexation was formed with Zn(II) and Ag(I) which resulted in the colorless solutions (Dilli and Tong, 1999). In case of Co(II), few stability problems of the PDTC complex have been reported with increasing back pressure of the column with successive runs and a blue complex at the head of the guard column. For better understanding the interaction of protein with dithiocarbamates, authors applied RP-HPLC/UV followed by matrix assisted laser desorption/ioni-

zation/MS for the analysis of diethylcarbamoyl adducts on cysteine residues of globin chains in hemolysates of Disulfiram-administered rats (Dilli and Tong, 1999; Tonkin et al., 2000; Tonkin et al., 2003). Acetonitrile/water/TFA was used as a linear gradient for parent and modified globin chains in chromatography. The peaks collected were treated with sinapinic acid and subjected to MALDI/MS. In the same investigation, the authors developed a new protocol with LC/MS/MS for the analysis of diethylcarbamoyl-cysteine in protein preparations which was extracted from the spinal cord. Recently, authors applied size exclusion chromatography and RP-HPLC followed by tandem MS for investigating the fate of PDTC in exposed rats (Valentine et al., 2006). The same research team reported a methodology for the determination of various DTCs based on the reaction of thio-carbonyl moieties with toluene-3,4-dithiol (TdT) resulting in toluenetriithiocarbonate (TTC; ultimately measured using RP-HPLC) (Johnson et al., 2003). Finally, authors recommended their methods being complementary to existing applications as their assay is capable of determining cumulative exposure of DTCs as various reaction products with proteins are detected.

6. Concluding remarks

A strong and rapid covalent bonding ability of these compounds toward inorganic species is challenging for the development of reliable, sensitive, selective and robust analytical measurements used for monitoring trace and ultra-trace levels of metals in different matrices of environmental importance. All the methods described in this review appear to be the latest trends in enviro-analytical science and environmental chemistry aimed at the extraction and analysis of the highest number of inorganic ions in a single-step with various DTCs. The main advantages of DTCs are as follows: (a) stability of metal-DTC complexes than any other organic analytical ligands (b) single step synthesis (c) convenient preparation in an ordinary laboratory (d) fairly soluble in water and useful for the development of solvent miniaturization protocols. DTC mode of action in biological system is not yet fully explored which may be the consequence of the versatile reactivity of the dithio-group comprising interactions.

7. Future Perspectives

Undoubtedly, the nature of DTCs (either aliphatic or aromatic) is crucial for considering the stability of the complexes to test their full extraction efficiency of inorganic ions in complex matrices. Efforts should be made to design new DTCs for the sensitive and selective studies in the field of analytical, bio and electro-analytical sciences due to their versatile applications.

New developments could be expected regarding the synthesis of novel and stable DTCs for the quantification and separation of inorganic ions. The applications of DTCs as a strong binding agent toward metal ions in materials science will be developed in the future, resulting in more facile and sensitive analytical protocols in the field of environmental chemistry.

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