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Review

The Liquid-Liquid Extraction of Toxic Metals (Cd, Hg and Pb) by Calixarenes

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Contents

Abstract

Toxic metals (Cd, Hg and Pb) are mostly present in the environment due to natural phenomenon and human activities as well. Exposure of these non-essential elements in the environment causes severe effects. They are known to cause problems in humans as well as in aquatic life. In this work, we demonstrate various studies regarding liquid-liquid extraction of selected ions with different functionalized calixarenes. This review article briefly discusses several molecular designs of calixarenes for divalent ion (Cd^{2+}, Hg^{2+} and Pb^{2+}) recognition; as well as the relationship between structure and selectivity of the macrocycles is elaborated. The article does not, however, attempt to cover all of the different approaches to these toxic metal ions extraction.

Keywords: Calixarenes, Liquid-Liquid Extraction, Ion Recognition, Toxic Metals, Supramolecular Chemistry.

Introduction

Toxicants are those species that are harmful to living organisms due to their detrimental effects for biological processes. The organisms that are affected by the poison/toxic material depend upon the type and amount of toxicants. In case of human beings the degree of

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harm done by a toxicant also depends strongly upon its exposure to skin, inhalation, or through ingestion. The environmental contaminants such as Pb^{2+}, Cd^{2+} and Hg^{2+} have been exploited by a number of research groups [1-5]. These targeted metal ions are mostly present in the environment due to fossil fuel combustion, paint, battery and fertilizer industries as well as oil refineries, smelting plants and wastewater [6, 7].

Exposure to these elements causes severe effects on humans in all over the world [8-10]. These highly toxic metals are known to cause health problems such as brain damage [11-13], nephropathy [14-16], sluggishness [17, 18], hyperirritability [19], restlessness [20], infertility [21] and a number of diseases in early aged children [13, 22]. The removal of these trace heavy metal ions are tested by number of methods i.e. membrane filtration, osmosis, precipitation, oxidation/reduction, microbiological activity, ion exchange and extraction etc [23-25].

In recent years, much attention has been paid to chemical separation techniques and the design and synthesis of new extraction reagents for ions and molecules. This attention results in part from environmental concerns, efforts to save energy and recycling at the industrial level. In this respect, the supramolecular chemistry has provided a much better solution to the search for molecular structures that can serve as building blocks for the production of sophisticated molecules by anchoring functional groups oriented in such away that they delineate a suitable binding site. This was achieved with the development of macrocyclic molecules such as synthetic crown ethers, cryptands, spherands [26], natural cyclodextrins [27,28] and calixarenes [29,30].

Calix[n]arene-based macrocycles have attracted much attention because of their unique molecular structure and simple single-pot synthesis in supramolecular chemistry [26,29,31,32]. These molecules are generally *ortho*-substituted calix[n]arenes capable of alkali, alkaline earth and heavy metal ion recognition [33-35]. It has been reported that ester function derived from calixarenes possess remarkable tendency to bind IA group cations with unique size-selectivity [36-38] as well as with ions and molecules of biological and environmental relevance [23]. Recently, a number of studies have been explored on the subject of the liquid-liquid, extraction or complexation of targeted ions [39-44]. In the present review, we describe the liquid-liquid extraction of selected metal ions (i.e. Pb^{2+}, Cd^{2+} and Hg^{2+}) by using calix[n]arenes.

Principles for Choosing an Extractant

Two strategies can be used in choosing extractants, these are steric and electrostatic stabilization. Steric stabilization is usually achieved with a non-ionic extractant or polymer, and electrostatic stabilization with an ionic extractant or polymer. An extractant with a high hydrophile-lipophile balance (HLB) is used for aqueous media, and one with a low HLB for non-polar organic liquids. Metal ions are charged, and this property allows for electrostatic extraction to be effective. The metals Cd, Hg and Pb are present as divalent cations and an anionic extractant will have a strong electrostatic attraction with these cations. Another factor is the nature of the binding site of the extractant, since non-polarizable (hard) anions preferentially bind to non-polarizable (hard) cations, and polarizable (soft) anions to polarizable (soft) cations. The divalent metal cations of Cd, Hg and Pb are soft. An additional factor that needs to be considered when choosing an extractant is the reversibility of the system. Ideally the extractant should be highly selective for the targeted cation, but it should readily release the metal ion under changed conditions and thus be repeatably used.

The amount of extractant used should be adequate to give monolayer coverage. This is preferred because tail group of the extractant should be compatible with the extracting solvent, and a bilayer with a tail-to-tail attraction leads to the metal compatible hydrophilic head group being at the outer periphery rather than the hydrophobic tail group.

Choice of Extractant

In selecting an extractant the choice of functionality to act as an anchoring head group is important. The binding of the coordinating group to the metal ion must be stronger than its hydration. The use of oligomers such as calixarenes having multiple absorption anchoring groups also need to be considered; as this allows for additivity of binding sites to be achieved.

The attention must also be givin to the solubility of the tail of the complexant in solvent because it acts as a boundary between the metal and the aqueous layer. An extractant is most effective if the complexant preferentially associates with the metal ion, and the organic moieties with the solvent into which the metal ion is being extracted. When the complexant binds the metal ion, a monolayer usually achieves the maximum extractability that can be attained for that system. The use of less than a monolayer leaves open sites on the metal ion that can be hydrated and if more than a monolayer is absorbed then the second molecular layer will likely be orientated in the opposite direction from the first layer, thereby reducing the compatibility of the copper nanoparticle with the vehicle (Figure 1).

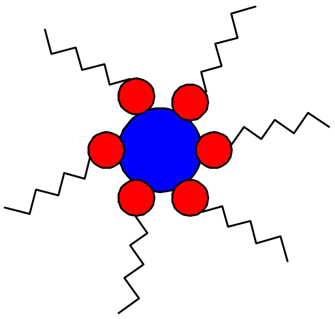


Figure 1. **Representation of a layer of extractant with a metal ion. The coordinating groups of the extractant are in red and the metal ion in blue.**

The quantity of complexant m_d required disperse a given mass of metal ion m_c in a given volume of liquid V can be calculated from the surface area of the metal ion (A_c), the molar mass of the surfactant M_d and the molar area coverage of the dispersant A_d by equation 1:

$$M_d = \frac{m_d m_c A_c}{A_d} \quad (1)$$

Multiple head groups in polymeric dispersants can be advantageous because they can have multiple anchoring sites on the copper nanoparticle (Figure 2). This may lead to increased attraction between the metal ion and the complexant and since the later occupies multiple sites on the metal ion, lower concentrations can be used.

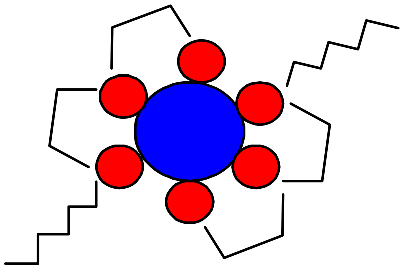


Figure 2. **Representation of a layer of a polymeric extractant onto a metal ion. The coordinating groups of the extractant are in red and the metal ion in blue.**

Design of Extractant - Effect of Chain Length

The compounds used as extractants have long-chain alkyl $(CH_2)_n$ or ethoxy groups. These groups are linked together by either carbon-carbon single bonds. These single bonds allow for 3-dimensional vibrations and rotations, which gives them a high degree of flexibility. An explanation for the need to use dispersants that have flexible long-chain tail groups is that through combinations of vibrations and rotations these groups occupy more space than do short-chain tail groups and that this space is not accessible for a second copper nanoparticle to approach. In order to quantify this excluded volume effect we have carried out calculations on propane (C_3H_8), hexane (C_6H_{12}) and decane ($C_{10}H_{22}$). These three alkyl chain compounds are shown structurally in Figure 3. All the structures are linear and in each case the C-C-C angle will be close to 109°.28 the tetrahedral angle.

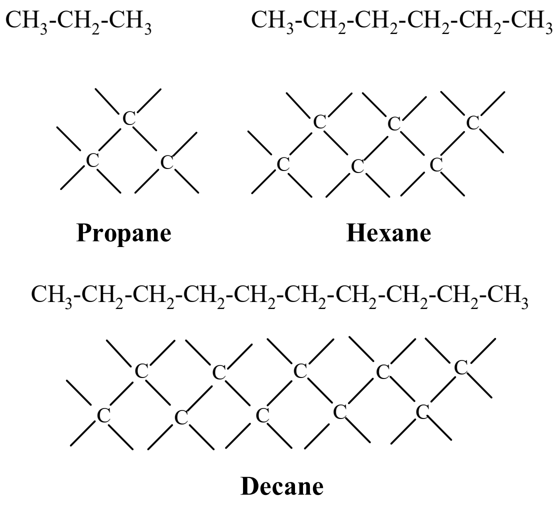


Figure 3. **Linear Structures of propane, hexane and decane.**

The computational results are collected in Table 1.

Table 1. **Computational Data on Alkanes.**

Alkane	Length (A°)*	Excluded Volume $(A^{o\,3})^{\Psi}$	Van der Waals Volume $(A^{o\,3})$ж	Molecular Volume $(A^{o\,3})$☼	Molecular Surface $(A^{o2})^{\Phi}$
Propane	4.1	36.1	56.2	77.4	103.5
Hexane	6.7	157.5	81.9	106.3	146.0
Decane	12.0	904.8	132.4	176.0	231.7

* *Length (Angstroms A°)* – end to end (heavy atoms) distance in extended conformation. For propane this is the C_1 to C_3 distance; for hexane this is the C_1 to C_6 distance and for decane this is the C_1 to C_{10} distance.

$^{\Psi}$ *Excluded" Volume (A^{o3})* – volume based on length (d) as $1/6.\pi d^3$. The excluded volume for a given object is defined as that volume surrounding and including a given object, which is excluded to another object. The excluded volume is always defined for a pair of objects.

ж *Van der Waals Volume (A^{o^3}) – volume based on van der Waals radii.* Two atoms that are not covalently bound cannot approach each other closer than a certain minimal distance. The closest proximity depends upon the type of atoms involved. This phenomenon can be described by assigning a value called a van der Waals radius to each atom type in such a way that the sum of these quantities for a given atom pair is equal to their closest possible distance. The van der Waals radii here are the "touching points" of the hydrogen atoms in the alkyl or ethoxy chains. The van der Waals volume is the volume of a molecule in which every heavy atom is represented by its van der Waals radii molecular surface, which is the surface formed by a sphere (typically 1.4 °A radii) rolled over the molecule in van der Waals representation.

۞ *Molecular Volume (A^{o^3})*–volume occluded by rolling a spherical probe of 1.4°A. This is the volume occupied by one mole of the compound, which is numerically equal to the molecular weight divided by the density. The molecular volume is the volume of the above excluded volume, or the volume that cannot be occupied due to the non-zero size of a molecule.

Φ *Molecular Surface (A^{o^2})*–area occluded by rolling a spherical probe of 1.4 °A. This is the equivalent of obtaining the surface area.

However, these data (Table 1) show that because of the distance cubed dependence on the distance, there is a large increase in the "excluded" volume as the length of the chain increases. This "excluded" volume represents the space "occupied" by the flexible alkyl (or ethoxy) chain and it is space that cannot be occupied by a second copper nanoparticle. The larger this "excluded" volume the more effective is the dispersant at keeping the copper nanoparticles separated. A second aspect of this "excluded" volume is that large values allow for low concentrations of the compound to be effective in providing a high level of coverage of the nanoparticle and therefore a high degree of effectiveness as a dispersant.

Pearson's Hard Soft [Lewis] Acid Base (HSAB) Principle

In the 1960's Pearson explained the differential complexation behavior of metals and ligands (dispersants) in terms of electron-pair donating Lewis bases and electron-pair accepting Lewis acids [45-48]. Association between them is shown in equation 2.

$$\text{Lewis acid} + \text{Lewis base} \rightarrow \text{Lewis acid/Lewis base complex} \quad (2)$$

Pearson classified Lewis acids and Lewis bases as being hard, borderline, or soft. According to Pearson's hard soft acid base (HSAB) principle:

Hard acids prefer to bind to hard bases and soft acids prefer to bind to soft bases.

Pearson classified a very wide range of atoms, ions, molecules and molecular ions as hard, borderline or soft Lewis acids or Lewis bases, moving the analysis from traditional metal/ligand inorganic chemistry into the realm of organic chemistry. Tables 2 and 3 show short lists classifying Lewis acids and basses into these three categories.

Table 2. **Classification of Lewis Acids.**

Hard	Soft
H^+, Na^+, Ca^{2+}, Fe^{2+}	Hg^{2+}, Cd^{2+}, Pb^{2+}

The important observations from Table 2 is that mercury, cadmium and lead are soft, and that other metals that are likely to be found in the environment are hard.

Table 3. **Classification of Lewis Bases.**

Hard	Soft	Borderline
H_2O, OH^-, Cl^-, RCO_2H (acids)	R_2S (sulfides), $RCH=CH_2$	$C_6H_5NH_2$ (aniline)
ROH (alcohols), R_2O (ethers),	(alkenes), C_6H_6 (benzene), CO	C_6H_5N (pyridine)
RNH_2 (amines)		

The classification in the original work was mostly based on equilibrium constants for reaction of two Lewis bases competing for a Lewis acid.

Klopman's FMO Analysis

In 1968, Klopman [49] attempted to quantify Pearson's HSAB principle using Frontier Molecular Orbital (FMO) theory. Klopman proposed that:

Hard [Lewis] acids bind to hard [Lewis] bases to give charge-controlled (ionic) complexes. Such interactions are dominated by the +/– charges on the Lewis acid and Lewis base species.

and

Soft [Lewis] acids bind to soft [Lewis] bases to give FMO-controlled (covalent) complexes. These interactions are dominated by the energies of the participating frontier molecular orbitals (FMO), the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO).

Using this analysis, the contributing aspects of charge-controlled and FMO-controlled Lewis acid/base complexation are separated and quantified.

Combining Pearson's and Klopman's Ideas leads to the concepts that:

Hard Lewis acids have or are:

- Atomic centers of small ionic radius
- High positive charge
- Species do not contain electron pairs in their alence shells
- Low electron affinity
- Likely to be strongly solvated
- High energy LUMO's

Soft Lewis acids have or are:

- Large radius
- Low or partial positive charge
- Electron pairs in their valence shells
- Easy to polarize and oxidize
- Low energy LUMO's, but large magnitude LUMO coefficients

Hard Lewis bases have or are:

- Small, highly solvated, electronegative atomic centres: 3.0-4.0
- Species that are weakly polarisable
- Difficult to oxidize
- High energy HOMO's

Soft Lewis bases have or are:

- Large atoms of intermediate electronegativity in the range of 2.5-3.0.
- Easy to polarize and oxidize
- Low energy HOMO's but large magnitude HOMO coefficients.

Borderline species have intermediate properties

There is a qualifier by Klopman saying that it is not necessary for species to possess all properties. HSAB is not a theory, since it does not explain variations in the strength of chemical bonds. The word 'prefer' in the HSAB Principle implies a rather modest effect, and HSAB should be used as a guide to choosing Lewis acid-Lewis base pairs and not as a rigid rule.

Chemical Hardness

In 1983 Pearson and Parr [50] extended the qualitative HSAB theory with a quantitative definition of chemical hardness. When the electronegativity, as defined in the Mullikan scale, is the first derivative in a plot of energy versus the amount of electrons with fixed nuclear charge in an atom or molecule, then the chemical hardness is the second derivative. Hardness and electronegativity are therefore related, and in this sense hardness is a measure of resistance to deformation or change. A value of zero in Table 4 denotes maximum softness.

Table 4. **Chemical Hardness.**

Na^+	21.1	H_2O	7.0
Ca^{2+}	19.7	NH_3	6.9
Fe^{3+}	13.1	H_2S	5.3
Cd^{2+}	10.3	CN^-	5.3
Pb^{2+}	8.5	Cl^-	4.7
Hg^{2+}	7.7	SH^-	4.1

Hydration Energies

A factor that must be taken into consideration when is the hydration of the metal ions since transfer from an aqueous medium into a non-aqueous medium involves loss of hydration. Since the hydration energy of a metal ion is less that the solvation energy, this difference must be overcome by the complexation. The respective hydration free energies for the divalent ions of Cd, Hg and Pb in kJ mol^{-1} are –1755, -1760 and –1425 [51]. Comparative heats of hydration are collected in Table 5.

Table 5. **Hydration Energies.**

Ion	Hydration free energy ΔG in kJ/mol	Ion	Hydration free energy ΔG in kJ/mol
Cd^{2+}	-1755	H^+	-1050
Hg^{2+}	-1760	Na^+	-365
Pb^{2+}	-1425	Ca^{2+}	-1505

The heats of hydration of Cd^{2+}, Hg^{2+} and Pb^{2+} show that the values for Cd^{2+} and Hg^{2+} are essentially the same, but the value for Pb^{2+} is significantly smaller. As a result the hydration energies can be ignored when comparing the extraction of Cd^{2+} and Hg^{2+} from aqueous solution, but the lower free energy of hydration of Pb^{2+} means that from thermodynamics it will be preferentially extracted, and this must be taken into consideration when the results from a synthetic strategy are considered. By comparison the hydration free energies for H^+, Ca^{2+} and Na^+ are included in Table 5. These data show that all three of these ions have lower hydration free energies than does either Cd^{2+} or Hg^{2+}, which means that they will only be displaced if the binding site preferably complexes with Cd^{2+} or Hg^{2+}.

Metal Ion Extraction

The extraction data for 3 are analyzed by a classical slope analysis method. Assuming the extraction of an ion-pair $[M^{n+}, A^{n-}]$ by the anion receptor [L] according to the following equilibrium in equation 3.

$$m(L)_{org} + nA^{n-}_{aq} + nM^{n+} \rightleftharpoons ((L)_{m}, A^{n-}_{n}, M^{n+}_{n})_{org} \qquad (3)$$

The extraction constant K_{ex} is then defined by equation 4.

$$K_{ex} = \frac{[((L)_{m}, A^{n-}_{n}, M^{n+}_{n})]_{org}}{[M^{n+}]^{n}\,[A^{n-}]^{n}_{aq}\,[L]^{m}_{org}} \qquad (4)$$

Equation 4 can be rewritten as equation 5.

$$\log D_A = \log K_{ex} + m \log [L]_{org} \qquad (5)$$

where the distribution ratio D_A is defined as ratio of the concentrations of an ion-pair $[M^{n+}, A^{n-}]$ in the two phases (equation 6)

$$D_A = [M^{n+}, A^{n-}]_{org} / [M^{n+}, A^{n-}]_{aq} \qquad (6)$$

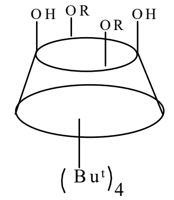
Consequently a plot of log D_A vs. log [L] leads to a straight line whose slope allows the stoichiometry of the extracted species to be determined. phase into dichloromethane at 25°C.

Calixarenes as Extractants

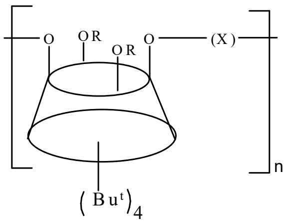
The calix[4]arene platform has proven to be an important building block in supramolecular chemistry [26, 29, 52]. In particular, cation complexing ligands containing calix[4]arenes have been used to obtain more selective metal ion receptors. These molecules are generally O-substituted calix[4]arenes capable of alkali, alkaline earth, and heavy metal ion recognition [33]. Herein the present approach highlights a series of examples for the liquid-liquid extraction of selected toxic metals (i.e. Pb^{2+}, Cd^{2+} and Hg^{2+}) with modified calixarenes.

Calixarenes with different chelating groups

It has been explored earlier that a calixarene with diester and/or dinitrile functionalities (1 and 2) at its *lower rim* (narrow rim) can selectively extracts lead/mercury from an aqueous to the organic phase in liquid-liquid extraction processes [53].



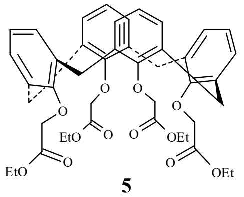
1 R = $CH_2COOC_2H_5$
2 R = CH_2CN



3 R = $CH_2COOC_2H_5$
4 R = CH_2CN

In order to see the extraction properties of more than one calix[4]arene units together the telomers (**3** and **4**) of compounds **1** and **2** were prepared [53]. The extraction results of telomer **3** are more or less similar to its monomer **1** showing preference toward lead; while **4** shows a significant increase in extraction efficiency as compared to **2** (Table 6).

Recently, our group has explored Pb^{2+} selective extraction behavior of ester derivatives of calix[n]arenes [54]. It has been observed that the hexaester derivative of calix[6]arene (**6**) is more selective and efficient ionophore as compared to tetraester derivative of calix[4]arene (**5**) for the extraction of Pb^{2+} from aqueous to the organic phase. The tetraester calix[4]arene is an efficient extracting agent and prefers Na^+ over lead [36-38,55,56]; may be due to the nature as well as compatibility between the ionic radii of Na^+ and cavity size of ligand **5.**



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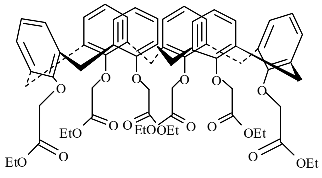

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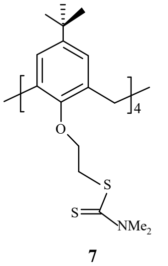
Solvent extraction with chelate and macrocyclic ligands for soft metal ions requires rapid selective complexation, high stability against hydrolysis, minimal affinity for alkali and alkaline earth metal ions, high metal extractant binding strength and reversible complexation allowing for metal recovery [57]. Since, heavy metals form strong bonds with sulfur, favored functionalities are hydrogen sulfides (HS^-), thiolates (RS^-), thioethers (R-S-R'), dithiocarbamates ($R_2NCS_2^-$) and substituted ureas (RNHC(S)NHR') [58].



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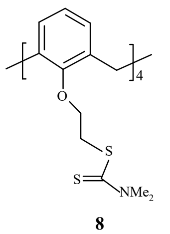

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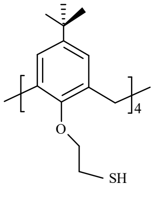

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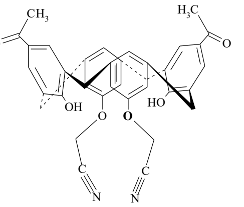
However, an early attempt was made by Roundhill and coworkers [59] to extract the toxic metals with calix[4]arenes modified with sulfur containing functionalities. Compounds **7**-**9** were found to be effective extractants for Hg^{2+} (Table 6).

Table 6. **Complexation of Hg^{2+}, Pb^{2+} and Cd^{2+} with Substituted Calix[4]arenes.**

Compounds	*% Extraction*			*References*
	Hg^{2+}	Pb^{2+}	Cd^{2+}	
1	33.3	82.0	23.6	53
2	40.0	6.6	2.0	53
3	27.9	76.2	55.9	53
4	63.9	55.3	44.8	53
5	---	78.5	---	54
6	---	94.9	---	54
7	81	<3	<4	59
8	85	11	9	59
9	86	<6	<3	59
10	71.58	13.9	<1.0	60
11	82.0	58.0	16.0	60



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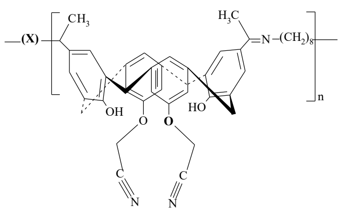
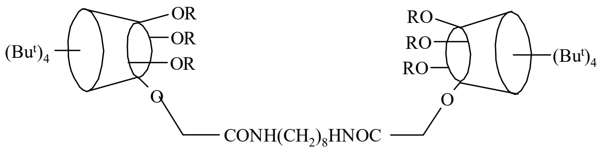


11 X = N=

Memon and Yilmaz [60] have noticed that the polymerizable groups and their attachment either at narrow or wide rim have remarkable affect on the extraction properties of the modified calixarenes. Compound **10** with dinitrile anchoring groups shows good selectivity toward Hg^{2+}, while its oligomer shows remarkable enhancement in the extraction of Pb^{2+} and Hg^{2+} (Table 6).

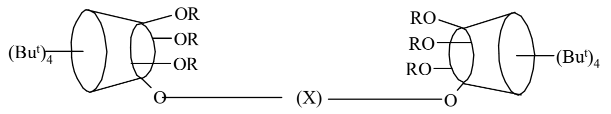
Biscalixarenes

In the past decades several double (or multiple) calixarenes have been synthesized and titled as biscalixarenes [61]. Moreover, biscalixarene derivatives **12-22** were synthesized to observe the extraction properties of two joint calixarene units. The extraction results of **12** and **13** show main difference in selectivity towards the toxic metals. Compound **12** extracts Hg^{2+} in high proportion while the compound **13** shows high affinity for both $Hg^{2+}$and Cd^{2+} ions. The extraction results (Table 7) suggest that the ketonic binding groups are efficient in phase transfer reactions.



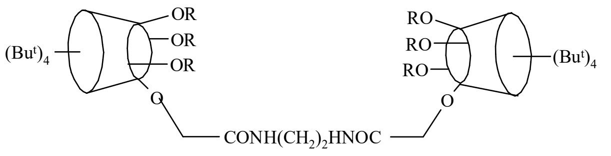
12 R = $CH_2COOC_2H_5$
13 R = CH_2COCH_3

In earlier studies we have focused on biscalix[4]arene with ester and keto groups appended at *lower rim* [61], while in compounds (**14-17**) possessing soft base (C≡N group) on their *lower rims* show stronger affinity for softer metal cation i.e. Hg^{2+} [62]. The extraction efficiency of compounds **14-17** are compiled in Table 7, which shows remarkable Hg^{2+} selectivity.



	(X)	**R**
14	CH_2COCH_2	R = CH_2 CN
15	$CH_2CH_2OCH_2CH_2$	R = CH_2 CN
16	$CH_2CONH(CH_2)_2$ $NHCOCH_2$	R = CH_2 CN
17	CH_2CO $NH(CH_2)_8$ $NHCOCH_2$	R = CH_2 CN

Memon *et al.* [63] reported that the compounds **18** and **19** with different bridge have got different extraction behavior as compared to **12** and **13**.

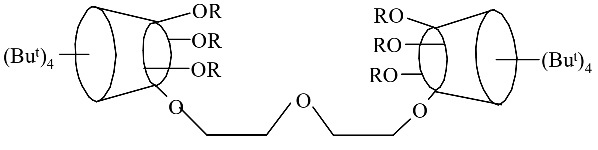


18 R = CH_2COCH_3
19 R = $CH_2COOC_2H_5$

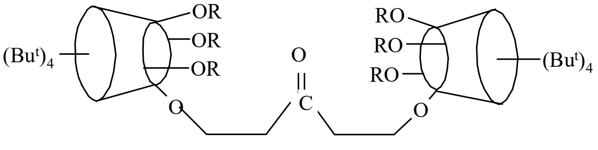
However, it has been noticed that biscalix[4]arenes are effective extractant for both Hg^{2+} and Cd^{2+}. The compound **18** shows selectivity for Hg^{2+}, while the compound **19** is an effective extractant but not selective (Table 7).

The synthesis of the compounds **20**-**22** were reported in our previous studies [64]. A preliminary evolution of binding efficiencies of these compounds was carried out by solvent extraction. The results are summarized in Table 7.

From the extraction results it is revealed that **20** and **21** extract almost all the metal ions used in the extraction studies, whereas compound **22** was particularly selective for Hg^{2+}. From these observations it has been concluded that the size of the ligand, nature and ionic diameter of the metal ions, the conformation of calixarene and the effectiveness and aggregation of functional groups are also important factors in these studies. These results may reflect the "Hard and Soft Acids and Basis" concept introduced by Pearson [65] and cation-π interactions have also been exhibited by the organized groups, which favor the effective extraction with the more polarizable transition metal ion especially Hg^{2+} which is known as soft metal cation.



20 R = $CH_2COOC_2H_5$



21 R = $CH_2COOC_2H_5$
22 R = CH_2COCH_3

Table 7. **Extraction of Hg^{2+} and Cd^{2+} with Biscalixarenes.**

Compounds	*% Extraction*		*References*
	Hg^{2+}	Cd^{2+}	
7	94.0	49.5	61
8	90.2	83.0	61
9	78.1	8.7	62
10	73.2	3.5	62
11	53.0	3.0	62
12	72.0	4.8	62
13	65.6	9.6	63
14	68.4	13.1	63
15	83.6	37.0	64
16	60.6	19.5	64
17	77.2	4.5	64

Bifunctional calixarenes with crown moieties

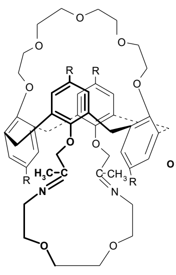
Over last decades researchers have tryed to put together the special properties of crowns and calixarenes in one molecule hence, more elaborate structures are beginning to emerge. Single bridged calixcrowns with poly(oxyethylene) linkage in 1,2 and 1,3 position, calixspherands, double or triple calixarenes with various connecting chains or conformationally constrained spacers have been reported [66].

Generally crown ethers are regarded as hard ionophores and have ability for the selective extraction of alkali metal cations. On the other hand Schiff bases have shown a potential ability of forming stable complexes with soft metal cations, such as Hg^{2+}, Cd^{2+}, Pb^{2+} etc. Compound **23**, which extracts these metal ions efficiently (Table 8), but lakes selectivity.

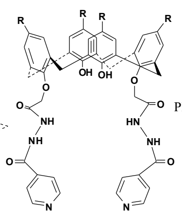
Table 8. **Exraction of Hg^{2+}, Pb^{2+} and Cd^{2+} with Bifunctional Calixarenes.**

Compounds	*% Extraction*			*Reference*
	Hg^{2+}	Pb^{2+}	Cd^{2+}	
23	99.0	95.2	95.2	66
24	96.9	---	64.7	67
25	83.3	82.3	47.3	68

The bifunctional calix[4]arene-based ionophores having various binding sites were synthesized to estimate their binding ability toward cations and anions through phase transfer systems. The extraction results (Table 8) show that compound **24** is effective not only for transition metal ions but also for dichromate anions [67]. Chiral calix[4](azoxa)crown-7 (**25**) in the *cone* conformation has been employed for the extraction of toxic metal ions [68]; showing a dramatic change in the separation science. Compound **25** possesses dual nature i.e. it may act as a receptor for ions as well as neutral molecules (enantiomers).



23 R = *tert*-butyl



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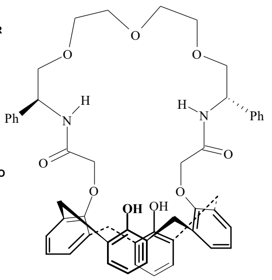
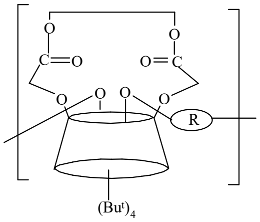


25

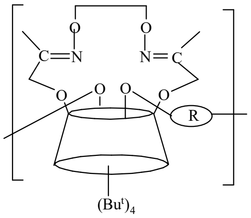
It has been evaluated that **25** is a good extractant for the transition metals (Table. 8), that may be due to size, arrangement of functional groups and/or nature of the targeted ions.

Telomers with calix-crowns

Recently, in order to see the extraction properties of more than one calix[4]arene units together, different calix[4]arene based telomers were synthesized and their extraction properties were evaluated (Table 9). Yilmaz and coworkers have concisely reported that this strategy is well and practicable for two-phase extraction processes. The ionophores **26** and **27** can effectively extract cadmium/mercury from an aqueous to the organic phase in liquid-liquid extraction processes [69].

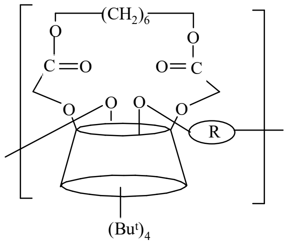


26 $R = CH_2(CH_2OCH_2)_2CH_2$



27 $R = CH_2(CH_2OCH_2)_2CH_2$

In another work, the synthesis and exploration of metal extraction efficiency of Schiff bases of calixarene unit and their telomers (**28** and **29**) has been evaluated [70]. The extraction ability of **28** and **29** toward the divalent transition metal ions (i.e. Hg, Cd and Pb) was found good but with no remarkable selectivity for these metal ions.



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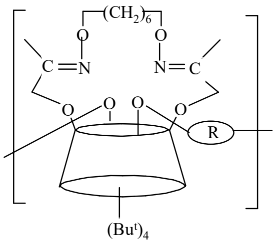
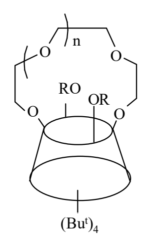
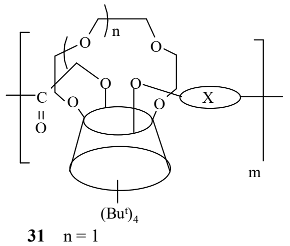


29 $R = CH_2(CH_2OCH_2)_2CH_2$

Besides this, calix[4]crowns and their telomers (**30-32**) were also used for the extraction purposes of non-essional toxic metal ions.



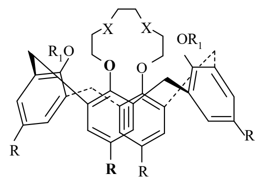
n = 2
30 $R = CH_2COOC_2H_5$



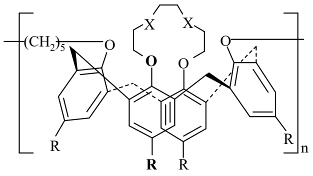
31 n = 1
32 n = 2
X = $CH_2CONH(CH_2)NH$

Memon *et al.* [71] have reported interesting extraction results of compounds **30-32**. The compound **30** was observed as a selective ionophore for mercury and lead only; while in the case of telomers (**31** and **32**) no specificity has been noticed except a remarkable increase in their extraction efficiency toward all metal ions used in the experiments.

A novel approach towards the synthesis of oligomeric calix[4]arene-thiacrowns as ionophores for the transition metals has been carried out by Uysal *et al.* [72].



33 R = *tert*-butyl ; R_1 = H, X= S



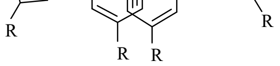
34 R = *tert*-butyl ; X= S

The liquid-liquid extractions have clarified that the monomer and oligomer both ionophores possess similar extraction behavior.

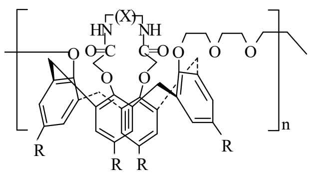
Table 9. **Liquid-Liquid Extraction (E%) of Hg^{2+}, Pb^{2+} and Cd^{2+} Calix[4]arene Based Telomers.**

Compounds	*% Extraction*			*References*
	Hg^{2+}	Pb^{2+}	Cd^{2+}	
26	94.8	---	75.8	69
27	90.0	---	80.6	69
28	95.0	69.0	60.2	70
29	77.6	59.2	74.6	79
30	90.0	95.0	44.4	71
31	91.8	92.7	66.0	71
32	93.0	94.3	99.6	71
33	97.6	12.8	6.2	72
34	94.0	35.5	25.1	72
35	98.9	97.1	94.8	73
36	92.2	91.5	88.2	73
37	96.7	97.1	96.6	73
38	98.2	98.1	95.9	73
39	97.8	96.4	97.7	73
40	98.9	97.8	96.3	73

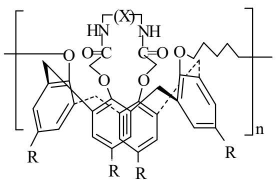
The synthesis and binding properties of calix(aza)crown monomers and their oligomers (**35-40**) is a new innovation [73]. The phase transfer studies reveal the importance of azocrown moieties in the calixarene frame work.



35 R = *tert*-butyl ; R_1=H ; X= $(CH_2)_6$
36 R = *tert*-butyl ; R_1=H ; X= $(CH_2OCH_2)_2$



37 R= *tert*-butyl ; X= $(CH_2)_6$
38 R= *tert*-butyl ; X= $(CH_2OCH_2)_2CH_2$

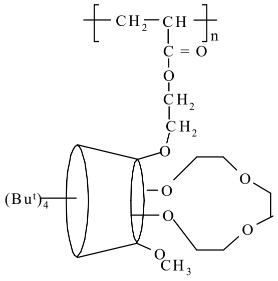


39 R= *tert*-butyl ; X= $(CH_2)_6$
40 R= *tert*-butyl ; X= $(CH_2OCH_2)_2CH_2$

All the monomers and oligomers of calix(aza)crowns (**35-40**) show good efficiency (more than 90%) for the extraction of transition metal ions (Table 9).

Calixarenes based polymers

Subsequently, efforts have been made to attach modified calixarenes in a polymeric backbone. A fascinating examples of such systems is the polymers (**41** and **42**) containing pedant calix[4]crown-4 [74]. Both polymers are efficient for the extraction of mercury/cadmium ions (Table 10).



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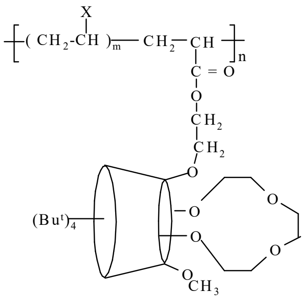
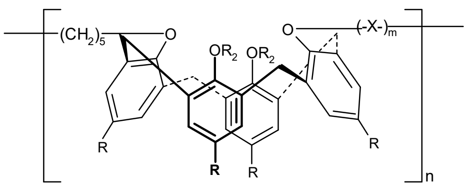
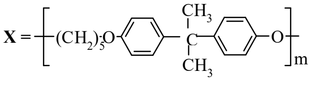


42 X = Phenyl

The copolymers (**43** and **44**) contaning calix[4]arene unit with nitrile functionalities at *lower rim* have achieved the goal of efficient removal of transition metal ions [75].



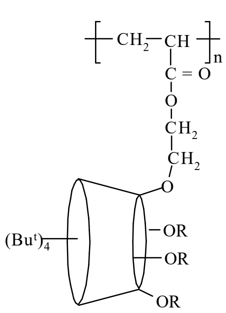
43 R = *tert*-butyl ; $R_2 = CH_2CN$
44 R= H ; $R_2 = CH_2CN$



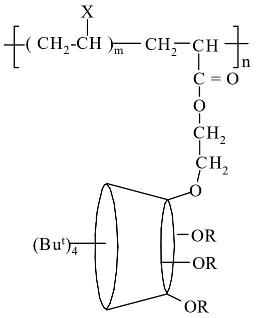
$X = \left[(CH_2)_5O-C_6H_4-C(CH_3)_2-C_6H_4-O \right]_m$

These polymers (**43** and **44**) have lost the selective nature of their precursors toward Hg^{2+} exploring the importance of selecting the polymeric backbone for the support to these macrocycles while designing such systems.

The development of Hg^{2+} selective polymers was achieved by the synthesis of **45** and **46**, showing an excellent strategy of the research group in this field [76]. Since, the alkylnitrile derivatives of calixarenes have proved to be very selective for Hg^{2+} [53, 61].

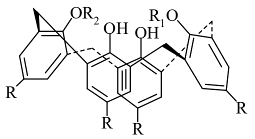


45 R = CH2CN

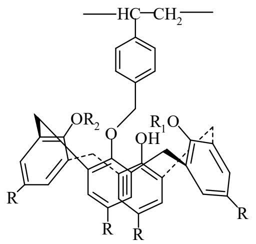


46 R = CH2CN, X = Ph

Therefore in connection with that study, the work presented by Gungor *et al.* [77] were focused on the investigation of extraction behavior of benzonitrile derivatives of calix[4]arenes and their polymeric analogues (**47-52**).



47 R = *tert*-Butyl
$R_1, R_2 = CH_2CN$
49 R = *tert*-Butyl
$R_1 = H, R_2 =$ CN CH_2
51 R = *tert*-Butyl
$R_1, R_2 =$ CN CH_2



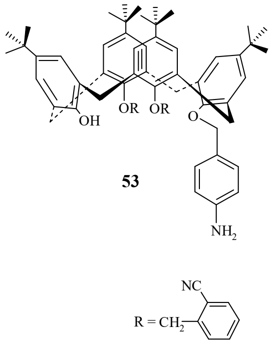
48 R = *tert*-Butyl
$R_1, R_2 = CH_2CN$
50 R = *tert*-Butyl
$R_1 = H, R_2 =$ CN CH_2
52 R = *tert*-Butyl
$R_1, R_2 =$ CN CH_2

Most surprising results have been found in case of aryl nitrile derivatives of calix[4]arenes **49** and **51**; that appeared as Hg^{2+} selective like their precedor **47**. In addition to this, compounds **49** and **51** also show a little affinity toward Cd^{2+}, which imparts a characterstic difference between benzonitrile and alkylnitrile groups. To compare the extraction characteristics of their polymeric analogues **48**, **50** and **52** with the monomers **47**, **49** and **51**, comparable extractions have been performed. It is observed that **48**, **50** and **52** are not selective, but show more or less a similar extraction behavior toward all metal cations.

Table 10. **Extraction of Hg^{2+}, Pb^{2+} and Cd^{2+} with Calixarene Based Polymers.**

Compounds	*% Extraction*			*References*
	Hg^{2+}	**Pb^{2+}**	**Cd^{2+}**	
41	96.6	---	80.0	74
42	90.3	---	42.9	74
43	94.5	93.2	90.6	75
44	92.2	91.0	86.0	75
45	56.9	---	7.1	76
46	34.0	---	<1.0	76
47	40.0	6.6	2.0	77
48	89.3	78.0	57.45	77
49	38.0	1.0	10.6	77
50	90.0	65.3	45.6	77
51	41.8	1.0	8.1	77
52	32.0	43.4	34.4	77
53	80.0	76.0	52	78
54	95.0	86.0	86.0	78
55	98	13	6	79
56	84.9	6.6	<1.0	79
57	59.1	60.0	<1.0	79

In connection with this work, a similar type of study was carried out by Tabakci *et al.* [78] with benzonitrile functionalities. From the extraction data given Table 10, it is apparent that **53** show good extraction behavior toward all metal cations because of the basic amino group. On comparison of the extraction characteristics of calix[4]arene derivative to its polymeric ionophore (**53** and **54**), comparable extractions have been performed. The copolymer **54** shows significant extraction of transition metal cations, with the relative order Hg^{2+} >> Cd^{2+}=Pb^{2+} being observed.



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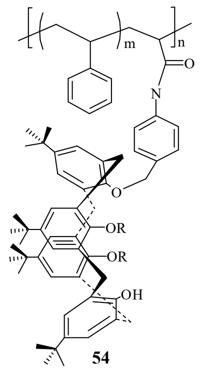

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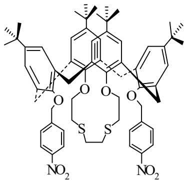
Generally, soft heavy metals form strong bonds with sulfur, therefore favored functionalities are thiolates, thioether, dithiocarbamates and substituted thioureas [57-59, 72, 79]. An extension of our previous studies [72], calix[4]arene-thiacrown derivative **33** has been modified and copolymerized successively. Among the monomers only **55** has proved to be selective ionophore for Hg $^{2+}$ but **56** was found as a good extractant for both Hg^{2+}, and Pb^{2+}. The copolymer **57** has entirely different approach toward these metal ions in two-phase extraction systems. It shows almost equal preference toward Hg^{2+}, Pb^{2+} and Cd^{2+} [79].



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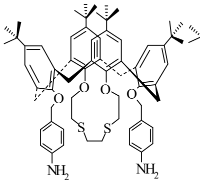

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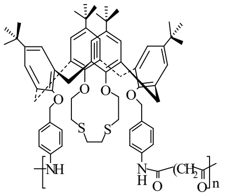

57

In short, it is apparent that ester, nitrile and thioether functionalities containing calixarenes are effective extractants for Hg^{2+}, Pb^{2+} and Cd^{2+} due to the soft nature of these metal ions as compared to competing cations [80]. The effectiveness in transferring these cations by calixarene based ionophores indicates that the binding ability toward metal cations belong to soft acids in Pearson's classification [81,82]. This is consistent with the HSAB principle because these groups are more polarizable than phenolic oxygens.

Conclusion

Significant achievements have been made over the years in developing hosts for metal ions extraction. In order to understand the liquid-liquid extraction phenomenon of calixarene based ionophores, two steps need to be considered. Firstly, designing of calix[4]arene framework with sophisticated anchoring groups in a particular conformation. Secondly, the nature, size as well as the geometry of guest specie (ions or neutral molecules) are very important The difference between the isomeric calixarenes less apparent, but it dose appear that there may be preference for one isomer being a better extractant for transfering guest species i.e. ions/molecules. Interstingly, a perticular isomer is the one that has effective functionalies in a potentially chelating geometry with hydophobic or hydrophilic groups projecting into the *lower/upper rim* binding cavity.

Acknowledgements

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