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Coordination of Al(III) in the environment and in biological systems

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Contents

Abstract

The tendencies of donor atoms and donor groups to form stable Al(III) complexes are described, and ligands with very basic oxygen donors are compared with chelating ligands having less basic donor atoms. Deprotonated forms of aliphatic α-hydroxy acids, and aromatic hydroxyl or polyhydroxy ligands, have the highest affinities for Al(III). Critical (selected) stability constants, and related protonation and deprotonation constants are given for Al(III) complexes of oxygen donor ligands and aminocarboxylates, including ligands that undergo deprotonation in the presence of metal ions to produce very basic donor oxygens. The hydrolysis of Al(III) leaves a small but appreciable concentration of Al(OH)$_3$ in solution, which may account for transport of Al(III) ion the environment. The presence of fluoride ion causes increased solubility and transport of Al(III). Desferriferrioxamine-B forms a very stable complex of Al(III) and the ligand has been suggested for the treatment of aluminum overload. Also, 1,2-dimethyl-3-hydroxy-4-pyridinone (DMHP, L1) forms a very stable aluminum(III) chelate and may also find application for the removal of Al(III) from the body.

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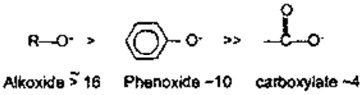
1. Coordination chemistry of Al(III)

The aquo aluminum ion is the "hardest" of the trivalent metal ions, with an effective ionic radius of 0.50 Å, which is smaller than other commonly encountered trivalent metal ions. Trivalent boron has an ionic radius of 0.23 Å, but does not form positive ions in aqueous solution. The "acidity" of an aquo metal ion is measured by its affinity for the OH^- ion, as indicated in Table 1 for aquo ions of Group IIIb. Acidity of a metal ion is controlled by size and charge, and also by covalence of the M–O bond [4]. It is seen that, while Al^{3+} is the smallest metal ion, and has a strong tendency to hydrolyze in aqueous solution, it is the least strongly hydrolyzed of the trivalent metal ions listed in Table 1.

Because Al^{3+} is a very hard metal ion, it has high affinity for hard anions. Among the "hardest" donors is the oxide ion, which is found generally in polymeric Al(III) species, usually coordinated to two or more Al(III) ions. Although OH^- and F^- are isoelectronic, OH^- ion has much higher affinity for Al^{3+}, because of the partially covalent nature of the Al–O coordinate bond, and the fact that the Al^{3+} –F^- bond is almost purely ionic. These ligands will be discussed in greater detail below.

For reasons described in detail elsewhere [5], the most stable Al^{3+} complexes are formed by multidentate ligands with negative oxygen donors, and the affinities of these ligands for metal ions also increase with the basicity of the ligand donor groups. The monodentate negative oxygen donors that are frequently found in multidentate ligands that are effective for Al(III) are listed in Scheme 1 in order of decreasing basicity, along with their approximate log protonation constants.



Scheme 1.

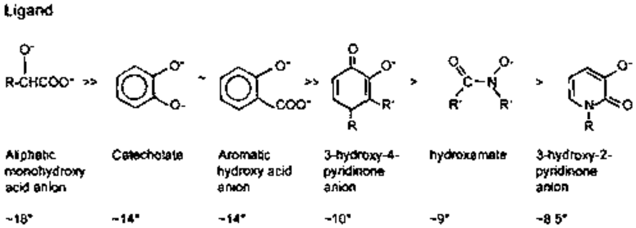
The protonation constants of the above donors indicate that their affinity for Al(III) varies with the basicity, which is measured in aqueous solution by the protonation constant. Thus ligands with high affinity for Al(III) also have high affinity for the

Table 1
Ionic radii and hydroxide affinities of trivalent metal ions

Metal ion	Al(III)	Ga(III)	In(III)	Tl(III)
Ionic radius (Å) [1]	0.50	0.62	0.82	0.95
log K_1 $(OH)^-$ [2,3]	9.01	11.4	10.0	13.4
log K_{sp}	−33.5	−37	−36.9	−45.2

hydrogen ion, and proton competition must also be considered when dealing with Al(III)–ligand equilibrium in aqueous solution.

These donor groups may be combined in various ways with each other and with other organic groups to produce bidentate ligands of varying basicity. Bidentate pairs that are effective for Al(III), and other hard trivalent metal ions, arranged in order of decreasing basicity, are shown in Scheme 2.



Scheme 2.

As before, the affinities of these donors for Al(III) parallel the protonation constants. For multidentate ligands with more than two donor groups, other factors such as preorganization of the ligand are also important. Some of these factors will be discussed below with individual chelating agents. The factors governing the stabilities of multidentate ligands have been described in detail in several reviews [5–7].

The selected protonation constants and Al(III) binding constants are given in Table 2 for some well-known chelating agents, some of which have high affinity for Al(III). It is noted that certain ligands with aliphatic hydroxyl groups, and some ligands with aromatic hydroxyl groups, have protonation constants of these functional groups that are too high to measure by conventional potentiometry and spectrophotometry. Hence the stability constants cannot be expressed in terms of the fully deprotonated ligand, even though the proton is displaced by the Al^{3+} ion. In such cases the equilibrium constant with Al(III) ion is expressed as a displacement constant, and the free anion of the ligand (which cannot be attained in the absence of metal ion) never appears in the equation. Thus for the displacement of one proton from the aliphatic (α) hydroxyl groups of gluconic acid, HL, we have

$$\log \frac{[\mathrm{AlL}^{2+}]}{[\mathrm{AlH}_{-1}\mathrm{L}^{+}][\mathrm{H}^{+}]} = 2.87$$

Here the $-n$ subscript indicates the number of additional protons displaced from the ligand.

2. Al(III) in the environment — $Al(OH)_3$ and fluoride complexes

The tertiary purification of water consists of the slow precipitation of solid, gelatinous $Al(OH)_3$ which gradually forms around any solid particles present, including dust particles and bacteria, followed by their removal by filtration. Thus water purified in this way is a saturated solution of $Al(OH)_3$.

Table 2
Critical stability constants of aluminum(III) complexes ($\mu = 0.10$ M, T = 25.0 °C)

Ligand	Quotient Q	log Q
1. HOH, HL	$[HOH]/[L^-][H^+]$	13.78
	$[AlL^{2+}]/[Al^{3+}][L^-]$	8.47
	$[AlL_2^+]/[Al^{3+}][L^-]^2$	16.8
	$[AlL_3]/[Al^{3+}][L^-]^3$	(24.7)
	$[AlL_4^-]/[Al^{3+}][L^-]^4$	(31.5)
	$[Al_2L_2^{4+}]/[Al^{3+}]^2[L^-]^2$ ($\mu = 1$)	20.0
	$[Al_3L_4^{5+}]/[Al^{3+}]^3[L^-]^4$	42.0
	$[Al_{13}O_4L_{24}^{7+}]/[Al^{3+}]^{13}[L^-]^{32}$ ($\mu = 1$)	336.5
2. HF, HL	$[HL]/[L^-][H^+]$	2.94
	$[AlL^{2+}]/[Al^{3+}][L^-]$	6.42
	$[AlL_2^+]/[Al^{3+}][L^-]^2$	11.63
	$[AlL_3]/[Al^{3+}][L^-]^3$	15.5
	$[AlL_4^-][Al^{3+}][L^-]^4$	18.1
3. Iminodiacetic acid (IDA), H_2L ($\mu = 0.5$)	$[HL^-]/[L^{2-}][H^+]$	9.22
	$[H_2L]/[HL^-][H^+]$	2.59
	$[AlL^+]/[Al^{3+}][L^{2-}]$	8.10
	$[AlL_2^-]/[AlL^+][L^{2-}]$	6.97
4. *N*-Methyliminodiacetic acid (MIDA), H_2L ($\mu = 0.5$)	$[HL^-]/[L^{2-}][H^+]$	9.46
	$[H_2L]/[HL^-][H^+]$	2.32
	$[AlL^+]/[Al^{3+}][L^{2-}]$	7.55
5. Nitrilotriacetic acid (NTA), H_3L	$[HL^{2-}]/[L^{3-}][H^+]$	9.46
	$[H_2L^-]/[HL^{2+}][H^+]$	2.52
	$[H_3L]/[H_2L^-][H^+]$	(1.8)
	$[AlL]/[Al^{3+}][L^{3-}]$	11.4
	$[AlHL^+]/[AlL][H^+]$	1.90
	$[AlL]/[AlOHL^-][H^+]$	5.09
6. *N*-(Phosphonomethyl)imino-diacetic acid, H_4L	$[HL^{3-}]/[L^{4-}][H^+]$	(10.29)
	$[H_2L^{2-}]/[HL^{3-}][H^+]$	5.57
	$[H_3L^-]/[H_2L^{2-}][H^+]$	2.44
	$[H_4L]/[H_3L^-][H^+]$	2.0
	$[AlL^-]/[Al^{3+}][L^{4-}]$	14.7
	$[AlHL]/[AlL^-][H^+]$	7.4
7. *N*-(2-Hydroxyethyl)iminodiacetic acid(HIDA), H_2L	$[HL^-]/[L^{2-}][H^+]$	8.68
	$[H_2L]/[HL^-][H^+]$	2.20
	$[H_3L^+]/[H_2L][H^+]$	(1.5)
	$[AlL^+]/[Al^{3+}][L^{2-}]$	7.74
8. *N*-(2-Hydroxyethyl)ethylenedinitrilotriacetic acid (HEDTA), H_3L	$[HL^{2-}]/[L^{3-}][H^+]$	9.70
	$[H_2L^-]/[HL^{2-}][H^+]$	5.39
	$[H_3L]/[H_2L^-][H^+]$	2.67
	$[AlL]/[Al^{3+}][L^{3-}]$	14.4
	$[AlHL^+]/[AlL][H^+]$	2.14
	$[AlL]/[AlOHL^-][H^+]$	4.89
	$[AlOHL^-]/[Al(OH)_2L^{2-}][H^+]$	9.19
9. Ethylenedinitrilotetraacetic acid (EDTA), H_4L	$[HL^{3-}]/[L^{4-}][H^+]$	10.19
	$[H_2L^{2-}]/[HL^{3-}][H^+]$	6.13
	$[H_3L^-]/[H_2L^{2-}][H^+]$	2.69
	$[H_4L]/[H_3L^-][H^+]$	2.00
	$[AlL^-]/[Al^{3+}][L^{4-}]$	16.5
	$[AlHL]/[AlL^-][H^+]$	2.5

Table 2 (*continued*)

Ligand	Quotient *Q*	log *Q*
	$[\mathrm{AlL}^-]/[\mathrm{AlOHL}^{2-}][\mathrm{H}^+]$	5.83
	$[\mathrm{AlOHL}^{2-}]/[\mathrm{Al(OH)_2L}^{3-}][\mathrm{H}^+]$	10.31
10. *trans*-1,2-Cyclohexylenedinitrilotetraacetic acid (CDTA), H_4L	$[\mathrm{HL}^{3-}]/[\mathrm{L}^{4-}][\mathrm{H}^+]$	(12.3)
	$[\mathrm{H_2L}^{2-}]/[\mathrm{HL}^{3-}][\mathrm{H}^+]$	6.12
	$[\mathrm{H_3L}^-]/[\mathrm{H_2L}^{2-}][\mathrm{H}^+]$	(3.49)
	$[\mathrm{H_4L}]/[\mathrm{H_3L}^-][\mathrm{H}^+]$	2.40
	$[\mathrm{AlL}^-]/[\mathrm{Al}^{3+}][\mathrm{L}^{4-}]$	19.6
	$[\mathrm{AlHL}]/[\mathrm{AlL}^-][\mathrm{H}^+]$	2.29
	$[\mathrm{AlL}^-]/[\mathrm{AlOHL}^{2-}][\mathrm{H}^+]$	7.82
11. Trimethylenedinitrilotetra-acetic acid (TMDTA), H_4L	$[\mathrm{HL}^{3-}]/[\mathrm{L}^{4-}][\mathrm{H}^+]$	10.30
	$[\mathrm{H_2L}^{2-}]/[\mathrm{HL}^{3-}][\mathrm{H}^+]$	7.88
	$[\mathrm{H_3L}^-]/[\mathrm{H_2L}^{2-}][\mathrm{H}^+]$	2.63
	$[\mathrm{H_4L}]/[\mathrm{H_3L}^-][\mathrm{H}^+]$	2.1
	$[\mathrm{AlL}^-]/[\mathrm{Al}^{3+}][\mathrm{L}^{4-}]$	16.32
12. (2-Hydroxytrimethylene)dinitrilotetraacetic acid, H_4L	$[\mathrm{HL}^{3-}]/[\mathrm{L}^{4-}][\mathrm{H}^+]$	9.49
	$[\mathrm{H_2L}^{2-}]/[\mathrm{HL}^{3-}][\mathrm{H}^+]$	6.98
	$[\mathrm{H_3L}^-]/[\mathrm{H_2L}^{2-}][\mathrm{H}^+]$	2.57
	$[\mathrm{H_4L}]/[\mathrm{H_3L}^-][\mathrm{H}^+]$	(1.7)
	$[\mathrm{AlL}^-]/[\mathrm{Al}^{3+}][\mathrm{L}^{4-}]$	15.2
	$[\mathrm{AlL}^-]/[\mathrm{AlOHL}^{2-}][\mathrm{H}^+]$	6.70
	$[\mathrm{AlOHL}^{2-}]/[\mathrm{Al(OH)_2L}^{3-}][\mathrm{H}^+]$	8.70
13. Ethylenebis(oxyethylenenitrilo)-tetraacetic acid (EGTA), H_4L	$[\mathrm{HL}^{3-}]/[\mathrm{L}^{4-}][\mathrm{H}^+]$	9.40
	$[\mathrm{H_2L}^{2-}]/[\mathrm{HL}^{3-}][\mathrm{H}^+]$	8.78
	$[\mathrm{H_3L}^-]/[\mathrm{H_2L}^{2-}][\mathrm{H}^+]$	2.66
	$[\mathrm{H_4L}]/[\mathrm{H_3L}^-][\mathrm{H}^+]$	2.0
	$[\mathrm{AlL}^-]/[\mathrm{Al}^{3+}][\mathrm{L}^{4-}]$	13.90
	$[\mathrm{AlHL}]/[\mathrm{AlL}^-][\mathrm{H}^+]$	3.97
	$[\mathrm{AlL}^-]/[\mathrm{AlOHL}^{2-}][\mathrm{H}^+]$	5.20
	$[\mathrm{AlOHL}^{2-}]/[\mathrm{Al(OH)_2L}^{3-}][\mathrm{H}^+]$	8.42
14. Diethylenetrinitilopentaacetic acid (DTPA), H_5L	$[\mathrm{HL}^{4-}]/[\mathrm{L}^{5-}][\mathrm{H}^+]$	10.48
	$[\mathrm{H_2L}^{3-}]/[\mathrm{HL}^{4-}][\mathrm{H}^+]$	8.60
	$[\mathrm{H_3L}^{2-}]/[\mathrm{H_2L}^{3-}][\mathrm{H}^+]$	4.28
	$[\mathrm{H_4L}^-]/[\mathrm{H_3L}^{2-}][\mathrm{H}^+]$	2.6
	$[\mathrm{H_5L}]/[\mathrm{H_4L}^-][\mathrm{H}^+]$	2.0
	$[\mathrm{H_6L}^+]/[\mathrm{H_5L}]\mathrm{H}^+]$	(1.6)
	$[\mathrm{AlL}^{2-}]/[\mathrm{Al}^{3+}][\mathrm{L}^{5-}]$	18.7
	$[\mathrm{AlHL}^-]/[\mathrm{AlL}^{2-}[\mathrm{H}^+]$	4.3
	$[\mathrm{AlL}^{2-}]/[\mathrm{AlOHL}^{3-}][\mathrm{H}^+]$	7.2
15. Triethylenetetranitrilohexaacetic acid (TTHA), H_6L	$[\mathrm{HL}^{5-}]/[\mathrm{L}^{6-}][\mathrm{H}^+]$	10.62
	$[\mathrm{H_2L}^{4-}]/[\mathrm{HL}^{5-}][\mathrm{H}^+]$	9.49
	$[\mathrm{H_3L}^{3-}]/[\mathrm{H_2L}^{4-}][\mathrm{H}^+]$	6.10
	$[\mathrm{H_4L}^{2-}]/[\mathrm{H_3L}^{3-}][\mathrm{H}^+]$	4.06
	$[\mathrm{H_5L}^-]/[\mathrm{H_4L}^{2-}][\mathrm{H}^+]$	2.75
	$[\mathrm{H_6L}]/[\mathrm{H_5L}^-][\mathrm{H}^+]$	2.3
	$[\mathrm{H_7L}^+]/[\mathrm{H_6L}][\mathrm{H}^+]$	(1.8)
	$[\mathrm{AlL}^{3-}]/[\mathrm{Al}^{3+}][\mathrm{L}^{6-}]$	21.0
	$[\mathrm{AlHL}^{2-}]/[\mathrm{AlL}^{3-}][\mathrm{H}^+]$	5.85
	$[\mathrm{Al_2L}]/[\mathrm{AlL}^{3-}][\mathrm{Al}^{3+}]$	9.2

Table 2 (*continued*)

Ligand	Quotient Q	log Q
16. 1,2-Dimethyl-3-hydroxy-4-pyridinone (DMHP), HL	$[HL]/[L^-][H^+]$	9.77
	$[H_2L^+]/[HL][H^+]$	3.68
	$[AlL^{2+}]/[Al^{3+}][L^-]$	12.20
	$[AlL_2{}^+]/[AlL^{2+}][L^-]$	11.05
	$[AlL_3]/[AlL_2{}^+][L^-]$	9.37
17. 1-Methyl-3-hydroxy-2-pyridinone (MH2P), HL	$[HL]/[L^-][H^+]$	8.89
	$[AlL^{2+}]/[Al^{3+}][L^-]$	9.41
	$[AlL_2{}^+]/[AlL^{2+}][L^-]$	17.79
	$[AlL_3]/[AlL_2{}^+][L^-]$	25.10
18. Acetonhydroxamic acid, HL	$[HL]/[L^-][H^+]$	9.36
	$[AlL^{2+}]/[Al^{3+}][L^-]$	7.95
	$[AlL_2{}^+]/[AlL^{2+}][L^-]$	15.29
	$[AlL_3]/[AlL_2{}^+][L^-]$	21.47
19. Desferriferrioxamine-B, H_4L^+	$[H_4L^+]/[H_3L][H^+]$	10.79
	$[H_3L]/[H_2L^-][H^+]$	9.55
	$[H_2L^-]/[HL^{2-}][H^+]$	8.96
	$[HL^{2-}]/[L^{3-}][H^+]$	8.32
	$[AlHL^+]/[Al^{3+}][HL^{2-}]$	24.14
	$[AlHL^+]/[AlL][H^+]$	9.43
	$[AlH_2L^{2+}]/[AlHL^+][H^+]$	1.2
20. Lactic acid, HL ($\mu=6$)	$[HL]/[L^-][H^+]$	3.57
	$[AlL^{2+}]/[Al^{3+}][L^-]$	2.36
	$[AlL_2{}^+]/[[Al^{3+}][L^-]^2$	4.42
	$[AlL_3]/[Al^{3+}][L^-]^3$	5.8
21. Malic acid, H_2L ($T=37\,°C$, $\mu=0.15$)	$[HL^-]/[L^{2-}][H^+]$	4.68
	$[H_2L]/[HL^-][H^+]$	3.20
	$[AlL^+]/[Al^{3+}][L^{2-}]$	4.60
	$[AlL_2{}^-]/[Al^{3+}][L^{2-}]^2$	7.62
	$[AlHL^{2+}]/[AlL^+][H^+]$	2.27
	$[AlHL_2]/[AlL_2{}^-][H^+]$	3.69
	$[AlL_2{}^-]/[AlOHL_2{}^{2-}][H^+]$	3.31
22. Citric acid, H_3L	$[HL^{2-}]/[L^{3-}][H^+]$	5.70
	$[H_2L^-]/[HL^{2-}][H^+]$	4.35
	$[H_3L]/[H_2L^-][H^+]$	2.90
	$[AlL]/[Al^{3+}][L^{3-}]$	7.98
	$[AlHL^+]/[AlL][H^+]$	2.94
	$[AlL]/[AlH_{1-}L^-][H^+]$	3.31
	$[AlH_{-1}L^-]/[Al(OH)(H_{-1}L)^{2-}][H^+]$	6.23
($\mu=0.6$)	$[Al_3(OH)_4L_3{}^{4-}][H^+]^4/[Al^{3+}]^3[L^{3-}]^3$	14.43
	$[Al_3(OH)_4(H_{-1}L)_3{}^{7-}][H^+]^7/[Al^{3+}]^3[L^{3-}]^3$	−10.91
23. D-Gluconic acid, HL	$[HL]/[L^-][H^+]$	3.44
	$[AlL^{2+}]/[Al^{3+}][L^-]$	1.98
	$[AlL^{2+}]/[AlH_{-1}L^+][H^+]$	2.87
	$[AlH_{-1}L^+]/[AlH_{-3}L^-][H^+]^2$	9.29
24. DL-Tartaric acid, H_2L	$[HL^-]/[L^{2-}][H^+]$	3.97
	$[H_2L]/[HL^-][H^+]$	2.82
	$[AlH_2{}^-]/[Al^{3+}][L^{2-}]^2$	7.65
	$[AlH_{-1}L][H^+]/[Al^{3+}][L^{2-}]$	1.18

Table 2 (*continued*)

Ligand	Quotient *Q*	log *Q*
	$[AlH_{-1}L]/[AlH_{-2}L^-][H^+]$	5.15
	$[AlL_2^-]/[AlH_{-1}L_2^{2-}][H^+]$	3.72
	$[AlH_{-1}L_2^{2-}]/[AlH_{-3}L_2^{4-}][H^+]^2$	12.67
	$[AlH_{-4}L_3^{7-}][H^+]^4/[Al^{3+}][L^{2-}]^3$	−15.92
	$[AlH_{-4}L_3^{7-}]/[AlH_{-5}L_3^{8-}][H^+]$	10.89
	$[AlH_{-5}L_3^{8-}]/[AlH_{-6}L_3^{9-}][H^+]$	12.7
	$[H_2L]/[HL^-][H^+]$	2.80
(T = 20 °C)	$[AlL+][H^+]/[Al^{3+}][HL^-]$	−0.2
	$[AlL_2^-][H^+]/[AlL^+][HL^-]$	−2.8
	$[AlL_3^{3-}][H^+]/[AlL_2^-][HL^-]$	−6.5
26. Sulfoxine, H_2L	$[HL^-]/[L^{2-}][H^+]$	8.42
	$[H_2L]/[HL^-][H^+]$	3.95
	$[AlL^+]/[Al^{3+}][L^{2-}]$	8.7
	$[AlL_2^-]/[Al^{3+}][L^{2-}]^2$	16.6
	$[AlL_3^{3-}]/[Al^{3+}][L^{2-}]^3$	23.2
27. Catechol, H_2L	$[HL^-]/[L^{2-}][H^+]$	(13.3)
	$[H_2L]/[HL^-][H^+]$	9.26
	$[AlL^+][H^+]^2/[Al^{3+}][H_2L]$	−6.0
	$[AlL_2^-][H^+]^2/[AlL^+][H_2L]$	−9.10
	$[AlL_3^{3-}][H^+]^2/[AlL_2^-][H_2L]$	−13.61
	$[AlHL_2]/[AlL_2^-][H^+]$	6.05
	$[AlHL_3^{2-}]/[AlL_3^{3-}][H^+]$	8.05
28. 4-Sulfocatechol, H_3L (T = 20 °C)	$[HL^{2-}]/[L^{3-}][H^+]$	(12.8)
	$[H_2L^-][HL^{2-}][H^+]$	8.50
	$[AlL][H^+]^2/[Al^{3+}][H_2L^-]$	−4.7
	$[AlL_2^{3-}][H^+]^2/[AlL][H_2L^-]$	−7.7
	$[AlL_3^{6-}][H^+]^2/[AlL_2^{3-}][H_2L^-]$	−11.6
29. Tiron, H_4L	$[HL^{3-}]/[L^{4-}][H^+]$	(12.5)
	$[H_2L^{2-}]/[HL^{3-}][H^+]$	7.62
	$[AlL^-][H^+]^2/[Al^{3+}][H_2L^{2-}]$	−3.2
	$[AlL_2^{5-}][H^+]^2/[AlL^-][H_2L^{2-}]$	−6.6
	$[AlL_3^{9-}][H^+]^2/[AlL_2^{5-}][H_2L^{2-}]$	−10.3
30. Chromotropic acid, H_4L	$[H_2L^{2-}]/[HL^{3-}][H^+]$	5.35
	$[AlL^-][H^+]^2/[Al^{3+}][H_2L^{2-}]$	−3.81
	$[AlL_2^{5-}][H^+]^2/[AlL^{1-}][H_2L^{2-}]$	−8.0
31. Dopamine, H_3L^+	$[HL^-]/[L^{2-}][H^+]$	(13.1)
	$[H_2L]/[HL^-][H^+]$	10.36
	$[H_3L^+]/[H_2L][H^+]$	8.88
	$[AlHL^{2+}]/[Al^{3+}][HL^-]$	13.32
	$[Al(HL)_2^+]/[Al^{3+}][HL^-]^2$	23.99
	$[Al(HL)_3]/[Al^{3+}][HL^-]^3$	30.63
32. L-DOPA, H_3L	$[HL^{2-}]/[L^{3-}][H^+]$	13.4
	$[H_2L^-]/[HL^{2-}][H^+]$	9.81
	$[H_3L]/[H_2L^-][H^+]$	8.75
	$[H_4L^+]/[H_3L][H^+]$	2.20
	$[AlHL^+]/[Al^{3+}][HL^{2-}]$	12.72
	$[Al(HL)_2^-]/[Al^{3+}][HL^{2-}]^2$	22.62
	$[Al(HL)_3^{3-}]/[Al^{3+}][HL^{2-}]^3$	28.43

In Fig. 1 are shown the Al(III) hydrolytic species formed when the total analytical concentration of Al(III) is 1.0×10^{-6} M. The equilibrium concentrations of the soluble complexes are calculated from the data in Table 2, and the value of K_{sp} is given in Table 1. At this concentration of Al(III) there are no polymeric species (which are formed at higher concentration). Solid $Al(OH)_3$ (written as AlH_{-3}) precipitates at pH 5, and predominates over soluble complexes between about pH 5.2 and 9. At higher pH the soluble aluminate, $Al(OH)_4^-$, indicated here as AlH_{-4}, predominates and it is the only species present above pH 10.

In the presence of 1.0×10^{-5} M fluoride, the distribution curves in Fig. 2 show

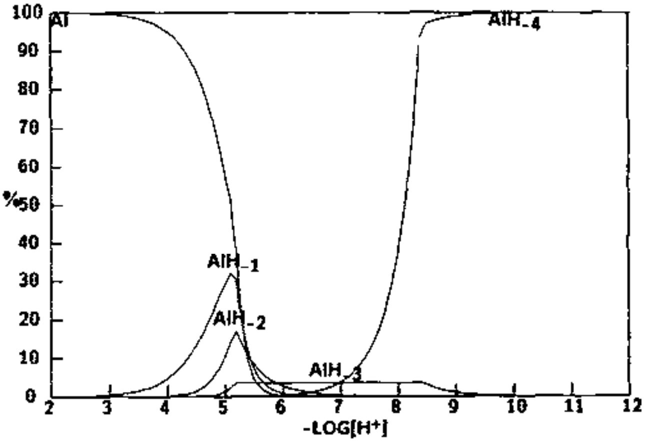


Fig. 1. Relative molar concentrations of hydrolytic species formed from the aqua aluminum(III) ion as a function of $-\log[H^+]$. Total analytical concentration of aluminum(III) species is 1.00×10^{-6} M. $T = 25.0$°C; $\mu = 0.100$ M.

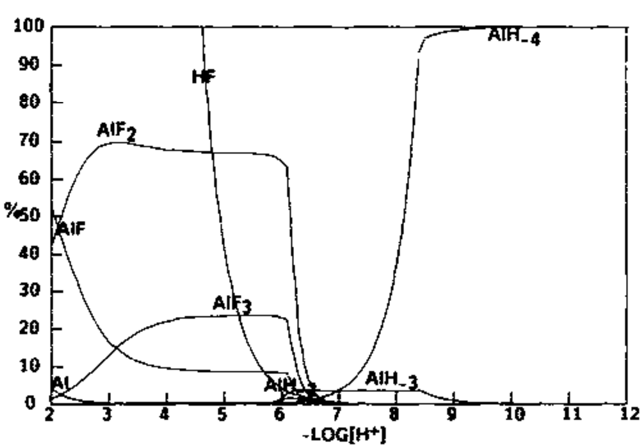


Fig. 2. Relative molar concentrations of complex species formed from 1.0×10^{-6} M aquo aluminum(III) ion and 5.0×10^{-5} M fluoride ion. $T = 25.0$°C; $\mu = 0.100$ M.

that the fluoride complexes AlF_2^+, AlF_3 and AlF_4^- predominate in acid solution until $Al(OH)_3$ precipitates. Also, it is seen that these complexes of Al(III) keep it from precipitating as the hydroxide until pH 6 is reached. In alkaline solution the complex formed is the aluminate anion, just as it forms in the absence of fluoride (Fig. 1).

In Figs. 1 and 2, it is seen that the excess solid $Al(OH)_3$ maintains a constant concentration of the complex $Al(OH)_3$. Thus it is seen that the concentration of the soluble $Al(OH)_3$ complex in aqueous solution (at saturation) is about 5×10^{-8} M, not an insignificant concentration. This indicates that Al(III) is free to move about (at low but appreciable concentration) in aqueous solution in the environment in the absence of more effective precipitating agents. It is also apparent from a comparison of Figs. 1 and 2 that fluoride ion increases the concentration and mobility of Al(III) in natural waters.

3. Al(III) complexes of multidentate ligands

Multidentate ligands with negative oxygen donors bind Al(III) with affinities that increase with the number of donor groups, and with the basicities of the donor groups. The coordination number is six in most of its complexes. The most basic groups, the aliphatic and aromatic hydroxyl donors, are generally protonated at low pH, even with Al(III) present, but become more available and effective at high pH. The less basic donors, such as the carboxylate anion, are generally available at low pH, but bind Al(III) less strongly.

The relative tendencies of the ligands listed in Table 2 to bind Al(III), and the concentration of complexes formed, can be calculated from the equilibrium constants listed in Table 2. Some representative examples of the relative effectiveness of pairs of ligands are illustrated in Figs. 3–8.

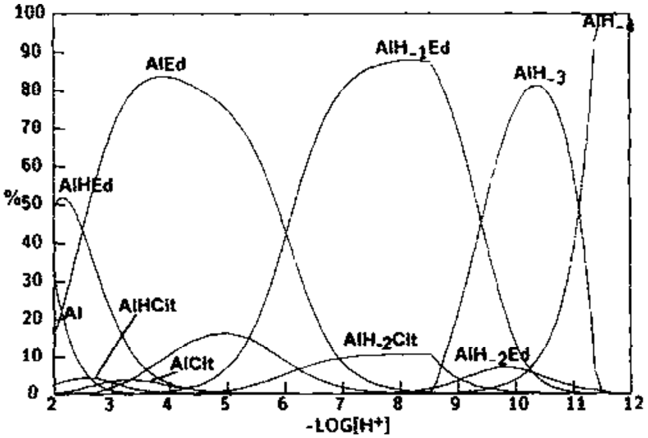


Fig. 3. Relative molar concentrations of complex species formed from 1.0×10^{-3} M Al(III), 1.0×10^{-3} M EDTA, and 1.0×10^{-3} M citric acid, Ed = $EDTA^{4-}$; Cit = $citrate^{3-}$; $T = 25.0°C$; $\mu = 0.10$ (KCl).

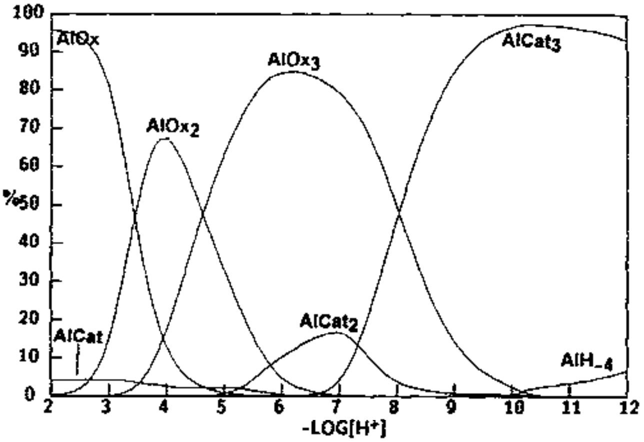


Fig. 4. Relative molar concentrations of complex species formed from 1.0×10^{-3} M Al(III) (=100%), 3.0×10^{-3} M sulfoxine, and 3.0×10^{-3} M sulfocatechol. Sulfoxine anion = Ox; sulfocatechol = Cat; $T = 25.0°C$; $\mu = 0.10$ (KCl).

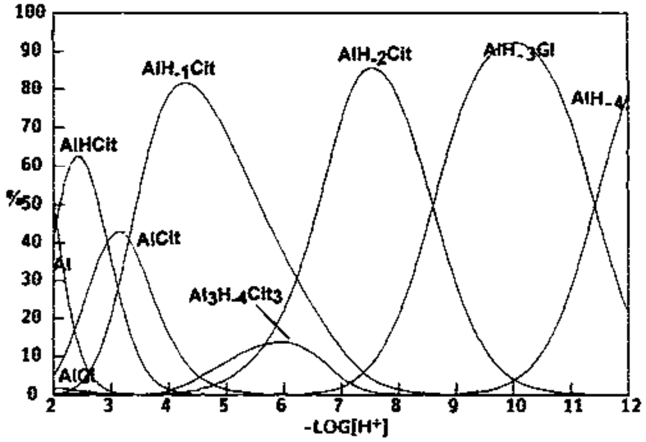


Fig. 5. Relative molar concentrations of complex species formed from 1.0×10^{-3} M Al(III) (=100%), 1.0×10^{-2} M citric acid, and 1.0×10^{-2} M gluconic acid. Citric acid = H_3L = Cit; gluconic acid = HL = Gl; $T = 25.0°C$; $\mu = 0.10$ (KCl).

Fig. 3 illustrates the competition between the well-known hexadentate chelating agent ethylenediaminetetraacetic acid, EDTA, and the terdentate chelating agent, citrate anion. It is seen that the four carboxylate donors of EDTA, and the fact that it forms five chelate rings, result in the formation of a much more stable complex of Al(III) than is formed by the citrate anion, which for steric reasons can bind Al(III) with only two of its carboxylate donor groups, in spite of the fact that it also binds Al(III) with an aliphatic alkoxide oxygen. Fig. 3 indicates that EDTA complexes of Al(III) predominate over citrate complexes at all pH values shown. The discontinuity

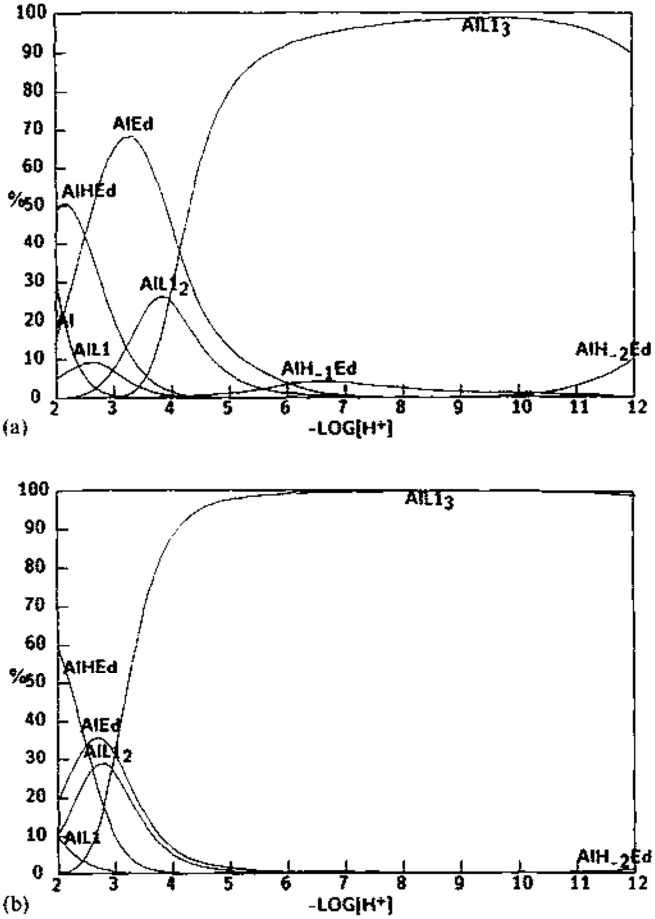


Fig. 6. (a) Relative molar concentrations of complex species formed from 1.0×10^{-3} M Al(III), 3.0×10^{-3} M 1,2-dimethyl-3-hydroxy-4-pyridinone (L1), and 1.0×10^{-3} M EDTA. L1 = HL; EDTA = H_4L = Ed; $T = 25.0$°C; $\mu = 0.10$ (KCl). (b) As (a), except at 100 times the concentration.

at pH 8.5 is due to the precipitation of $Al(OH)_3$. The curve labeled AlH_{-3} does not represent a soluble species, as other curves do, but rather represents the relative amount of solid $Al(OH_3$ that is formed. It is seen that at very high pH the aluminum hydroxide is dissolved to form the soluble aluminate, labeled AlH_{-4}.

4. Chelate ring size

The relative affinities of ligands with chelate rings of different sizes for metal ions of varying ionic radii have been described [5–7]. The geometry of chelate rings is such that five-membered chelate rings prefer larger metal ions, while six-membered chelate rings best combine with small metal ions with least strain. Examples of the

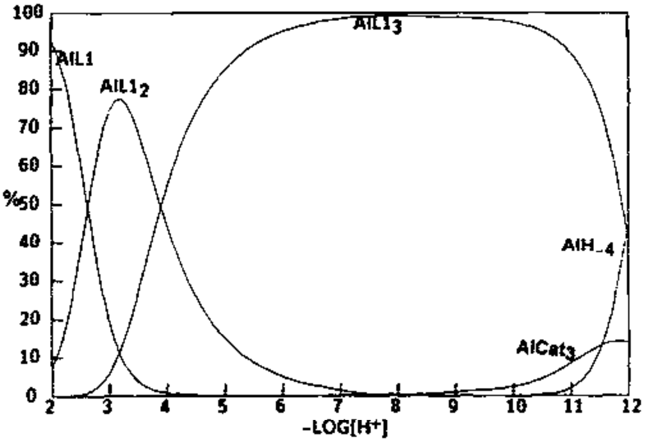


Fig. 7. Relative molar concentrations of complex species formed from 1.0×10^{-3} M Al(III), 3.0×10^{-3} M L1, and 3.0×10^{-3}M catechol. L1 = HL; catechol = H_2L = Cat; $T = 25.0$°C; $\mu = 0.10$ M (KCl).

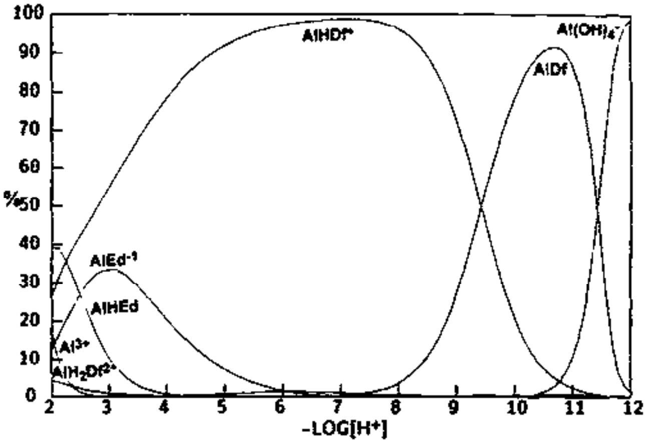


Fig. 8. DFO more effective than EDTA for binding Al(III). EDTA = H_4E; DFO = H_3L or H_4L^+; Al^{3+} = M^{3+}. Total concentrations of components, $T_{EDTA} = T_{DFO} = T_{Al(III)} = 0.0010$ M; $T = 25.0$°C; $\mu = 0.100$ M (KCl).

chelate ring size principle can be found in the structures of the citrate complexes [8,9]. Tridentate coordination of citrate with metal ions may lead to two six-membered chelate rings, or one five-membered and one six-membered chelate ring. However, the very small Al(III) ion forms the structure, indicated by Fig. 9(c), containing two six-membered chelate rings [9]. Unpublished molecular-mechanics calculations by the present authors show that only metal ions with M–O bond length of 1.90 Å or less should form citrate chelates with two six-membered chelate rings, rather than structures with one five-membered and one six-membered chelate ring. The average Al–O bond length in the Al(III) citrate complex is 1.91 Å,

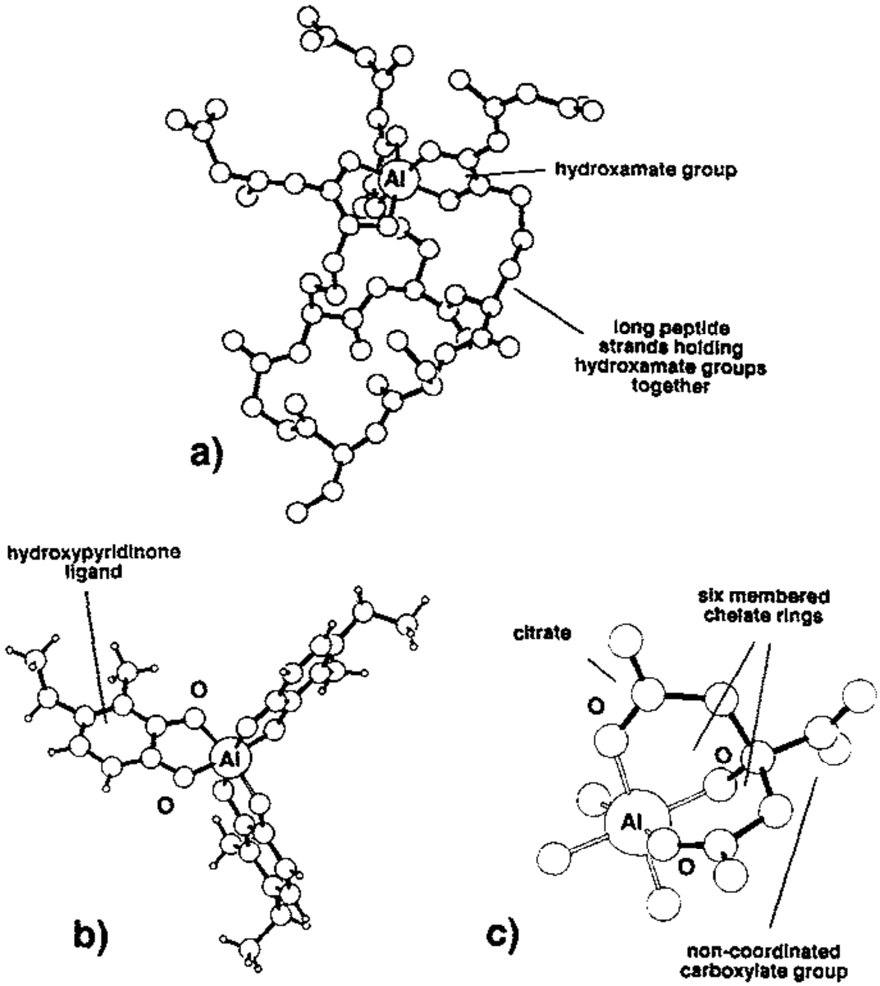


Fig. 9. Structures of some complexes of Al(III) of interest in its solution chemistry: (a) Al(III) complex of desferriferrichrome-A, redrawn with coordinates available in Ref. [12]; (b) tris(1-ethyl-2-methyl-hydroxy-4-pyridinone)aluminum(III) complex, redrawn using coordinates available in Ref. [10]; (c) citrate complex of Al(III), redrawn with coordinates available in Ref. [9].

and both five–six, and six–six chelate rings are present in the crystal lattice of Al(III) citrate.

Fig. 4 compares the affinities of the Al(III) ion for two bidentate ligands; sulfoxine and the much more basic sulfocatechol. It is seen that the sulfoxine complexes predominate at and below pH 8, where hydrogen ion competition ties up the catechol derivative in its protonated forms. Above pH 8, however, the tris-sulfocatechol complex predominates, and it becomes the only complex present above pH 11.

A similar situation is illustrated in Fig. 5, wherein the less basic citrate ligand competes with the gluconate anion, which becomes very basic when one to three aliphatic hydroxyl groups dissociate. Here it is seen that citrate complexes predominate up to pH 8.5, but are converted to gluconate complexes in more alkaline solution.

In Figs. 6(a) and 6(b) are illustrated the relative effectiveness of EDTA and 1,2-dimethyl-3-hydroxy-4-pyridinone (L1) in complexing Al(III). The pryidinone has the advantage of having two oxygen donors, relatively low pK values, and fairly high binding constants for Al(III). It is seen in Fig. 6(a) that, at a 3:1 molar ratio of L1 to EDTA, the pyridinone is the more effective ligand by far, with the EDTA complex amounting to no more than a few molar percent of the complexes present. Since L1 is only bidentate and forms 1:3 chelates with Al(III), it is subject to the dilution effect, which increases its dissociation in dilute solution. Therefore at higher concentration (Fig. 6(b)) it is even more effective, with no EDTA complexes appearing above pH 5. The structure of Al(III) with three hydroxypyridinone ligands coordinated to it is seen in Fig. 9(b) [10].

In Fig. 7, on the other hand, two bidentate ligands are compared. The ligand L1 has a somewhat lower affinity for Al(III) than does catechol, but much lower affinity for hydrogen ion. Therefore the complexes of L1 predominate over those of catechol over the whole pH range shown (2–12). In fact the 3:1 catechol complex does not appear except as a minor species at very high pH. Because both ligands are bidentate, they have the same dilution effect, and the distribution curves in Fig. 7 are therefore not changed by a change in concentration.

5. Al(III) complexes in biological systems

Aluminum overload is not a very common condition, but may result from physiological disorders which can lead to increased aluminum intake in excess of the slow natural process of elimination. It has also been produced in dialysis therapy, but dialysis encephalopy syndrome, a severe disabling disease, is now less common because of the avoidance of aluminum parts in dialysis equipment. Aluminum overload is also of interest since excessive amounts are usually present in patients suffering from Alzheimer's disease, although whether or not the condition actually causes the disease has not been established, and aluminum overload may merely be a side-effect.

Desferriferrioxamine-B (desferal, DFO) is a microbial siderophore that has long been used for the treatment of Cooley's anemia and other forms of iron overload [11,12]. A structure of the Al(III) complex of DFO has not been reported, but that of the similar trishydroxamate desferriferrichrome-A is seen in Fig. 9(a) [13]. DFO is now recommended for the treatment of aluminum overload [14–22]. Also, it has been shown above (Figs. 6(a) and 6(b)) that the pyridinone L1 has very high affinity for Al(III) and could also be used as a chelating agent to remove aluminum from the body [23]. In addition to the possible use of DFO and L1 as chelating agents for the treatment of aluminum overload, the new chelating agents that have been developed for the treatment of iron overload [24,25] should also have high affinity for Al(III) and should be effective in the treatment of aluminum overload.

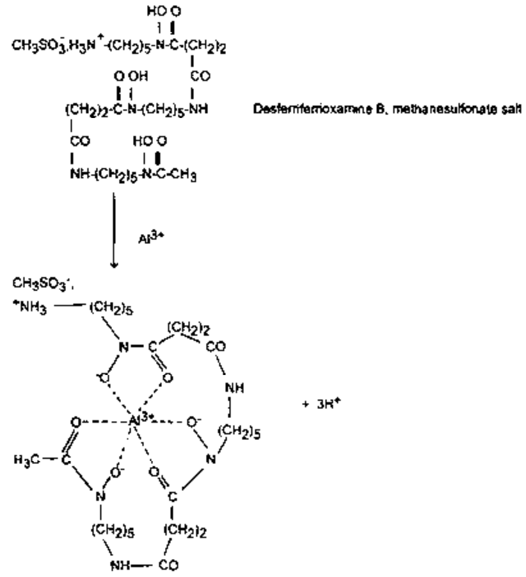
Because of its medicinal importance, it is of interest to compare the affinity of

DFO for aluminum(III) with that of other ligands. The stability constant for the aluminum(III) DFO chelate, formed in accordance with the following reaction, is listed in Table 2 as $10^{24.14}$ for the species with a proton on the terminal aliphatic amino group. It is this form which exists at physiological pH. With these data it is possible to calculate the species present in solutions containing DFO and a competing chelating agent.

$$\log\left(\frac{[\mathrm{AlHL}^{+}]}{[\mathrm{Al}^{3+}][\mathrm{HL}^{2-}]}\right)=24.14$$

$$\log\left(\frac{[\mathrm{AlHL}^{+}]}{[\mathrm{AlL}][\mathrm{H}^{+}]}\right)=9.43$$

Fig. 8 clearly demonstrates the remarkable affinity of DFO for aluminum(III). The aluminum(III)–DFO chelate predominates over the EDTA chelate between pH 3 and 11.5 (Fig. 8), with the latter ($[\mathrm{MHE}]+[\mathrm{ME}^{-}]$) accounting for about 50% of the metal ion only below pH 3, and disappearing entirely at and above pH 6. The aluminum(III)–DFO chelate is eventually converted to $\mathrm{Al(OH)_4}^{-}$, but only above pH 11.



Scheme 3.

Fig. 10 shows the correlation between log K_1 and log K_1(OH) for the desferriferrioxamine (DFO) and citrate complexes of aluminum(III) and a number of other metal ions. DFO is hexadentate and very stable, while the citrate ligand, as shown above, is probably terdentate, giving rise to considerably less stable complexes. As mentioned above, because of the high stability of its Al(III) complex (pM = 19.4 at

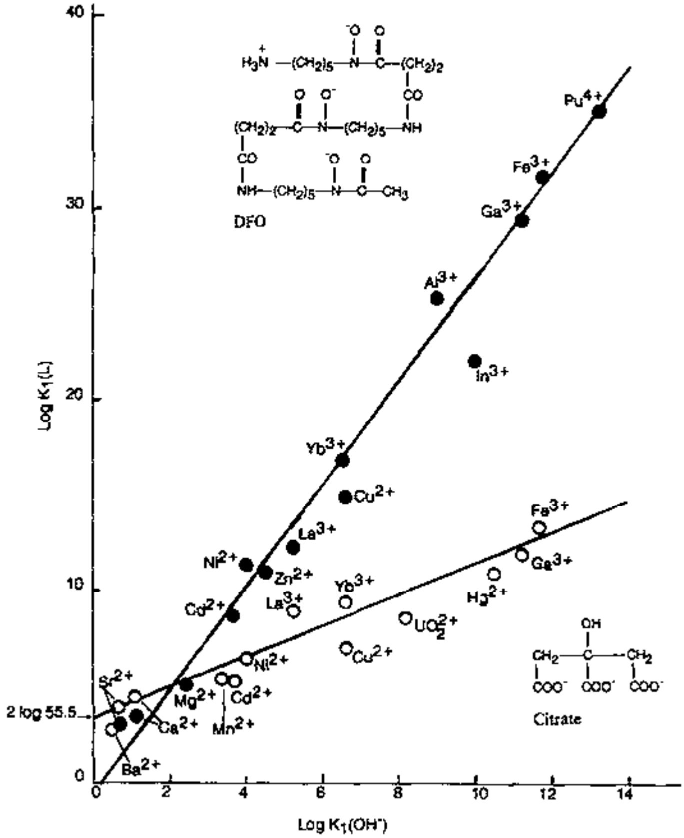
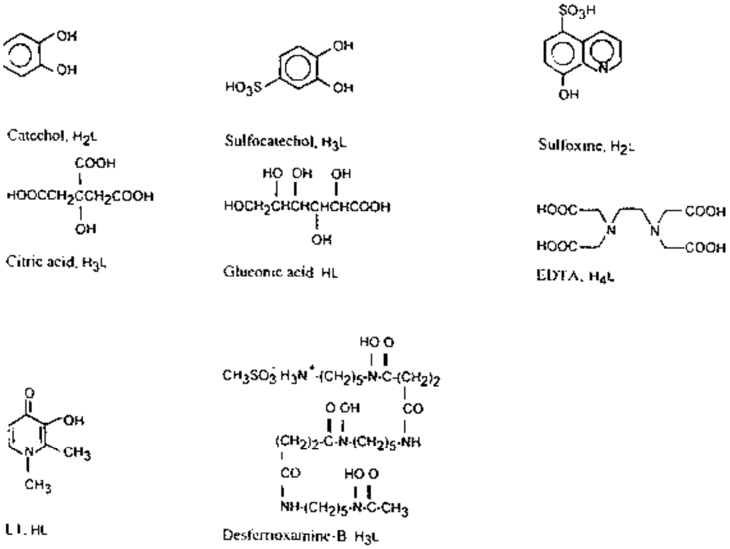


Fig. 10. Correlation between log K_1 of the Al(III) DFO and citrate chelates and log $K_1(OH^-)$. Formation constants data from Ref. [3].

physiological pH with 100% excess free ligand, compared with $Al(OH)_3$, which precipitates when pM is lower than 11.0), and its low toxicity, DFO seems to be the drug of choice for the treatment of aluminum overload.

Two important factors control the correlations in Fig. 10. First, more basic donor atoms in the ligand, and an increase in the number of donor atoms on the ligand, lead to steeper slopes and higher selectivity. Second, the magnitude of the intercept depends on the level of preorganization of the ligand. Analysis of the chelate effect [26,27] suggests that the formation of chelate rings should produce additional stabilization, giving an intercept of $(n-1)$ log 55.5, where n is the number of donor atoms of the chelating ligand. Thus the terdentate, rather rigid, citrate anion gives the expected intercept of 2 log 55.5. The hexadentate but very flexible DFO anion, however, with long chains between pairs of donor groups, has no chelate effect, and is characterized by a very low intercept.



Scheme 4.

6. Summary

The hydrolytic behavior of Al(III) described above indicates that it can be a component of natural waters, and even of purified drinking water, and that transport of Al(III) through environmental aqueous systems may take place readily. Effective complexing agents for Al(III), such as L1 and DFO, may be used as chelating agents for the treatment of aluminum overload, and DFO has been recommended for that purpose.

The structural formulas of the ligands described in detail in this paper are given in Scheme 4. For more information on Al(III) complexes, the reader is referred to previous papers on this subject [11,14,16] and to data on critical (selected) stability constants [2,3].

Acknowledgements

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