1.3: Chemical Properties Relative to Storage and Transport

Iron

Iron is the most abundant transition element in the Earth's crust and, in general, in all life forms. An outline of the distribution of iron in the Earth's crust[20,21] is shown in Table 1.2. As can be seen, approximately one-third of the Earth's mass is estimated to be iron. Of course, only the Earth's crust is relevant for life forms, but even there it is the most abundant transition element. Its concentration is relatively high in most crustal rocks (lowest in limestone, which is more or less pure calcium carbonate). In the oceans, which constitute 70 percent of the Earth's surface, the concentration of iron is low but increases with depth, since this iron exists as suspended particulate matter rather than as a soluble species. Iron is a limiting factor in plankton growth, and the rich fisheries associated with strong up-welling of ocean depths result at least in part from the biological growth allowed by these iron supplies. Properties that dominate the transport behavior of most transition metal ions are: (l) redox chemistry, (2) hydrolysis, and (3) the solubility of the metal ions in various complexes, particularly the hydroxides.

Table 1.2 - Iron: its terrestrial distribution.[a]

a) Data from References 1a and 20

One third of Earth's mass, most abundant element by weight

- Distribution in crustal rocks (weight %):
  - igneous 5.6
  - shale 4.7
  - sandstone 1.0
  - limestone 0.4
- Ocean (70% of Earth's surface):
  - 0.003 - 0.1 ppb, increasing with depth; limiting factor in plankton growth
- Rivers:
  - 0.07 - 7 ppm
- K_{sp} for $Fe(OH)_3$ is approximately 10^{-39}, hence at pH 7 $[Fe^{3+}]$ 10^{-18} M

As an example of the effects of solubility, consider the enormous variation in the concentration of iron in rivers, depending on whether the water is from a clear mountain stream running over rock or a muddy river carrying large amounts of sediment. However, the amount of dissolved iron in the form of free ferric ion or its hydrolysis products, whatever the source of water, is extremely low. As can be seen from the solubility of hydrated Fe(III) ($K_s \sim 10^{-18}$ M) (Table 1.2), the concentration of free ferric ion is extraordinarily low at neutral pH; so significant concentrations of soluble iron species can be attained only by strong complex formation.

One example of the versatility of iron as a function of its environment is how the ligand field can strongly alter the structural and ligand exchange properties of the metal ion (Figure 1.3). The ligand field can also alter the redox properties. For high-spin ferric ion, as found in the aquo complex or in many other complexes (including the class of microbial iron-transport agents called siderophores, to be discussed later), the coordination geometry is octahedral or pseudo-octahedral. In the relatively weak ligand field (high-spin ground state), the complex is highly labile. In a strong ligand field, such as an axially ligated porphyrin complex of ferric ion, or the simple example of the ferrocyanide anion, the low-spin complex is exchange-inert. Similarly, the high-spin octahedral ferrous complexes are exchange-labile, but the corresponding axially ligated porphyrin complexes, or the ferrocyanide complexes, are spin-paired (diamagnetic) and ligand exchange-inert. Large, bulky ligands or constrained ligands, such as those provided by metalloprotein and enzyme sites, can cause a tetrahedral environment, in which both ferrous ion and ferric ion form high-spin complexes.

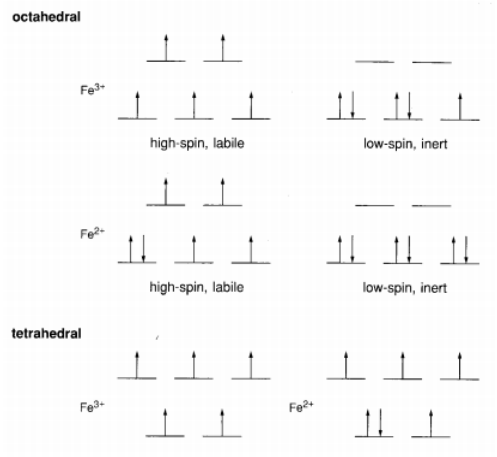

Figure 1.3 - Versatility of Fe coordination complexes.

The distribution of specific iron complexes in living organisms depends strongly on function. For example, although there are many different iron complexes in the average human, the relative amounts of each type differ more than 650-fold (Table 1.3). The total amount of iron in humans is quite large, averaging more than three and up to five grams for a healthy adult. Most of the iron is present as hemoglobin, the plasma oxygen-transport protein, where the function of the iron is to deliver oxygen for respiration. A much smaller amount of iron is present in myoglobin, a muscle oxygen-storage protein. For transport, the most important of these iron-containing proteins is transferrin, the plasma iron-transport protein that transfers iron from storage sites in the body to locations where cells synthesizing iron proteins reside; the major consumers of iron in vertebrates are the red blood cells. However, at any given time relatively little of the iron in the body is present in transferrin, in much the same way that at any given time in a large city only a small fraction of the population will be found in buses or taxis. Other examples of iron-containing proteins and their functions are included in Table 1.3 for comparison.

Table 1.3 - Average human Fe distribution

Protein	Function	Oxidation State of Fe	Amount of Fe (g)	Percent of Total
Hemoglobin	Plasma O_2 transport	2	2.6	65
Myoglobin	Muscle O_2 storage	2	0.13	6
Transferrin	Plasma Fe transport	3	0.007	0.2
Ferritin	Cell Fe storage	3	0.52	13
Hemosiderin	Cell Fe storage	3	0.48	12
Catalase	H_2O_2 metabolism	2	0.004	0.1
Cytochrome *c*	Electron transport	$\frac{2}{3}$ (1.3.1)	0.004	0.1
Other	Oxidases, other enzymes, etc.		0.14	3.6

An example of different iron-coordination environments, which alter the chemical properties of iron, is the difference in the redox potentials of hydrated Fe^{3+} and the electron-transport protein cytochrome *c* (Table 1.4). The coordination environment of iron in cytochrome *c* is illustrated in Figure 1.4. For example, the standard reduction potential for ferric ion in acid solution is 0.77 volts; so here ferric ion is quite a good oxidant. In contrast, cytochrome *c* has a redox potential of 0.25 volts. A wide range of redox potentials for iron is achieved in biology by subtle differences in protein structure, as listed in Table 1.4. Notice the large difference in the potential of cytochrome *c* and rubredoxin (Figure 1.5), 0.25 volts vs. -0.06 volts, respectively. In polynuclear ferredoxins, in which each iron is tetrahedrally coordinated by sulfur, reduction potentials are near -0.4 volts. Thus, the entire range of redox potentials, as illustrated in Table 1.4, is more than one volt.

Table 1.4 - Fe redox potentials

Complex	Coord. no., type	Fe^{3+}/Fe^{2+} E^o (mV)
$Fe(OH_2)_6^{3+}$	6, aquo complex	770
Cytochrome a_3	6, heme	390
HIPIP	4, $Fe_4S_4(SR)_4^-$	350
Cytrochrome *c*	6, heme	250
Rubredoxin	4, $Fe(SR)_4$	-60
Ferredoxins	4, $Fe_4S_4(SR)_4^{2-}$	-400

Zinc, Copper, Vanadium, Chromium, Molybdenum, and Cobalt

The chemical properties of the other essential transition elements simplify their transport properties. For zinc there is only the +2 oxidation state, and the hydrolysis of this ion is not a limiting feature of its solubility or transport. Zinc is an essential element for both animals and plants.[8,9,20,21] In general, metal ion uptake into the roots of plants is an extremely complex phenomenon. A cross-sectional diagram of a root is shown in Figure 1.6. It is said that both diffusion and mass flow of the soil solution are of significance in the movement of metal ions to roots. Chelation and surface adsorption, which are pH dependent, also affect the availability of nutrient metal ions. Acid soil conditions in general retard uptake of essential divalent metal ions but increase the availability (sometimes with toxic results) of manganese, iron, and aluminum, all of which are normally of very limited availability because of hydrolysis of the trivalent ions.

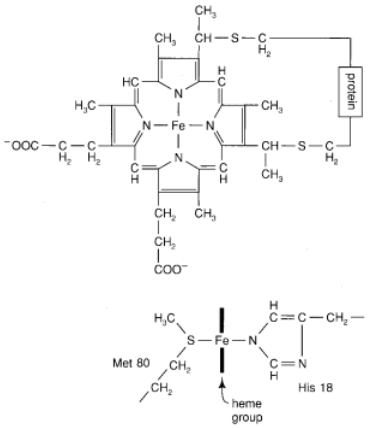

Figure 1.4 - Heme group and iron coordination in cytochrome c.

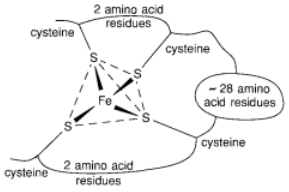

Figure 1.5 - $Fe^{3+/2+}$ coordination in rubredoxin.

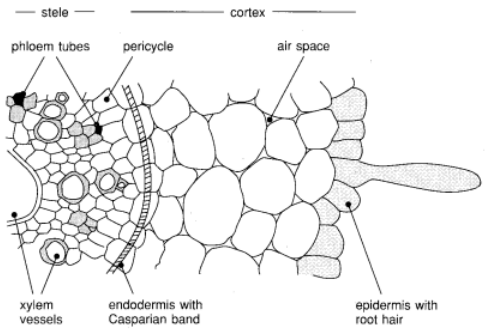

Figure 1.6 - Transverse section of a typical root.[20] The complex features of the root hair surface that regulate reductase and other activities in metal uptake are only beginning to be understood.

Vanadium is often taken up as vanadate, in a pathway parallel to phosphate.[18] However, its oxidation state within organisms seems to be highly variable. Unusually high concentrations of vanadium occur in certain ascidians (the specific transport behavior of which will be dealt with later). The workers who first characterized the vanadium-containing compound of the tunicate, *Ascidia nigra*, coined the name tunichrome.[22] The characterization of the compound as a dicatecholate has been reported.[23]

Quite a different chemical environment is found in the vanadium-containing material isolated from the mushroom *Amanita muscaria*. Bayer and Kneifel, who named and first described amavadine,[24] also suggested the structure shown in Figure 1.7.[25] Recently the preparation, proof of ligand structure, and (by implication) proof of the complex structure shown in Figure 1.7 have been established.[26] Although the exact role of the vanadium complex in the mushroom remains unclear, the fact that it is a vanadyl complex is now certain, although it may take a different oxidation state *in vivo*.

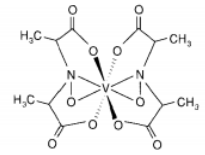

Figure 1.7 - A structure proposed for amavadine.[27]

The role of chromium in biology remains even more mysterious. In human beings the isolation of "glucose tolerance factor" and the discovery that it contains chromium goes back some time. This has been well reviewed by Mertz, who has played a major role in discovering what is known about this elusive and apparently quite labile compound.[27] It is well established that chromium is taken up as chromic ion, predominantly via foodstuffs, such as unrefined sugar, which presumably contain complexes of chromium, perhaps involving sugar hydroxyl groups. Although generally little chromium is taken up when it is administered as inorganic salts, such as chromic chloride, glucose tolerance in many adults and elderly people has been reported to be improved after supplementation with 150 - 250 mg of chromium per day in the form of chromic chloride. Similar results have been found in malnourished children in some studies in Third World countries. Studies using radioactively labeled chromium have shown that, although inorganic salts of chromium are relatively unavailable to mammals, brewer's yeast can convert the chromium into a usable form; so brewer's yeast is today the principal source in the isolation of glucose tolerance factor and has been used as a diet supplement.

Although chromium is essential in milligram amounts for human beings as the trivalent ion, as chromate it is quite toxic and a recognized carcinogen.[30] The uptake-reduction model for chromate carcinogenicity as suggested by Connett and Wetterhahn is shown in Figure 1.8. Chromate is mutagenic in bacterial and mammalian cell systems, and it has been hypothesized that the difference between chromium in the +6 and +3 oxidation states is explained by the "uptake-reduction" model. Chromium(III), like the ferric ion discussed above, is readily hydrolyzed at neutral pH and extremely insoluble. Unlike Fe^{3+}, it undergoes extremely slow ligand exchange. For both reasons, transport of chromium(III) into cells can be expected to be extremely slow unless it is present as specific complexes; for example, chromium(III) transport into bacterial cells has been reported to be rapid when iron is replaced by chromium in the siderophore iron-uptake mediators. However, chromate readily crosses cell membranes and enters cells, much as sulfate does. Because of its high oxidizing power, chromate can undergo reduction inside organelles to give chromium(m), which binds to small molecules, protein, and DNA, damaging these cellular components.

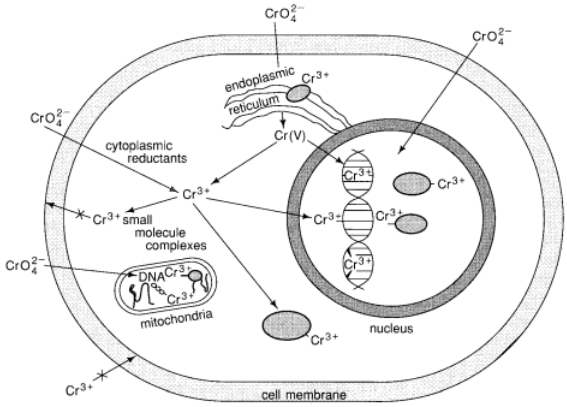

Figure 1.8 - The uptake-reduction model for chromate carcinogenicity. Possible sites for reduction of chromate include the cytoplasm, endoplasmic reticulum, mitochondria, and the nucleus.[27]

In marked contrast to its congener, molybdenum is very different from chromium in both its role in biology and its transport behavior, again because of fundamental differences in oxidation and coordination chemistry properties. In contrast to chromium, the higher oxidation states of molybdenum dominate its chemistry, and molybdate is a relatively poor oxidant. Molybdenum is an essential element in many enzymes, including xanthine oxidase, aldehyde reductase, and nitrate reductase.[19] The range of oxidation states and coordination geometries of molybdenum makes its bioinorganic chemistry particularly interesting and challenging.

The chemistry of iron storage and transport is dominated by high concentrations, redox chemistry (and production of toxic-acting oxygen species), hydrolysis (pK_a is about 3, far below physiological pH), and insolubility. High-affinity chelators or proteins are required for transport of iron and high-capacity sequestering protein for storage. By comparison to iron, storage and transport of the other metals are simple. Zinc, copper, vanadium, chromium, manganese, and molybdenum appear to be transported as simple salts or loosely bound protein complexes. In vanadium or molybdenum, the stable anion, vanadate or molybdate, appears to dominate transport. Little is known about biological storage of any metal except iron, which is stored in ferritin. However, zinc and copper are bound to metallothionein in a form that may participate in storage.
