22 BIOLOGICAL PERSPECTIVE

The detailed structural studies of several biological examples of polynuclear iron(III) discussed in the preceding chapter can be correlated with the biological roles of polynuclear iron(III) (see chapter 22). Phosvitin is a major dietary constituent of avian egg yolk, the inhibition of iron absorption of which is associated with resistance to digestive proteolytic enzymes[106] and with binding of about fifty moles of iron/mole protein in a polynuclear fashion[97]. Nutritional studies have shown that dietary phytic acid (inositolhexaphosphoric acid) and phosphates greatly depress iron uptake[1], presumably by forming highly insoluble iron(III) phosphate compounds. Binding of iron by phosvitin—primarily through the phosphate groups of the serine phosphate side chains—does not lead to precipitation but still effectively makes the iron unavailable for absorption by maintaining it in a macromolecular complex. However, scant information is available on the competition for dietary iron among the variety of potential ligands and chelates available in the diet.

Gastroferrin is an endogenous macromolecular ligand secreted in the digestive tract that binds about two hundred moles of iron per mole of protein, also in a polynuclear array[117]. Consequently its role as a potential regulating agent in both normal and abnormal control of iron absorption is under investigation[108–10]. Although the protein also possesses blood-group activity, the biological implications of the simultaneous occurrence of iron(III) binding and blood-group activity are not known.

Ferritin functions as an efficient storage compound by binding iron atoms into a sphere of polymeric iron(III) that is much more compact than the iron(III) nitrate polymer and hydrolysate since it can accommodate in the same volume several times the number of iron atoms as the structural models. The iron(III) nitrate gel, however, appears to be close in density to the ferritin core. The cores are prevented from aggregating by a surrounding layer of polypeptide. By contrast haemosiderin appears to consist largely of aggregates of ferritin cores formed when the ferritin subunits are unavailable. However, haemosiderin iron is known to be formed directly, not via ferritin, particularly in iron-storage pathologies. Although the major function of iron-dextran is to provide iron rather than to store it, the structural features of a polymeric iron core solubilised by a protective organic coating that can be metabolised, seems appropriate for this role.

Sizable polynuclear clusters of iron(III) are now known to be widespread in biological systems. These clusters, which vary in iron content from the fifty iron atoms in phosvitin and two hundred in gastroferrin, to over four thousand in a complete ferritin core, involve antiferromagnetic coupling among the bound iron(III) ions. The polynuclear nature of these iron(III) species correlates well with their particular biological effect, for example inhibition of iron absorption and storage of iron. It is anticipated that other systems binding various amounts of polynuclear iron(III) will be discovered.

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