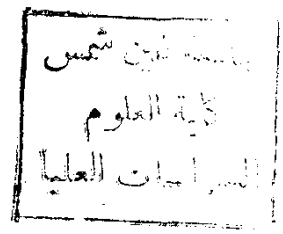
IRON DEFICIENCY AND HAIR GROWTH

A THESIS

Submitted to the Faculty of Science
University of Ain Shams



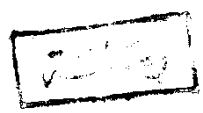
In Partial Fulfilment of the Requirements for
The Degree of M. Sc.
in Chemistry

546.126
N.M

2122

By
NAGI NAGUIB ABDEL MESSIH
B. Sc. 1975

1985



Central Library - Ain Shams University

Iron deficiency and hair growth

Thesis Approved by

Prof. Dr. Nazir Erian Milad

Professor of Inorganic chemistry.

Prof. Dr. Zenab El-Gothamy.

Professor of Dermatology.

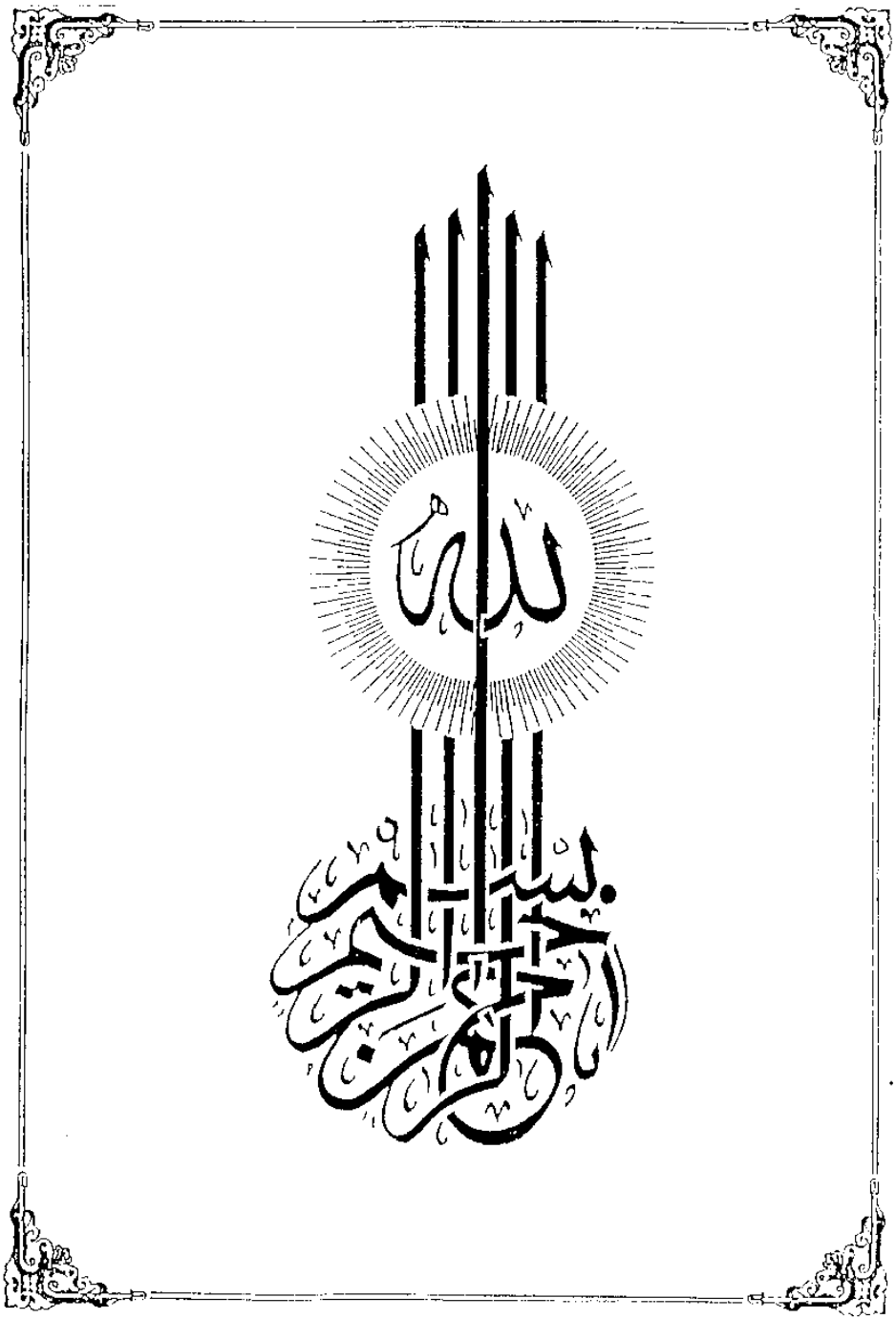
Dr. Mery Nagwa Ramsis.

Lecturer of Inorganic Chemistry.

Head of Chemistry

Department.

Central Library - Ain Shams University



Central Library - Ain Shams University

Note

The candidate has attended courses for one year in physical and inorganic chemistry covering the following topics:

1- Advanced surface chemistry.

2- " electro "

3- Statistical thermodynamics.

4- Quantum chemistry.

5- Solvent extraction.

6- Nuclear chemistry.

7- Inorganic reaction mechanism.

8- Stability constant.

9- Instrumental analysis.

He has successfully passed a written examination in these courses.

Prof. Dr.G.EL-DIN.M.MOUSSA

Head of Chemistry Department.

Central Library - Ain Shams University

ACKNOWLEDGEMENT

It is a great honour to me to take this opportunity to express my great indebtness and supreme gratitude to Professor Dr . Nazir Erian Milad Professor of Inorganic Chemistry, Faculty of Science, Ain Shams University and Professor Dr. Zinab El-Gothamy Professor of Dermatology, Faculty of Medicine, Ain Shams University for their Kind supervision direction and encouragement.

I would also like to thank Dr. Mery Nagwa Ramsis lecturer of Inorganic Chemistry, Faculty of Science, Ain Shams University, for her encouragements during the achievement of this work.

Last and not least, I would like to thank all those who were kind enough to help me with their encouragement, advice or facilities.

Nagi Naguib.

Central Library - Ain Shams University

CONTENTS

Central Library - Ain Shams University

Vitae

Nagi Naguib Abdel Messih born in Cairo (1954) received his secondary school education at Heliopolis secondary school, where he obtained the secondary school certificate in 1971. He joined the college of Science, University of Ain Shams, obtained the B.Sc degree in Chemistry in 1975. In 1981 he joined the graduate School of Chemistry at Ain Shams University and after passing successfully the necessary examinations in Inorganic, analytical and physical Chemistry in 1982 he started the research programme of the present study.

Central Library - Ain Shams University

CHAPTE I
INTRODUCTION

Central Library - Ain Shams University

CHAPTER I

Iron is a member of the group of transition metals which share two important properties, the ability to exist in several oxidation states and the ability to form stable complexes. It is these properties which have made the transition elements important components of electron and oxygen carrying proteins

Among the metallic elements, iron easily qualifies for preeminent interest in biochemistry and medicine. Not only is it the most abundant metal, but its biochemical functions are extremely diverse ranging from the activation of oxygen, nitrogen and hydrogen to the control of electron flow through numerous bioenergetic pathways. The human body contains 4-5 grams of iron. Zinc is second, among the metals, with about 2 grams. Other metals are present in much smaller (80, 20, 9, 6 and 1 mg) for Cu, Mn, Mo, Cr and Co, respectively[1] or genuinely "trace" quantities. Of the total iron a few hundred mg are found as an essential part of various oxidative enzymes and of myoglobin. About 3 g are present in haemoglobin and the rest, amounting to between 0.5 and 2.0 g. With a great individual variation, is situated

Central Library - Ain Shams University

in organs such as the liver, spleen and bone marrow, Owing to the normal breakdown of red blood cells some 20-25 mg of iron are liberated from haemoglobin each day and this quantity is liberated into the plasma. The same quantity is of course removed from the plasma and since the total quantity of plasma iron is only 3-4 mg, it can be seen that the turnover is very rapid indeed. In plasma iron is transported bound to a B_1 -globulin, transferrin.

Iron is stored in combination with the protein apoferritin as ferritin, a compound which is readily demonstrated on electron microscopy and which has magnetic properties. Although normally in cells most iron is stored in the form of ferritin , as iron overloading occurs a greater proportion is found in the protein complex haemosiderin, which is probably composed of increasing aggregations of denatured ferritin.

The daily loss of iron from the body is only of the order of about 1 mg in the male and an average of 2 mg. in women with normal menstruation.

The term sideropenia has been used to describe the condition of iron deficiency, recognized by a low serum iron concentration with a normal haemoglobin content.

Central Library - Ain Shams University

I.1 Chemistry of Iron

I.1.a. OXIDATION AND SPIN STATES.

In common with other first series transition metals, the valence electrons of iron belong to the 3 d subshell. Because the 3d electrons are of comparable energy, the transition metals can exist in a variety of oxidation states. In different chemical settings, iron is found in oxidation states as high as Fe (VI) and as low as Fe (II). In an aqueous environment, however only the oxidation states Fe (III) and Fe (II) are stable although Fe (IV) is implicated in intermediate products of the peroxidase reaction[2]. The stable forms of iron have 5 and 6 (d) electrons, respectively

In the free (gas phase) ions, Fe^{2+} and Fe^{3+}, the five 3d orbitals are of equal energy. The valence electrons distribute themselves among these orbitals with maximum unpairing of their spins, i.e. five unpaired electrons for Fe^{3+} and four for Fe^{2+}. This situation carries over to the normal "high-spin" complexes of Fe (III) and Fe (II). If the ligands bind very strongly, however, then they may destabilize some of the d orbitals sufficiently that electrons are paired up in the remaining ones. In most such cases the complexes are basically

Central Library - Ain Shams University

octahedral with two high-and three low-lying orbitals. Placement of the valence electrons in the latter produces "low spin" Fe (III) and Fe (II) complexes with one and zero unpaired electrons respectively.

A change in spin state has marked consequences not only on the electronic properties of the iron ion, (magnetism, absorption spectra, etc.) but also on its stereochemistry. The vacant orbitals in the low-spin complexes are those pointing at the ligands, which are therefore unencumbered in forming strong, short bonds. In high-spin complexes all the orbitals are partially filled and iron-ligand distances are consequently longer in effect an iron ion is bigger when high-spin than when low -spin. This size effect has important consequences for the chemistry of heme proteins. The porphyrin ring has a central cavity just big enough to accommodate a low-spin iron ion. When two strong axial ligands (e.g. imidazole and O_2) are bound, the iron sits in the heme plane, but when one of them is weak (e.g. water) or absent (as in deoxyhemoglobin) then the iron becomes high -spin and pops out of the plane (toward the strong axial ligand) The displacement of the iron atom upon deoxygenation of hemoglobin is believed to be a key facet

Central Library - Ain Shams University

of both reversibility and cooperativity in oxygen binding[3,4].

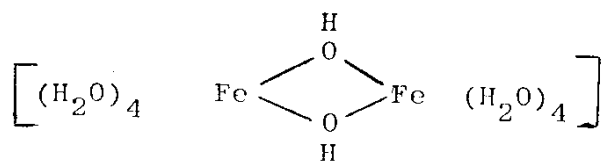
I.1.B. COMPLEXATION AND HYDROLYSIS.

Iron (III)

The Fe^{3+} ion is relatively small and highly charged It shows a marked preference for small anions such as F^-, CN^-, O^{2-}, OH^- and also RO^- i.e. alkoxide, phenolate and carboxylate ions. Its affinity for alkoxide ion is such that alcoholic OH groups are readily deprotonated at neutral pH upon coordination with Fe^{3+} ion. The binding of Fe^{3+} to hydroxy-acids and sugars is strong. Its affinity for hydroxide is demonstrated by the fact that the aquo-Fe^{3+} ion, $\left[Fe(H_2O)_6\right]^{3+}$, is a stronger acid than acetic acid, its pk_a is about 3.

Because the OH^- ion has a strong tendency to bridge polyvalent ions, the product of hydrolysis is not simply $(H_2O)_5\,Fe\,(OH)^{2+}$ but polynuclear complexes such as

(5)



At higher degrees of hydrolysis, large polycations are formed [6]. These are essentially amorphous particles of hydrous ferric oxide, with a positively charged surface.

Central Library - Ain Shams University

Their reactions with acid or other depolymerizing agents are slow, and become slower with time, probably as a result of dehydration[7]. They are stable in solution for long periods of time, but precipitate if the pH is raised to neutrality. This is prevented, however, if complexing agents (e.g. acetate [8,9] or fructose[10] are present which can coat the particles. A sufficient excess of complexing agent can prevent polymerization[9] or can reduce the size and increase the reactivity[10] of the polymers.

It is also possible to limit polymerization at the dimer stage via chelating agents which bind tightly to Fe^{3+} but leave one or two water molecules coordinated[6] These chelating agents include, for example, EDTA (ethylenediamine tetraacetate), NTA (nitrilotriacetate), and also porphyrins. In each of these cases the main species present at neutral pH is $(LFe)_2\ O$, where L is the chelating agent. It is not possible to tell, in the absence of structure data, whether the formula should be $(LFe)_2 O$ or $(LFe)_2\ (OH)_2$, which differ only by a water molecule. Both linear oxo and bent hydroxy bridges have been observed in crystal structures[10] the former being more common. The dimers are labile, and react rapidly with acid.

Central Library - Ain Shams University

The solubility product constant of $Fe(OH)_3$ is about 10^{-39}. This means that the equilibrium concentration of aqueous Fe^{3+} cannot exceed about 10^{-18}M at pH 7, although it can rise to 1 M at pH 1. This does not mean, of course, that significant quantities of ferric iron cannot be found in neutral solution but only that its chemistry depends completely on the nature of the complexed species and their hydrolysis product. Their reactions are apt to be slow, either because of polymerization, or because of the need to displace tightly bound chelating agents.

Iron (II)

The Fe^{2+} ion is less polarizing than the Fe^{3+}. It is a much weaker aquoacid, with a pk_a around 7, and the solubility product of $Fe(OH)_2$ is around 10^{-15}, allowing a $\left[(H_2O)_6\ Fe^{2+}\right]$ concentration near 0.1 M at pH 7. Its affinity for anionic oxygen -containing ligands is less pronounced than the Fe^{+3} ion. Both Fe^{2+} and Fe^{3+} ions appear to have comparable affinities for thiolate and sulfide ligands, as judged from the extensive chemistry of iron sulfur proteins and chemical analogs which has recently been developed [11].

Central Library - Ain Shams University