IRON IN LIVING ORGANISMS



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IRON



- Iron is essential to most living organisms
- Iron is the key component of hemoglobin
- Iron is integral part of many proteins and enzymes that maintain good health
- Iron is the most abundant transition metal in the brain
- Iron is considered as the most potent toxin
- Iron deficiency is the most widespread single deficiency worldwide.

IRON ON THE EARTH



- Iron is the most abundant metal on the Earth's.
- It makes up ~ 95% of all metals produced worldwide (~ 720 mln ton p. a.)
- It is the main element in steel; among its many uses are car panels, ship hulls and structural components for buildings.
- Iron has magnetic properties. Its presence in the Earth's core creates its magnetic field, which protects life on the Earth and suports migration.
- Iron is essential to living organisms, in particular, to humans.

IRON PROPERTIES AND FORMS



- Pure iron is a soft, silvery metal, which is highly chemically reactive.
- It quickly oxidizes (rusts) to form rust or iron oxides.
- In nature it exists in form of ores or minerals; e. g. magnetite (72% Fe) , hematite (70% Fe), goethite (72 %Fe),.....
- It is most common ferromagnetic element.

IRON IN LIVING ORGANISMS



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The Five Kingdom System



IRON IN HUMANS (1)

- he human bodies is stored as ferritin and hemosiderin remainder is stored as ferritin and hemosiderin in the liver, spleen and bone-marrow. A small amount is present as myoglobin, which acts as an oxygen store in muscle tissue.
- It plays a vital role in supporting life by taking part in oxygen transport and storage, electron transport and energy metabolism, DNA synthesis and many other functions neccesary to maintain life.
- In most organisms, intracellular concentration of Fe is from 10⁻⁵ to 10⁻¹⁸ M.

IRON IN HUMANS (2)





- Iron deficiency: people with severe iron deficiency suffer from a disease diagnosed as iron-deficiency anemia (IDA). IDA has been identified in a large percentage of the world's population with pregnant women, children, and teens at greatest risk for developing the disease.
 - Another form of iron deficiency is **sickle-cell anemia**, a genetic disorder. This disease is genetically recessive, meaning that one must have inherited a defective copy of the gene from both parents to develop the disorder. This disease is present mainly in Mediterrenean area countries.

IRON IN HUMANS (3)





- Iron overload; too much iron deposited in the body tissues (> 15 g) leads to <u>hemochromatosis</u>. It can result in serious damage to the body's tissues, including cirrhosis of the liver, heart failure, diabetes, abdominal pain, and arthritis.
- Elevated iron levels are also associated with 15 neurodegenerative disorders, e. g. Alzheimer's (AD), Huntington's (HD), Parkinson's (PD), etc. Estimated number of AD cases > 18 mln worldwide.

IRON IN HUMANS (4)



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Distribution of iron in a human body

tissue	blood	brain	liver	muscle	bone	dd-intake*
Fe	450	20-2000	250-1400	180	3-380	6-40
contet	mg/dm ³	ppm	ppm	ppm	ppm	mg









HUMANS – FORMS OF IRON



- Most of physiologically active iron (2/3) in a healthy human body is in red blood cells (RBCs) in hemoglobine (Hb), which makes up ~97% of the RBC's dry mass. Smaller amounts are present in myoglobin and in enzymes.
- 1/3 of whole iron is stored in form of ferritin and hemosiderin with their ratio ≈ 1 for healthy people.
- Trace amounts are in form of magnetite and/or *maghemite*.
- In all forms, iron exists as Fe²⁺ and Fe³⁺ ions.



FERRITIN (1)



- Ferritin is a metalloprotein that stores an excess iron in form of a hydrous ferric oxide-phosphate mineral [FeO(OH)]₈[FeO(H₂PO₄)] similar in structure to the mineral ferrihydrite. The protein is capable of storing as many as 4500 iron atoms in its interior, giving a concentration equivalent to 0.25M Fe inside the protein.
- In many organisms, including humans, the amount of ferritin is a good indicator of the sufficiency or deficiency of an organism's iron supply.



FERRITIN (2)



- Ferritins form hollow, spherical particles in which 2000 to 4500 iron atoms can be stored as Fe(III) (i.e. Fe³⁺ ions). Depending on the organism, ferritin particles are roughtly 8-12 nm in diameter, with several channels that appear to mediate iron transport to and from the interior. All ferritins are composed of 24 apoferritin monomers which associate to form a spherical particle shell apoferritin.
- Ferritin is found in all living organisms from bacteria to mammals. In animals, ferritin is found not only inside cells, but also circulating in plasma. Plasma levels of ferritin can be used as an index of iron storage deficiency.

HEMOSIDERIN



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• **Hemosiderin** is another iron-storage complex. Its molecular nature remains poorly defined, but it is always found within cells (as opposed to circulating in blood) and appears to be a complex of ferritin, denatured ferritin and other material. The iron within deposits of hemosiderin is very poorly available to supply iron when needed. Hemosiderin is most commonly found in **macrophages** and is especially abundant in the case of hemochromatosis and hemosiderosis; 4-11 times the amount of ferritin.

MAGNETITE & MAGHEMITE



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Biogentic magnetite (Fe₃O₄) and/or maghemite (γ-Fe₂O₃) have been found in many living organisms; from magnetotactic bacteria (1975) – (left) to human's brain (1992) – (right).





IRON - IDENTIFICATION



- Transmission electron microscopy (TEM); size and shape
- SQUID magnetometry; magnetic properties
- Mössbauer spectroscopy (MS); chemical form, magnetic state, valence state (Fe²⁺, Fe³⁺), superparamagnetic blocking temperature
- Magnetic force microscopy (MFM); shape and magnetic state

IRON – IDENTIFICATION (1)





 Fe_3O_4

FIGURE











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IRON – IDENTIFICATION (2) SQUID

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Comparison meningiomas vs hippocampi



IRON – IDENTIFICATION (3)



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Hb+ferritin

ferritin





- a oxyHb
- b deoxyHb
- **C** ferritin





NANO-IRON - PROPERTIES (1)



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Superparamagnetism = magnetism of small particles (1-20 nm) that are ferromagnetic in bulk



", blocked" state: e. g. $T_B = 300 \text{ K}$

Fe, d > 16 nm; for T > T_B fluctuations with frequency, f.

 $f = f_o \exp[\Delta E/k_B T]$







NANO-IRON - PROPERTIES (2)



- S. M. Dubiel et al.., Eur. Biophys. J., 28 (1999) 263
- Magnetic properties of human brain (globus pallidus) and liver



Thank you for your attention!





HEMOGLOBIN



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Hemoglobin or haemoglobin (Hb or Hgb) is the Fe-containing oxygen-transport metalloprotein in the red blood cells (RBCs). Its concentration is 16g/100 ml of whole blood i.e. $15 \cdot 10^{16}$ Hb molecules per 100 ml. The protein consists of four polypeptide chains, each of them holds a heme group with one Fe²⁺ atom.





Fe is stored as Fe(III) in a crystalline core - ferrihydrite

Fe exits as Fe(II) through the 3-fold channels



MAGNETOTACTICS

0.5µm



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• South seeking















ANEMIA



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- Too low level of healthy RBCs
- ~3 billion people suffer from it

Causes:

- excessive destruction of RBCs
- blood loss
- inadequate production of RBCs
- inherited disorders
- nutritional problems
- infections and diseases
- exposure to drugs or toxin







INHERITED DISORDERS



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Sickle Cell Anemia (SCA):most
 common among people of African heritage,
 but also Indian, Saudi Arabian, Caucasian
 and Mediterranean descent. About 1 of every
 625 Afro-American childeren is born with SCA



• Thalassemia: usually affects people of African, Mediterranean, and Southeast Asian origin, and marked by abnormal and short lived RBCs.



MAGNETITE (Fe_3O_4)



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Sites A (tetra) occupied by Fe³⁺ and sites B (octa) by Fe³⁺ and Fe²⁺ (A : B = 1 : 2). Ferrimagnetic with T_c \approx 850 K. M_s \approx 90 Am²/kg at RT.

















HEMATITE & GOETHITE



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Hematite (α -Fe₂O₃)

Goethite (α -FeOOH)



HEMOCHROMATOSIS



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Hemochromatosis, the most common form of iron overload disease, is an inherited disorder that causes the body to absorb and store too much iron. The extra iron builds up in organs and damages them.



Symptoms:

- arthritis
- liver diseases
- heart abnormalities
- cancer
- impotence











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BRAIN



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Highest content of iron:

- substantia nigra
- globus pallidus
- basal ganglia
- putamen
- red nucleus
- caudate nucleus







IRON IN BRAIN

Table 1 Iron concentrations (µg/g wet weight tissue) in various anatomical sites in PD and control post-mortem tissue as measured by absorption spectrophotometry

Anatomical region	Control $(n = 6)$	PD $(n = 6)$
Putamen	119.8 ± 11.6	148.5 ± 9.9
Caudate	99.6 ± 6.6	107.7 ± 13.4
Globus pallidus (lat)	207.0 ± 9.7	295.0 ± 12.5
Globus pallidus (med)	163.8 ± 18.3	113.7 ± 10.0
Substantia nigra	139.8 ± 13.1	280.9 ± 21.6
Frontal cortex (BA 10)	41.8 ± 8.2	51.4 ± 9.4
Parietal cortex (BA 39)	30.2 ± 9.3	42.7 ± 10.0
Temporal cortex (BA 21)	50.1 ± 8.5	49.3 ± 17.7

IRON in SN in PD



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Fe content	Tisue	Control (n=6)	PD (n=6)
[mmol/l]			
Pars	Total	7.8	14.3
Compacta	Extraneuronal	6.2 ± 1.3	8.5 ± 1.7
PC	Intraneuronal	15.2 ± 3.2	25.0 ± 6.6
	Melanin	20.5 ± 3.8	41.4 ± 5.6
Pars	Total	10.7	16.7
Reticulata	Extraneuronal	7.6 ± 1.0	13.8 ± 6.7
PR	Intraneuronal	8.1 ± 1.4	14.8 ± 7.3
	Melanin	-	-
SN	Total (PC+PR)	9.3 ± 1.2	15.5 ± 3.0



M. Morawski et al.., NIM Phys. Res. B, 231 (2005) 224

IRON IN SN



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Level of total Fe in the SN in PD is 1.3 –
3.4 times higher than in healthy controls.
Here this factor is 1.7.

M. Morawski et al.., NIM Phys. Res. B, 231 (2005) 224

HEMOSIDERIN



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Hemosiderin = Brownish pigment containing iron . Its deposits in muscle or nerve occur in: Hemosiderosis, Hemochromatosis, other systemic iron overload and local hemorrhage.





FENTON REACTION



Radicals (often referred to as free radicals) are atomic or molecular species with unpaired electrons on an otherwise open shell configuration. These unpaired electrons are usually highly reactive, so radicals are likely to take part in chemical reactions. Their chief danger comes from the damage they can do when they react with important cellular components such as DNA, or the cell membrane.



MIGRATION





Pigeon's beak





FERRITIN CORE



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• Ferrihydrite [FeO(OH)]₈ [FeO(H₂PO₄)]





FIVE KINDOM SYSTEM



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• MONERA



• PROTISTA



• PLANTAE



• FUNGI



• ANIMALS



AD & PD



- AD:Alzheimer's disease is a progressive brain disorder that gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities.
- PD: Parkinson's disease is a disorder that affects nerve cells, or neurons, in a part of the brain that controls muscle movement.
- Symptoms of PD may include:
- •Trembling of hands, arms, legs, jaw and face
- •Stiffness of the arms, legs and trunk
- Slowness of movement
- Poor balance and coordination

MACROPHAGES







Hippocampus



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Hippocampus



