



COPPER

Michaela Králíková, MD
Department of Biochemistry
Faculty of Medicine
Masaryk University

- **Cu⁺, Cu²⁺**
- **80 - 100 mg in organism, 90% in body tissues**
- **reference values Cu/S = 820 – 1400 μg/l**
males 11 - 22 μmol/l
females 12.5 - 24 μmol/l
- **Afroamericans 8 - 12% ↑**
- **90-95% in ceruloplasmin**
- **ceruloplasmin /S = 240 - 400 mg/l**

Metabolism

- **Absorption**
- **Transport and distribution in organism**
- **Excretion**

Absorption

- **10 - 70% of intake Cu**
- **RDI about 2 mg/d**
- **SOURCES:** sea fish, cereals, nuts, cocoa, liver
- **small intestine**
- **chelate complex with aminoacids (His), or metalothionein bounded**
- **competition with zinc**

Transport and distribution in organism

- **chelate Cu – AA transported to portal circulation, where Cu binds to albumin, His or transcuprein**
- **in liver 90% binds to newly synthesized ceruloplasmin**
- **in blood 90-93% in ceruloplasmin**

Excretion

- faeces (1.5 - 2 mg/d) – bile and shed mucosal Cu
- urine - 1 - 2% Cu absorbed ~ < 100 µg/d
assessment for dg and therapy control of **Wilson's disease**

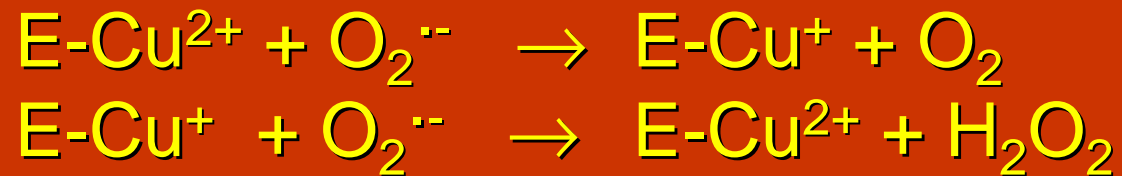
Importance

- Part of enzymes: **cyt c-oxidase, SOD, MAO, tyrosinase, dopamine- β -hydroxylase, lysyloxidase**
- Part of pigments, for example keratin
- Necessary for catecholamines metabolism, production of connective tissue , CNS and ercs function
- Antioxidative function

SOD



SOD 1 (cytosol), EC-SOD: contains Cu and Zn



Zn²⁺ - stabilisation function

SOD 2 (mtch): $\text{Mn}^{2+} \leftrightarrow \text{Mn}^{3+}$
← antioxidative activity

ceruloplasmin –

catalyses



(protects Fe²⁺ from participation in Fenton reaction)

← antioxidative activity

Cu in Fenton reaction



← prooxidative activity

Deficiency

- **inborn: Menkes disease**
- **obtained**

Menkes disease (Kinky (steely) - hair disease)

- GR heredity
- gene mutation of transport IC ATPase 7A → intestinal absorption impairment
- PCR prenatal dg
- ↓Cu, ceruloplasmin and Cu-enzymes
- most of children die within 3 years
- growth and skeletal defects, mental and physical retardation, brain and typical hair symptomatology

Obtained deficiency - causes

- **malnutrition**
- **parenteral nutrition without Cu supplementation**
- **zinc or long-term D-penicilamine therapy**
- **diarrhoea**

Obtained deficiency – clinical symptoms

- **hypochromic normocytic anemia**
- **neutropenia**
- **bone metabolism disorders (lysoxidase)**
- **GIT disorders**
- **depigmentations**
- **demyelination**

Toxicity

- ↑ Cu in hepatitis, acute leukemias, lymphomas, MM, melanoma, schizophrenia
- **Acute intoxication** - >250 mg Cu, nausea, emesis diarrhoea, epigastrium pain; shock, coma and acute hepatal and renal failure
- **Chronic intoxication** - cirrhosis (children in India, milk and water stored in brass vessels)

Wilson's disease

- AR heredity
- gene mutation of transport IC ATPase 7B →
- ↑ Cu absorptin, Cu bile elimination disorder, Cu-ceruloplasmin bound defect, ↓ or none ceruloplasmin synthesis
- manifests usually between 10th – 20th year
- ↓ **total Cu /S** (6.3 – 9.4 $\mu\text{mol/l}$), ↑ **free Cu /S**,
↓ **ceruloplasmin /S** (<0.2 g/l) , ↑ **urine excretion**
(> 1.57 $\mu\text{mol/d}$ = > 400 $\mu\text{g/d}$)

Wilson's disease

- **free copper attacks:**
- **liver:** icterus, anorexia, nausea, weight loss, haemorrhagic diathesis, cirrhosis
- **brain:** basal ganglion dysfunction → rigidity or tremor, dystonia, speech disorder
- **kidneys:** ↑ urine excretion
- **cornea:** brown-green Kayser-Fleischner ring

Wilson's disease

- ATP7B gene molecular PCR analysis – detection of latent disease
- Examination of relatives (brothers and sisters) is necessary!
- (Cu/S, ceruloplasmin/S, Cu/U; PCR)
- **Therapy:** D-penicillamine (1 - 2 g/d)
 - Zn (25 - 50 mg 3x per day between meals)
 - vit. B₆ (penicillamine is its antimetabolite)