Copper [Cu]

Table of contents

1	Ove	rview	1	
2	Mac	cro clinical perspective	2	
3	Cop 3.1	per metabolism Copper absorption	2	
	3.2	Copper Bioavailability	2	
4	Function			
	4.1	Metabolic Functions	3	
	4.2	Iron utilization	3	
	4.3	Vascular function	3	
	4.4		3	
	4.5	Skeleton	3	
	4.6	Oxidative damage defense	3	
	4.7	Myelination	3	
	4.8	Reproduction	3	
	4.9	Hormone synthesis	4	
5	Multi-Copper Oxidases (MCOs)			
	5.1	Ceruloplasmin	4	
	5.2	Hephaestin	4	
	5.3	Zyklopen	4	
Re	eferen	nces	5	

1 Overview

• Copper(Cu) is the 26th element in abundance in the crust of the earth¹.

- 29th periodic element
- 2 stable and 9 radioactive isotopes¹

2 Macro clinical perspective

- Cu is only needed in only trace amounts in humans. Total Cu in the body is >100 mg¹. The skeleton and muscles account for 1/2 of the Cu in the body¹.
- Most Cu in the body exists copper almost always exists in biological systems bound to proteins¹. Free copper in cells and in the body is extremely low¹
- High [Cu] is related to metabolic activity of organs¹. Kidney and liver have the highest [Cu], followed by the brain ($\sim 5 \mu g/g$), then the heart¹.

3 Copper metabolism

3.1 Copper absorption

- Copper absorption is considerably higher than for that of other trace elements $(\sim 55-75\%)^1$
- Relative amount of copper in the diet seems to be inversely correlated with percent intestinal absorption¹. Percent absorption increases during states of deficiency¹.
- Copper absorption occurs mainly in the upper small intestine¹

3.2 Copper Bioavailability

- Dietary factors (i.e. iron, vitamin C, and Zinc) have been reported to exert adverse effects on the bioavailability of copper¹
- Other factors impact Copper's bioavailability, such as lead poisoning, hemochromatosis, and excessive ingestion of soft drinks¹

4 Function

Through copper's enzymes (Multi-copper oxidases) copper has the unique ability to convert O_2 into H_2O without producing oxidative "exhaust"². This allows our bodies to manage O_2 without being negatively affected by its toxic and highly reactive nature²

4.1 Metabolic Functions

Copper plays a crucial role in energy transformation in the body¹. Copper impacts this process by acting as a cofactor for cytochrome c oxidase (Terminal enzyme in the electron transport chain)¹

4.2 Iron utilization

Copper is important in the normal utilization of iron in the body¹. From Intestinal iron absorption, iron release from stores (e.g. in macrophages of liver and spleen), iron incorporation into hemoglobin, and even preventing anemia¹.

4.3 Vascular function

- Blood coagulation is assisted by copper¹.
- Blood pressure control¹
- Cross-linking of connective tissues in arteries¹

4.4 Cardiac function

• Cross-linking of CT in heart¹

4.5 Skeleton

• Cross-linking of CT in bones¹

4.6 Oxidative damage defense

• Defense against oxidative damage¹

4.7 Myelination

• Myelination of brain and spinal cord¹

4.8 Reproduction

• Copper has a function in reproduction¹

4.9 Hormone synthesis

• Copper plays a role in hormone synthesis¹

5 Multi-Copper Oxidases (MCOs)

3 Multi-Copper oxidases have been detected in humans:²

- 1. Ceruloplasmin²
- 2. Hephaestin²
- 3. Zyklopen²

All 3 of these enzymes have a high specificity towards iron with the resulting ferroxidase activity being associated with ferroportin (the only known iron exporter protein in humans.)²

Ferroportin exports iron as Fe2+, but transferrin, the major iron transporter protein of blood, can bind only Fe3+ effectively. Iron oxidation in enterocytes is mediated mainly by hephaestin thus allowing dietary iron to enter the bloodstream²

5.1 Ceruloplasmin

Function: Release of iron from the liver relies on ferroportin and the ferroxidase activity of ceruloplasmin which is found in blood in a soluble form²

5.2 Hephaestin

Iron oxidation in enterocytes is mediated mainly by hephaestin thus allowing dietary iron to enter the bloodstream²

5.3 Zyklopen

Zyklopen is involved in iron efflux from placental trophoblasts during iron transfer from mother to fetus 2

References

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- 2. Vashchenko G, MacGillivray RTA. Multi-copper oxidases and human iron metabolism. $Nutrients.\ 2013;5(7):2289-2313.\ doi:10.3390/nu5072289$