

ABSTRACT

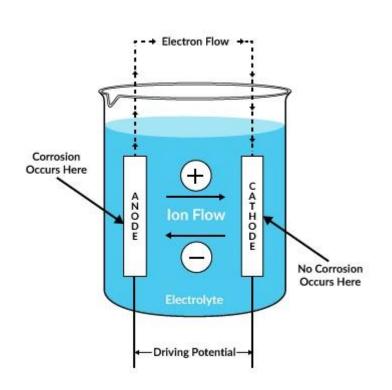
Though copper plays a vital role in the human body, an excess of inorganic copper may be fatal. Patients with the genetic recessive Wilson's Disease have an excess of copper that provides reducing effects that form free radials and peroxides that may cause damage to liver cells and the overall health of the body.

INTRODUCTION

By definition, Wilson's disease is a recessive genetic disorder that causes the body to remove copper inadequately. This results in a buildup of copper that will lead to symptoms such as swelling of the limbs, abdominal pain, personality shifts, incoordination, and unique Kayser-Fleischer rings around the irises.

Copper is one of three heavy metals essential for human life along with zinc and iron, but in excess, it can cause an imbalance with zinc and iron. Since the body is one big galvanic cell, zinc and copper electrodes are utilized for the oxidation states within the blood, nerves, bones, and connective tissue.

Copper that enters the body through organic means (food) is bound to organic ligands² that are nutritionally beneficial, unlike inorganic means such as ingesting pennies, electrical wires, etc. that can transform nutrition into a neurotoxin as strong as mercury or lead. An abundance of free copper causes a shortage of zinc and an inverse effect on the oxidative stress of the body, meaning cardiolipin (CL) fragments build up and damage the mitochondria, possibly leading to cell death. Therefore, as a treatment, zinc gluconate can be utilized to release copper back into the bloodstream to continue its elimination through the kidneys.¹



The human body acts as a galvanic cell as copper reduces molecular oxygen.¹³

COPPER FUNCTIONS IN THE BODY

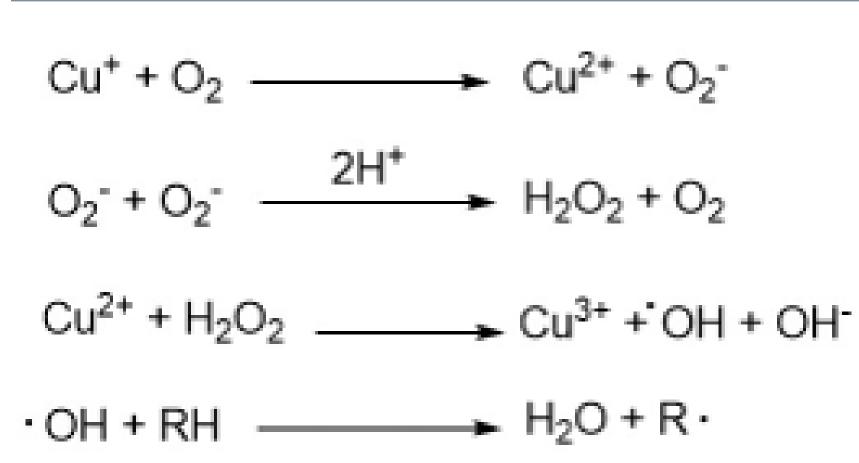
Typical uses of copper in the body³:

- Helps with the creation of red blood cells
- Keeps nerve cells and immune system in check
- Forms collagen for bones and connective tissue
- Aids in the reduction of free radicals that can damage cells
- Absorbs iron
- Makes energy

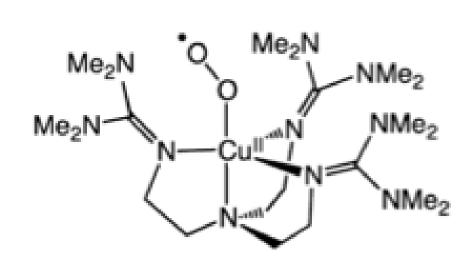
Copper Toxicity and Disease States: Wilson's Disease

Alexis Harris, Lilia Koelemay, Emily Howard

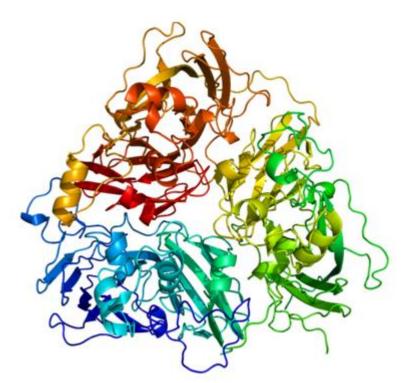
EFFECTS OF WILSON'S DISEASE



Copper II normally forms stable complexes with superoxide.^{4,5}



(TMG₃tren)Cu^{II}-OO'



hydrogen peroxide.⁹

Patients with Wilson's disease have a lack ceruloplasmin, a protein that binds the metal. Lower amounts of ceruloplasmin result in up to 50% more copper in the body than normal, which affects the liver, kidneys, and CNS.^{4,8}

Copper also reduces levels of oxidized glutathione, which removes

REFERENCES

¹Wilson's Disease Association. About Wilson's Disease. http://www.wilsonsdisease.org/about-wilson-disease (accessed Feb. 28, 2017).

²Wu, F., Wang, J., Pu, C., Qiao, L., Jiang, C. 2015. Wilson's Disease: A Comprehensive Review of Molecular Mechanisms. *Int. J. Mol. Sci.* 16.

³University of Maryland Medical Center, Copper, Ehrlich, S.D., Phoenix, AZ. Jan. 2, 2015. The Essentials of Copper: Your Body's Protective and Anti-Aging Metal, Pickart, L. http://skinbiology.com/copper-the-protective-antiaging-metal.html

⁴Aust, S. D.; Morehouse, L. A.; Thomas, C. E. Role of Metals in Oxygen Radical Reactions. *J. Free Radicals Biol. Med.* **1985**, *1*, 3-25.

⁵Tetsuro, T.; Yuri, O.; Atsushi, K.; Minoru, K.; Hideki, S.; Nobutaka, F.; Takashi, O.; Shinobu, I. Redox Properties of a Mononuclear Copper(II)-Superoxide Complex. Inorg. Chem. 2013, 52, 10431-10437.

⁶Hironori, N.; Ikuo, I.; Ayano, I.; Haruki, K.; Tsuyoshi, S.; Kei, M.; Tomoko, M.; Tohru, Y.; Kotaro, A.; Shigeo, K.; Shinji, U.; Kunihiko, K.; Masaki, T.; Tomoo, F.; Hirokazu, T. Relationship Between Oxidative Stress and Antioxidant Systems in the Liver of Patients With Wilson Disease: Hepatic Manifestation in Wilson Disease as a Consequence of Augmented Oxidative Stress. Pediatr. Res. 2006, 60, 472-477.

⁷Hochstein, P.; Kumar, S.; Forman, S. J. Lipid Peroxidation and the Cytotoxicity of Copper. Ann. N. Y. Acad. Sci. **1980**, 355, 240-248.

⁸Wikipedia. Ceruloplasmin. https://en.wikipedia.org/wiki/Ceruloplasmin (accessed Apr 7, 2017).

⁹Wikipedia. Glutathione. https://en.wikipedia.org/wiki/Glutathione (accessed Apr 7, 2017). ¹⁰National Institute of Diabetes and Digestive and Kidney Diseases. Wilson's Disease. https://www.niddk.nih.gov/health-information/liver-disease/wilsondisease (accessed Apr 8, 2017).

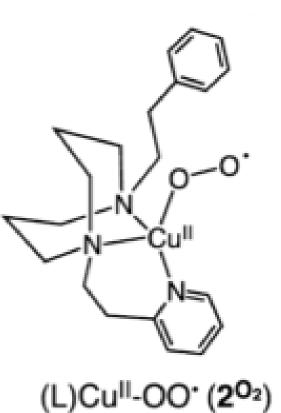
¹¹Gaetke, LM; Chow, CK. Copper Toxicity, Oxidative Stress, and antioxidant Nutrients. *Toxiciology*. **2003**. Vol 189, 147-163. ¹²University of Cambridge. Alternatives to aluminum metallization. https://www.doitpoms.ac.uk/tlplib/electromigration/alternatives.php (Accessed Apr. 8, 2017).

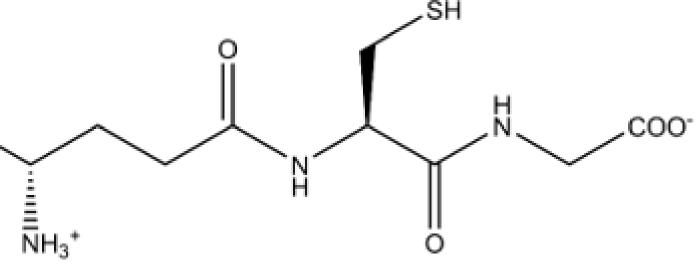
¹³Advanced Piping Products. Corrosion Part 2: The Nitty Gritty. http://blog.appinc.co/corrosion-part-2-the-nitty-gritty. (Accessed Apr 8, 2017).

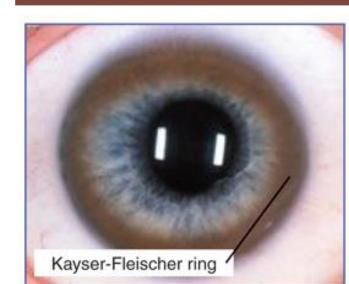
¹⁴ Fischer, P. W.; Giroux, A.; L'Abbe, M. R. The effect of dietary zinc on intestinal copper absorption. *Am. J. Clin. Nutr.* **1981**, *34*, 1670-1675.

cleave DNA.⁴

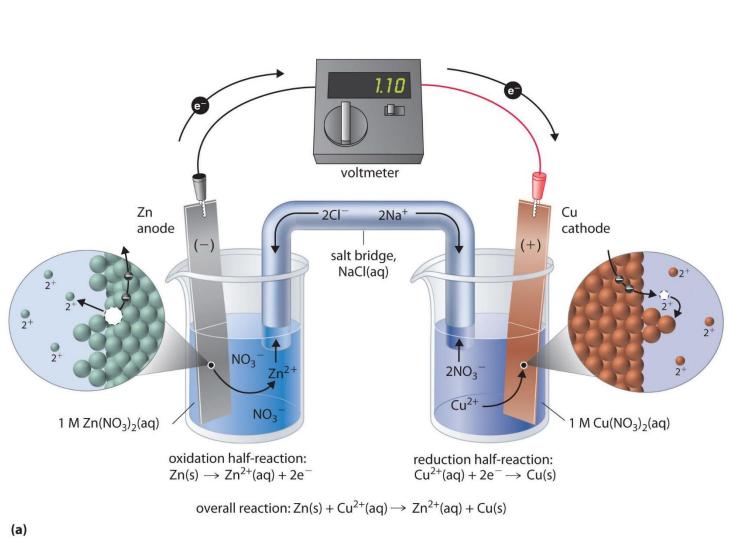
Copper is oxidized by molecular oxygen to form free radicals that can change the structure of hepatocyte organellar lipids and thiol-containing proteins, causing the liver damage seen in Wilson's Disease.³ The superoxide produced or a thiol present in the cell can oxidize copper further to product hydrogen peroxide, which can form oxidants that can







- copper is deposited after it enters the blood.¹¹
 - Manifested by Liver Cirrhosis (liver scar tissue)
 - Also causes the rupture of red blood cells (hemolysis)
 - Estimated lethal dose in adult human is 10-20 g¹¹
- Cupric and cuprous copper ions can both be reduced; and cuprous is capable of reacting with hydrogen peroxide and forming the hydroxyl radical (strongest biological oxidizing agent) which breaks DNA strands.¹¹
 - Copper catalyzes this process.
- Inorganic copper has an Face Centered Crystalline structure.
- Inorganic copper also causes an imbalance of zinc acting as a galvanic cell, which allows cardiolipin fragments to accumulate and lead to cell death.
- The treatment of copper toxicity includes taking zinc because it theoretically induces the synthesis of copper binding ligands and therefore allows the copper to be flushed from the system.¹⁴



CONCLUSIONS

While copper toxicity in a normally functioning human body only occurs with the ingestion of inorganic copper, those that suffer from Wilson's Disease accumulate an excess amount of organic (non-toxic) copper, and scientists do not exactly know the mechanism.





Kayser-Fleischer rings are one of the most visible symptoms of Wilson's Disease.¹⁰

AM CHEMISTRY TEXAS A&M UNIVERSITY

Chronic copper toxicity primarily affects the liver because it is the first place

