QUATERLY OF ENVIRONMENTAL ENGINEERING AND DESIGN
Vol. 172(52) 2018

**Katarzyna Kempka[*], Piotr Kamiński[†], Grażyna Malukiewicz[‡], Maria Bogdzińska[§]**

# COPPER AS AN ANSWER ON THE IMPACT OF OXYDESS STRESS ON THE EYES

*S u m m a r y*

*The eyes are exposed to many factors, that contribute to the deterioration of their condition. These include environmental conditions and the influence of reactive oxygen species ROS and oxidative stress. Research shows, that one of the most important tasks of created in such way state of emergency is maintenance of relative balance between oxidants (contributing to the formation of ROS) and antioxidants (restraining their effect). Some chemical elements, especially copper, play a key role in blocking ROS and are a key response to the detrimental effect of oxidative stress. The paper presents an overview of information on the impact of oxidative stress on the eyes and the defense mechanisms with the participation of copper.*

Key words: copper, reactive oxygen species, antioxidation, eyes, environment

## INTRODUCTION

The eyes are exposed to many harmful factors from the environment, i.e. directly from outside of the body (external factors), but also to the so called internal

[*] Department of Biotechnology, Faculty of Biological Sciences, University of Zielona Góra
[†] Department of Ecology and Environmental Protection, Department of Medical Biology, Collegium Medicum im. Ludwika Rydygiera in Bydgoszcz of the Nicolaus Copernicus University in Toruń
[‡] Department of Eye Diseases, Collegium Medicum Ludwika Rydygiera in Bydgoszcz of the Nicolaus Copernicus University in Toruń
[§] Department of Genetics and Fundamentals of Animal Breeding, Faculty of Animal Breeding and Biology, University of Technology and Life Sciences Jan and Jędrzej Śniadeckich in Bydgoszcz

factors. Environmental conditions, which include pollution of the environment with heavy metals, accelerates the formation of certain eye diseases (cataract, AMD macular degeneration, diabetic retinopathy, glaucoma). The interaction of reactive oxygen species ROS, both directly and indirectly (e.g atherosclerosis, cancer, immune disorders) in many physiological situations can contribute to the formation of highly dangerous to organism reactive oxygen species, that are direct cause for the formation of oxidative stress. The effect of this stress are numerous pathophysiological changes in internal organs [Asbell et al. 2005; Thiagarajan and Manikandan 2013]. However, there are chemical compounds that neutralize this adverse effect of ROS and oxidative stress. They are antioxidants. It is extremely important to maintain in the biological systems a balance between oxidants (compounds that contribute to the formation of ROS and oxidative stress), and antioxidants. The imbalance of this balance may cause many unfavourable changes, including in the eyes [Asbell et al., 2005; Iwaszkiewicz-Bilikiewicz 2008; Bartosz 2013; Thiagarajan and Manikandan 2013].

## CHEMICAL ELEMENTS AND OXIDATIVE STRESS IN THE EYES

Chemical elements are characterized by both oxidative and antioxidant effect. It has been shown that Fe, Cu, Zn, Mn, Co have the features of antioxidants. However, heavy metals (Cd, Pb, As, Be, Hg) are very strong oxidants. Between the elements there are simultaneously constant and often increasing significant interactions, both synergisms and antagonisms. These are very often the main factors in the formation and development of pathophysiological changes, and in their consequence - diseases, including eyes [Kabata-Pendias and Pendias 2001, Kabata-Pendias and Szteke 2004; Kabata-Pendias and Mukherjee 2007].

## REACTIVE OXYGEN SPECIES

Oxygen, essential for proper life cycle of cell, may in some circumstances be toxic. Full reduction of its molecule, is the basis of aerobic respiration and one of the basic metabolic reactions of each cell. It becomes dangerous during an incomplete reduction when RFT is created. Reactive oxygen species are radicals that behave as single molecules during the reaction. They exhibit paramagnetic properties and high reactivity. ROS are formed primarily during various oxygen reduction reactions. The then formed radicals showing greater reactivity than oxygen in the basic triplet state [Bartosz 2013]. The main danger associated with RFT is non specific reactions with individual components of cells, the final effect of which is damage. There are many types of ROS, and some of them are shown

in Table 1. The most reactive and at the same time dangerous radical is the hydroxyl radical [Bartosz 2013; Thiagarajan and Manikandan 2013; Bhatia, Sontakke, and Abhang 2017].

*Table. 1. Selected reactive oxygen species and related forms [Bartosz 2013 modified]*

| *Polish name* | *English name* |
|---|---|
| tlen singletowy | singlet oxygene |
| ozon | ozone |
| rodnik wodoronadtlenkowy | hydroperoxyl radical |
| anionorodnik ponadtlenkowy | superoxide radical anion |
| tlenek azotu | nitric oxide |
| kwas podchlorawy | hypochlorous acid |
| rodnik acyloksylowy | acyloxyl radical |

## COPPER ANTIOXIDANT EFFECT

There are some defense mechanisms in the organism that are directed against ROS. These are pro antioxidative reactions that use antioxidants (antioxidants). Their task is to block ROS. At the same time, they inhibit the formation of oxidative stress. The cells have specialized themselves in using metals to control oxygen metabolism to prevent the formation of ROS [Haddad 2012; Bartosz 2013; Thiagarajan and Manikandan 2013]. Copper is one of such metals. Its concentration in the human body should be 12.6-25.2 μmol * L-1. However, there are often some changes in the body that require increased copper demand. These include: biliary obstruction, arthritis, cirrhosis of the liver, some cancers [Gomółka and Szaynok 1997; Heisermann 1997; Kokot Hyla-Klekot and Kokot 2015].

Copper is one of the basic building blocks of the antioxidant enzyme - superoxide dismutase SOD, which is one of the best antioxidants found in animal organisms. The purpose of SOD is to bind ROS. Most often, it catalyzes the decomposition reactions, i.e. disproportionation of superoxide anion radicals to H2O2 hydrogen peroxide and molecular oxygen - according to the reaction [Shukla, Moitra, and Trivedi 1996; Behndig et al. 2001; Wills et al. 2008; Bartosz 2013]:

$$O_2^- + O_2^- + 2H^+ \xrightarrow{SOD} H_2O_2 + O_2$$

The neutralization of the superoxide anion radical with SOD is possible due to the presence of copper at two levels of oxidation, i.e. Cu+ and Cu2+. The occurring reactions are: oxidation of copper from the first stage and divalent copper is reduced [Bartosz 2013].

$$SOD - Cu^{+} + O_2^{-} + 2H^{+} \rightarrow SOD - Cu^{2+} + H_2O_2$$

$$SOD - Cu^{2+} + O_2^{-} \rightarrow SOD - Cu^{+} + O_2$$

It should be remembered that free copper ions are toxic. Due to the fact that the above reactions are alternating, copper ions are in continuous circulation and do not pose a threat to the organism [Bartosz 2013]. At the same time, two research teams led by Behding (2001) and Willis (2009) indicate that superoxide dismutase located in the cytosol, which in its structure has Cu and Zn ions, shows high antioxidant activity in the eye lens. It has been proven that in addition to ROS blocking, copper ions stimulate their own protective cells in their eyes. The purpose of these cells is to stabilize proteins and at the same time reduction of the tendency to oxidation [Behndig et al. 2001; Wills et al. 2008].

Copper may also contribute to the formation of ROS when it occurs in the free ion state in the body. The ionic concentration of this element in the eye lens was examined [Lin 1997]. It turned out that in people with some pathophysiological changes in the eyes, Cu concentration is higher than in healthy people. An excess of copper ions leads to unfavourable activation of the Fenton reaction, during which the superoxide anion radical is formed. This reaction is possible because copper ions readily undergo redox reactions [Lin 1997; Bartosz 2013].

## SUMMARY AND CONCLUSIONS

Copper ions have a fundamental influence on the functioning of the organism, especially the eyes. They play a very important role in antioxidative processes, when they block ROS and eliminate the effect of oxidative stress. Unfortunately, in addition to positive effects, they may have a toxic effect, because their excess leads to an increase in Fenton's reaction, which has the consequence of the formation of ROS. However, by determining the concentration of copper ions in the organism it can be observed that they play an essential role in cell protection. Based on the literature review, it can be concluded that in the future the determination of copper concentration in the body will be used as one of the parameters during the diagnosis of eye diseases, among others AMD, cataracts, diabetic retinopathy, or glaucoma. These diseases are more and more common, so it is important to look for new treatments and new methods of diagnosis. Determination of copper concentration could improve the diagnosis in ophthalmology.

## LITERATURE


1. ASBELL, PENNY A., DUALAN I., MINDEL J., BROCKS D., AHMAD M., EPSTEIN S. 2005. „Age-related cataract". The Lancet 365 (9459): 599–609.
2. BARTOSZ G. 2013. Druga twarz tlenu - wolne rodniki w przyrodzie. Warszawa: PWN.
3. BEHNDIG A., KARLSSON K., REAUME A.G., SENTMAN M-L., MARKLUND S.L. 2001. „In vitro photochemical cataract in mice lacking copper-zinc superoxide dismutase". Free Radical Biology and Medicine 31 (6): 738–744.
4. BHATIA G., SONTAKKE A.N., SUBODHINI A. 2017. „Role of oxidative stress in cataractogenesis". International Journal of Research in Medical Sciences 5 (6): 2390. https://doi.org/10.18203/2320-6012.ijrms20172087.
5. GOMÓŁKA E., SZAYNOK A. 1997. Chemia wody i powietrza. Wrocław: OficynaOficyna Wydawnicza Politechniki Wrocławskiej.
6. HADDAD, HANAA H. 2012. „The Effect of Heavy Metals Cadimium, Chromium and Iron Accumulation in Human Eyes". American Journal of Analytical Chemistry 03 (10): 710–13. https://doi.org/10.4236/ajac.2012.310094.
7. HEISERMANN D. 1997. Księga pierwiastków chemicznych. Warszawa: Prószyński i S-ka.
8. IWASZKIEWICZ-BILIKIEWICZ B. 2008. „Zaćma (cataracta) Cataract", Geriatryczne problemy kliniczne, 252–54.
9. KABATA-PENDIAS A., MUKHERJEE A.B. 2007. „Trace Elements from Soil to Human". Springer-Verlag.
10. KABATA-PENDIAS A., I SZTEKE B., red. 2004. „Żelazo i mangan w środowisku - problemy ekologiczne i metodyczne". PZH.
11. KABATA-PENDIAS A., PENDIAS H. 2001. Trace elements in soils and plants. 3rd ed. Boca Raton, Fla: CRC Press.
12. KOKOT F., HYLA-KLEKOT L., I KOKOT S. 2015. „Diagnostyka zaburzeń metalami śladowymi". W Badania laboratoryjne. Zakres norm i interpretacji. Warszawa: PZWL.
13. LIN J. 1997. „Pathophysiology of cataracts: copper ion and peroxidation in diabetics". Japanese journal of ophthalmology 41 (3): 130–137.
14. SHUKLA N., NANDITA JK., MOITRA J.K., TRIVEDI R.C. 1996. „Determination of lead, zinc, potassium, calcium, copper and sodium in human cataract lenses". Science of the total environment 181 (2): 161–165.
15. THIAGARAJAN, R., MANIKANDAN R. 2013. „Antioxidants and Cataract". Free Radical Research 47 (5): 337–45. https://doi.org/10.3109/10715762.2013.777155.

16. WILLS, N.K., SADAGOPA RAMANUJAM V.M., KALARIYA N., LEWIS J.R., VAN KUIJK F.J.G.M. 2008. „Copper and Zinc Distribution in the Human Retina: Relationship to Cadmium Accumulation, Age, and Gender". Experimental Eye Research 87 (2): 80–88. https://doi.org/10.1016/j.exer.2008.04.013.