

Long-term exposure to high copper: does it affect the production of pancreatic digestive enzymes?

Copper is one of the microelements vital to maintain the physiological functions of the living organisms. Owing to its physio-chemical properties, copper regulates functions of the enzymes involved in the processes of cell respiration, free radical detoxification and keeping the balanced iron levels in cells and tissues. Disturbance in the copper body balance can lead to the severe metabolic disorders. Cellular copper pool remains under precise control of copper transport proteins; it is also regulated after changes in cellular copper concentrations. A handful of diseases are caused by the distribution in cellular copper levels. One of these, Wilson's disease, affects the patients who have inefficient copper removal from their cells and thus they accumulate toxic levels of copper ions. In the absence of the appropriate treatment, Wilson's disease seriously affects the liver, or even causes neurological disorders in patients.

Several medical reports of the pancreas inflammation in sufferers of Wilson's disease are available in the specialists medical literature. The pancreas is the organ of digestive tract that produces pancreatic juice necessary to breaks foods. Animal studies showed that low levels of copper induce remodeling of the pancreatic structure: enzyme-producing cells are replaced by fibrosis. This massively decreases capacity of the organ for pancreatic juice production.

However, there are no reports on how the increased levels of copper affect the pancreas. Therefore, in my project, I aim to investigate whether high copper doses change the pancreatic structure and functions of the organ, that in turn lead to inflammation and fibrosis. Also, I plan to test whether lack of copper balance in cells induces an increase in reactive oxygen species, as well as it dysregulates metal ion (copper and calcium ions) mediated signals in the pancreatic cells. In order to verify our hypothesis, I will use a mouse model of the long-term copper exposure, the mice injected with solutions of copper salts. After the experiment, I will analyze cellular structure of the organ, its damage and fibrosis. Next, I will assess how high copper stress changes levels of the proteins that regulate transport of copper ions into or from the cell.

The proposed study will answer the question whether pancreatic cells tolerate the excessive copper levels, also in relation to regulation of iron levels in the cells. This project will deliver now-missing knowledge about the functions of pancreatic cells under the high copper stress. Finally, this project will help us to understand mechanisms that drive severe metabolic conditions of copper storage, mainly Wilson's disease.