Zinc and Cadmium: Size Really Does Matter

Abstract
Cadmium is an environmental pollutant that can be responsible for failures in the human body. Humans are exposed to cadmium by cigarette smoke, contaminated water, and plants grown in contaminated soils. Accumulation of cadmium from our environment can interfere with a specific DNA transcription factor responsible for coding a protein, sodium-glucose transporter (SLC7A1), which regulates re-absorption of glucose into the blood. Sp1 was found to lose its binding capability with specific CC-rich DNA. We are modeling transcription factor IIα, which has a comparable structure to Sp1, the protein in study. Transcription factor IIα readily accepts a cadmium ion in place of the normal zinc ion as it has a greater affinity for it. The cadmium ion is significantly larger than the zinc, so the structure of the protein is altered to accommodate the size difference. Both the tertiary and quaternary structures are affected by this shift. Some pertinent amino acids that are displaced: arg23, his21, his25, cys8, lys15, met18, and cys5. The helix’s shift causes the transcription factor to incorrectly bind to the DNA; thus, mRNA is not correctly transcribed and the glucose regulating protein is not produced. The lack of this protein results in numerous health concerns, namely glucosuria and kidney failure. Our task is to show the specific differences caused by the binding of cadmium to transcription factor Sp1. This research may help to expand knowledge of the specific health effects of toxic cadmium.

Cadmium Use
Cadmium is produced in the environment from the extraction, smelting, and refining of metals: zinc, lead, copper. Environmental cadmium peaked in the 1960’s, has been declining ever since. Cadmium is taken in through cigarette smoke, food, and water.

Cadmium’s Effect in the Body
- Flu-like symptoms
- Problems with respiratory tract
- Kidney damage
- Renal failure
- Bone pain, osteoporosis
- Kidney shrinkage
- Loss of ability to smell
- Arthritis

Cadmium and Zinc: Size
- The zinc atom has a smaller radius than the cadmium
- The diagram above displays this difference

How Cadmium Gets to You
- Cadmium is an industrial waste and is used in battery production
- These sources then leach into the environment
- Which then contaminates water and plants; esp. tobacco
- From these sources the body takes in cadmium
- The cadmium can then bind with zinc fingers in place of zinc

Effect of Cadmium on Sp1
- The greater size of the cadmium atoms causes the helix of the transcription factor to enlarge
- The larger helix causes amino acids responsible for DNA interaction to be displaced
- Not able to bind to the DNA; Sodium Glucose transporter is not produced
- Without the transporter, Glucose is not reabsorbed into the kidneys, instead, it is excreted in the urine

Conclusion
While cadmium is a known, highly toxic metal, its use in industry is still pervasive today. Due to its use in batteries and industry, humans will continue to face exposure, and its consequences. When bound with cadmium in place of zinc, it is believed to cause a lengthening of the helix, resulting in a displacement of the amino acids. This prevents correct binding to the DNA, preventing the proper regulation of production of Sodium Glucose Transporter; thus, glucose is not reabsorbed in the kidneys. This may cause glucosuria, Fanconi syndrome, and kidney failure. Knowledgeable on the effects on cadmium, we will hopefully have greater motivation to use other materials, preventing its harmful effects.

Transcription Factors
- Regulatory proteins that bind to DNA and stimulate transcription of specific genes in RNA synthesis
- Specific transcription factor must be present for the protein encoding genes to function

Zinc Fingers
- Finger-shaped fold in a protein
- Permits interaction with DNA and RNA
- Fold created by binding of amino acids to zinc atom

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