THE ROLE OF CELLULAR REDUCING AGENTS IN THE PROTECTION OF ZINC FINGER PROTEINS AGAINST TOXIC METAL IONS

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In recent years, there has been an increasing use of silver in medicine, especially in the form of silver nanoparticles (AgNPs), which is strengthened by the antimicrobial effect of Ag(I) ions. Today 30% of nanoparticulate products contain AgNPs. Not only medical devices or bone implants, but also products for everyday use, including cosmetics, bedding, sportswear, protective equipment and food containers, are coated with AgNP for their antibacterial properties [1]. The rapid spread of these coatings increases the environment's and also the population's exposure to Ag(I) ions. However, AgNPs and the Ag(I) ions they release intracellularly can also be toxic. The intracellular dissolution of AgNP is followed by the mass formation of Ag-S bonds, therefore thiol groups in proteins have been identified as cellular targets of Ag(I) ions. Similarly, Hg(II) is an extremely toxic metal ion mostly attributed to its interaction with S-donor atoms of biomolecules, thereby altering their structure. In cell culture experiments, inhibition of zinc finger proteins (ZFPs) has been identified as one of the mechanisms of toxicity of these metal ions [2].
The zinc finger (ZF) motifs of ZFPs are responsible for molecular recognition. The structure of the ZF motif is stabilized by the tetrahedral coordination of Zn(II) and the formation of a hydrophobic core. A ZFP can specifically recognize its target sequence in the DNA molecule only if Zn(II) coordinates to the protein and stabilizes its secondary structure. Therefore, potential competition with foreign metal ions may change the DNA-binding property of ZFPs and their original function [3].
At the same time, cysteine-containing peptides or proteins present in the cells may prevent the binding of these metal ions to the ZF motifs through competition due to their high affinity toward the toxic metal ions with a soft character. In our research project, the effect such molecules was investigated. The main goal of this research was to quantify the metal ion interaction with an artificial Cys2His2-type zinc finger protein (1MEY#) in the absence and presence of DNA. We also monitored the DNA recognition ability of 1MEY# in the absence and presence of interfering agents. The results to be presented are promising and suggest that the intracellular environment is well equipped for the defence of the cell against such toxic heavy metal ions.

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