Protective Mechanism of Zinc against Cadmium-Induced Rat Testicular Cancer
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Cadmium has been suspected as a carcinogen in human. It is known that in experimental animals, transtracheal administration of cadmium compounds produces lung cancer and parenteral administration specifically induces testicular tumors.

On the other hand, it is known that zinc can prevent cadmium-induced tumor formation in rat and mouse testes, but little is known about the mechanism involved. However, there is some evidence suggesting that zinc is protective through a direct interaction with cadmium in Leydig cells, the target cell population in the tissue.

In the present study, therefore, in order to elucidate the mechanism of the protective action of zinc against the tumorigenicity of cadmium in the rat testis, the cytotoxicity of cadmium in Leydig cells, the subnuclear distribution of the metal in intact Leydig cells and isolated Leydig cell nuclei and binding of the metal to purified Leydig cell DNA, obtained from control and zinc-treated rats, were examined in vitro.

Adult male Wistar (WF/NCr) rats were treated with zinc acetate (1.0 mmole/kg), once, s. c. 24 h before examination. Rat testicular Leydig cells were isolated by the collagenase dispersion method.

The in vivo zinc acetate treatment resulted in a marked reduction of cadmium chloride-induced cytotoxicity, as reflected by a reduced loss of cellular GOT. In both control and zinc-treated cells, the cadmium content in whole nuclei was higher in isolated nuclei than in intact cell nuclei, suggesting that subcellular components other than nuclei affect accumulation of cadmium in nuclei. In both intact cell nuclei and isolated nuclei from both control and zinc-treated groups, more than 85% of cadmium found in whole nuclei was associated with chromatin and the metal found in DNA was less than 3.6%. When the cadmium content of whole nuclei in corresponding experimental systems was compared between both control and zinc-treated cells, in both systems the metal content was lower in zinc-treated cells than in control cells. Such an decrease in cadmium content in whole nuclei of both experimental systems was partially due to the reduction of the metal content in several subnuclear components including DNA.

These results suggest that zinc may prevent the tumorigenicity of cadmium in the rat testis by reducing accumulation of the metal in nuclei and subnuclear components including DNA, as well as the metal-induced cytotoxicity.