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Effect of Zineb on Male Rats

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Zineb (Zinc ethylene bisdithiocarbamate) is widely used against a variety of plant fungi in agriculture. Reports show that zineb has caused poisoning in man(HAYES. 1976). While zineb as such has not produced any tumours in animals, its metabolite,ethylene thiourea(ETU) has produced hepatic tumors in mice(INNES et al.1969). Chronic feeding of zineb has resulted in sterility,resorption of fetuses and anomalous tails in rats(KORTE 1972).

Feeding of grains treated with zineb has induced drastic reduction in egg production,thinning of egg shells and often resulted in complete cessation of egg laying in poultry birds (PICCO 1962). Zineb has induced thyroid changes (SMITH et al.1953). SMITH(1976) has studied the possible teratogenic and carcinogenic effects of ethylene thiourea-a metabolite of dithiocarbamate in rats. PETROSONI et al.(1962) have shown that zineb gets converted into ethylene thiourea under different storage conditions. IVANOVA(1969) and IVANOVA et al.(1967,1968,1971) in adult rats and SEIFTER and EHRICH (1948)in weanling rats have studied the effect of dithiocarbamate onthyroid. It has shown that toxaphene an organochlorine insecticide stimulated thyroid growth,increase in iodine uptake and caused adrenal hypertrophy in bob white quail.

NELSON and WOODARD (1949) have studied the effect of pesticides on hypophyso-adrenal system while FREGLY et al. (1967),SHETENBERG and RYBAKOVA(1968), SYROVATKA et al. (1971) have investigated the effect of different pesticides on hypophyso-thyroid system in experimental animals. WASSERMANN et al. (1971) has paid attention to the effects of organochlorine insecticide on hypophyso-thyroid system in occupationally exposed people.

The present study deals with the histopathologic changes in thyroid and testis after repeated exposure of zineb for a period of 30 days and the possible mode of action of this compound in rats.

MATERIALS AND METHODS

Male albino rats of average body weight 250 g of Industrial Toxicology Research Centre's Colony were used in this study. Rats were housed in the air-conditioned(75±2°F)

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room of the animal house for one week prior to experimentation. Rats were fed with pellet diet and water ad libitum. Rats were divided in two groups having four animals each. Rats of one group were fed with peanut oil daily for 30 days and served as controls. Animals of the other group were orally treated with zineb at the dose of 1000 mg/kg/day in peanut oil for the same period. The animals of both the groups were sacrificed on day 30. Thyroid, pituitary and testis were taken out, weighed individually and fixed in formal saline solution. After routine processing paraffin section were cut at 6/um stained in haematoxylin-eosin and studied under microscope.

RESULTS

Rats treated with zineb did not show any clinical symptoms nor died during the period of experiment. Absolute and relative thyroid and pituitary weights are summerised in Table 1. The absolute as well as relative thyroid and pituitary weight showed a significant increase ($P<0.001$ and $P<0.05$) respectively, when compared to controls. There was no significant weight change in testis of experimental animals.

TABLE 1 - Absolute and Relative Weights of Pituitary and Thyroid in Male Rats Administered Zineb (1000mg/kg/day) for 30 Days.

	Absolute organ weight		Relative organ weight	
	Pituitary	Thyroid	Pituitary	Thyroid
Treated	0.0067[a] ± 0.0004	0.0300 [b] ± 0.0008	0.0027a ± 0.0002	0.0119 b ± 0.0003
Control	0.0050 ± 0.0004	0.0132 ± 0.0008	0.0020 ± 0.0002	0.0053 ± 0.0004

Number of animals in each groups are four.
a= $P<0.05$; b= $P<0.001$.

Thyroid

Microscopic examination of the thyroid of rats treated with zineb revealed increased follicular cell height, increased follicular area and diminished stain of colloid (Fig. 1). No such changes were observed in the thyroid of control rats (Fig. 2).

Testis

The testis of zineb treated animals also showed pathologic changes. The close observation indicated that several damaged tubules were lying in association with

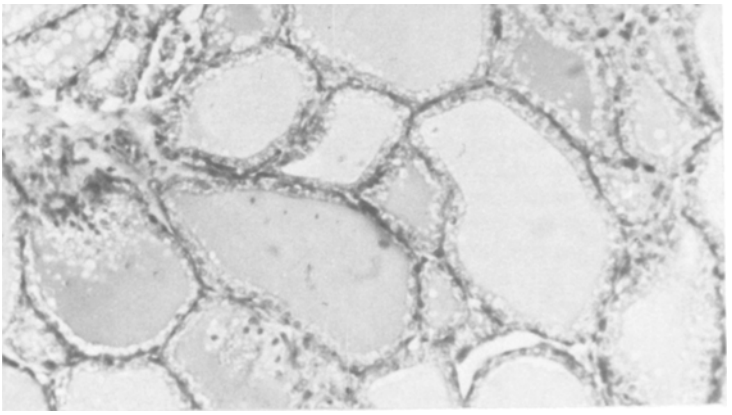

Fig. 1. Section of the thyroid after Zineb treatment for 30 days. H & E X 170.

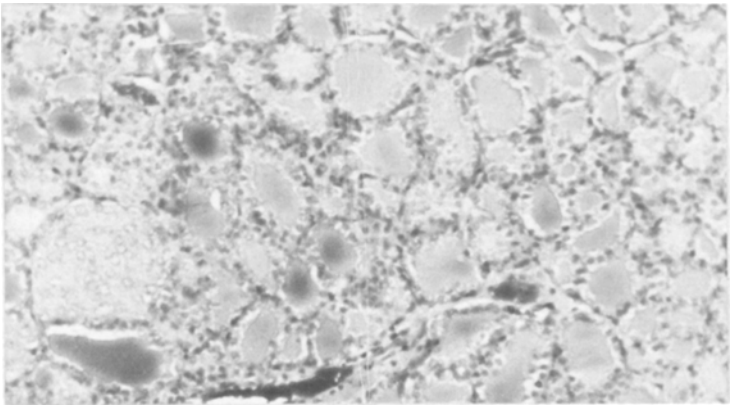

Fig. 2. Section of thyroid of control rats. H & E X 170.

normal seminiferous tubules. The lumen of the degenerated tubules were filled with necrosed cells and debris matter. Most of the tubules appeared necrotic and carried giant cells within them, often filled with oedematous fluid. The interstitial space did not show marked increase, nor the Ledig cells suffered any damage (Figs. 3, 4).

DISCUSSION

The results have shown that prolonged feeding of zineb has produced changes in the thyroid and testis of rats. There was however, no sign of poisoning nor death of animals after 30 days of repeated exposure to zineb.

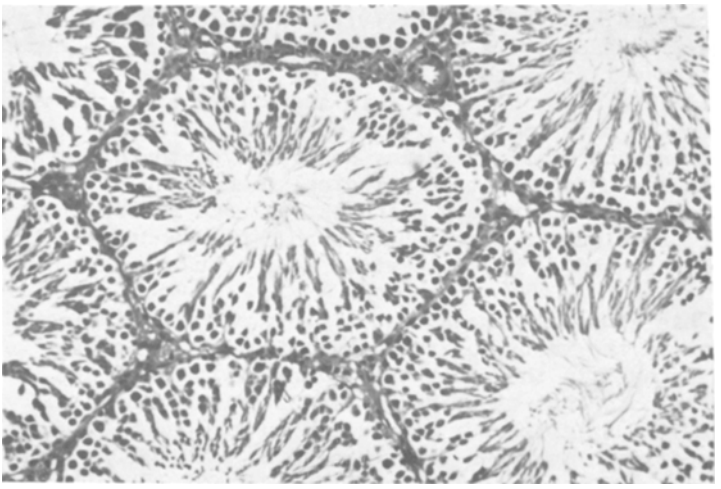

Fig. 3. Section of testis of control rats. H & E X 170.

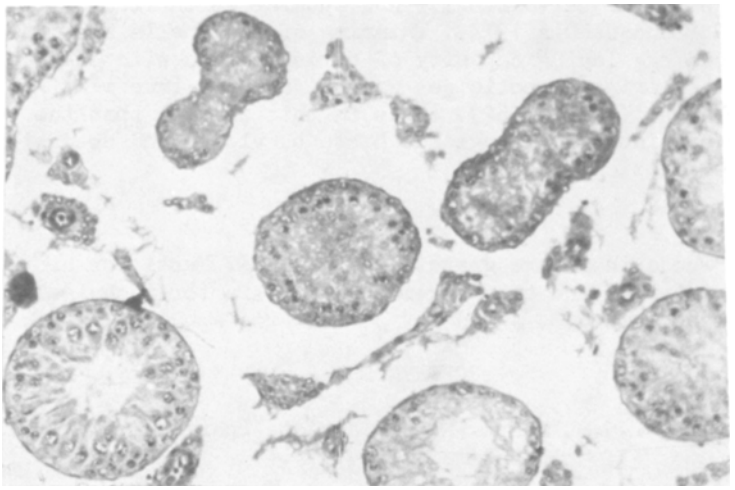

Fig. 4. Section of rat testis after Zineb treatment for 30 days. H & E X 170.

The increased weight of thyroid as well as its marked hyperplasia after zineb was very significant. These findings are in confirmity with the earlier reports (SEIFTER and EHRICH 1948, GRAHAM and HANSEN 1972). Zineb appears to block the conversion of iodide to iodine and this has resulted in the hypertrophy and marked hyperplasia ofthyroid, and decreased the synthesis of thyroxin. The fall of thyroid hormone has enhanced the synthesis and release of TSH (thyrotropic stimulating hormone)of the anterior

pituitary. SYROWATKA et al. (1971) have also noticed similar changes. Perhaps it is due to these changes that an increase in the weight of the pituitary of zineb treated rats has been noticed here. However, this needs further confirmation. The results have indicated that the action of zineb is a direct one and it is operating on hypophyso-thyroid system. The studies on the histopathological changes in pituitary, the bioassay of pituitary gland extract and radioiodine tracer technique to assess the thyroid gland activity is in progress and is hoped to yield more valuable data.

This study has shown that zineb produced pathologic changes in the testis of rats. Majority of the tubules were found damaged in the zineb treated rats. It is of significance to note that zineb has caused sterility in rats. (KORTE 1972). Testicular damage due to prolonged exposure to insecticide is known through several studies(DIKSHITH and DATTA 1972 a, b, DATTA and DIKSHITH 1973,DIKSHITH et al. 1975). Studies have also indicated that DDVP inflicts damage in the sertoli cells and tubular epithelium of rats (KRAUSE and HAMOLA 1974). Thinning of egg shells and reduced egg laying capacity of birds as seen with some organochlorine insecticides was found to be true with zineb also (PICCO 1962). It is in this context that the role of zineb as a fungicide hasto be viewed and used with proper caution.

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