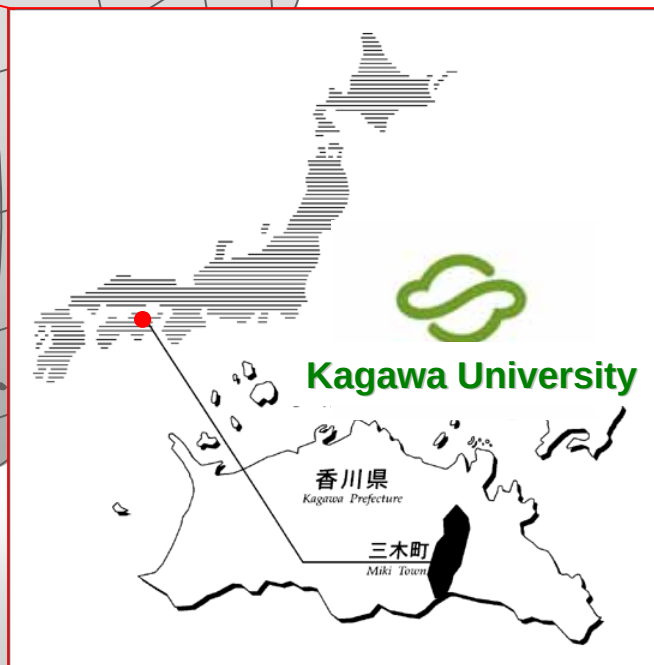
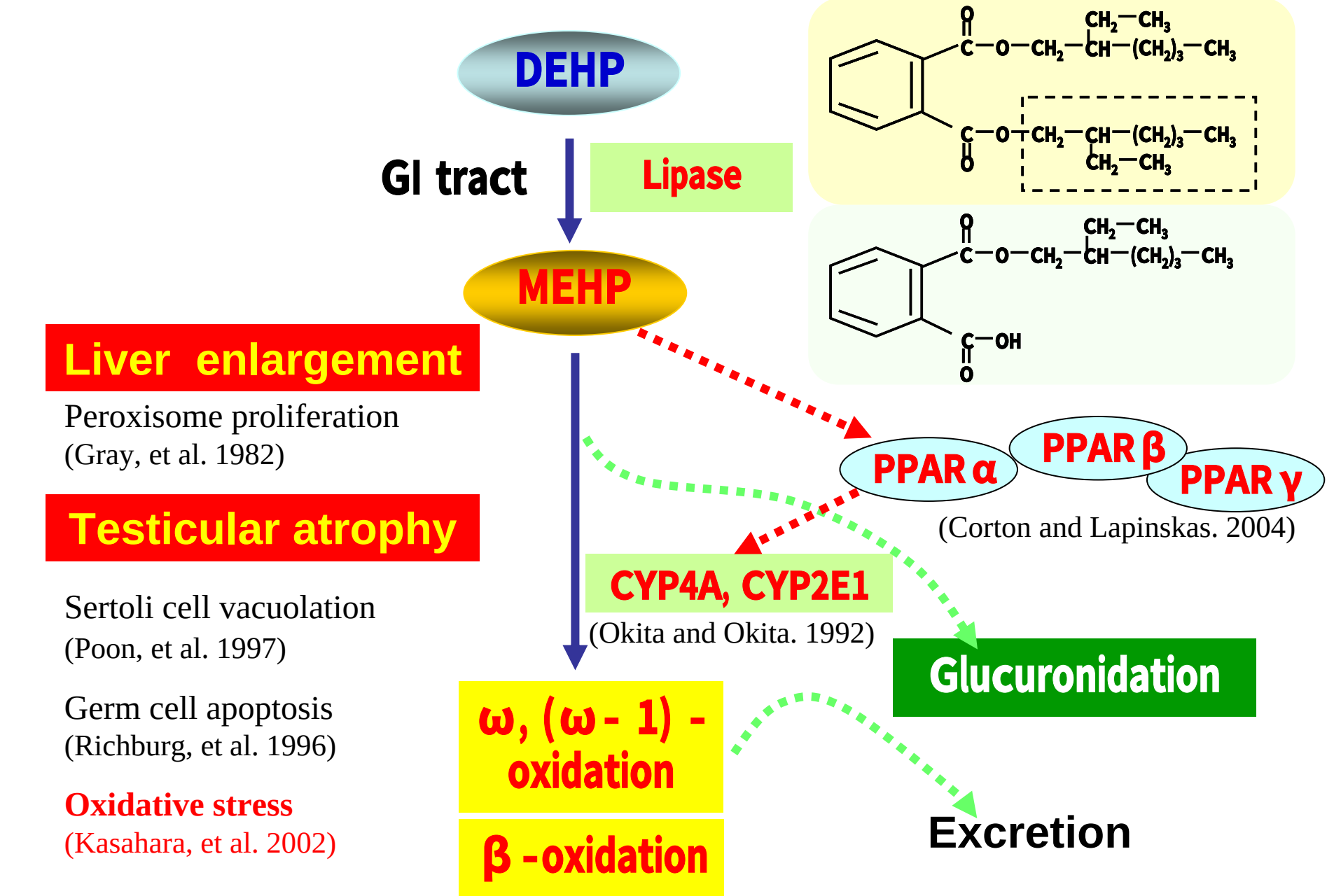
Germ cell apoptosis in rat testis is induced by oxidative stress via oral administration of di(2-ethylhexyl)phthalate, and is significantly prevented by treatment of antioxidant vitamins or special six-carbon monosaccharides.



Points of this study

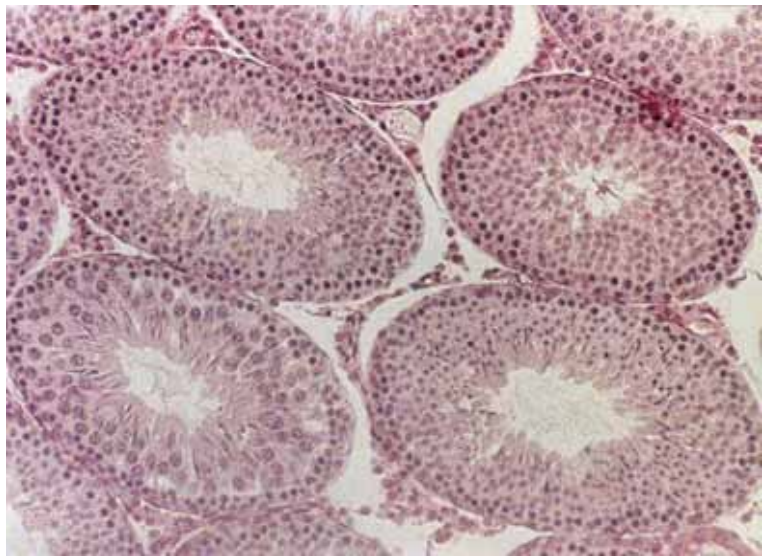
1. **Collaboration work of Departments of Cell Physiology, Hygiene and Public Health, and Urology, Faculty of Medicine, Kagawa University**
2. **Acute or subacute toxicity of DEHP**
3. **High doses (1-2%DEHP-containg diet for rats)**
4. **Oxidative stress causes apoptosis of germ cells and impairment of androgen secretion**
5. **Practical prevention approaches: Prevention of DEHP toxicity with antioxidant food additives**
6. **Molecular mechanism of the toxicity**



Metabolic map of DEHP after oral administration

Atrophic change of testis by DEHP

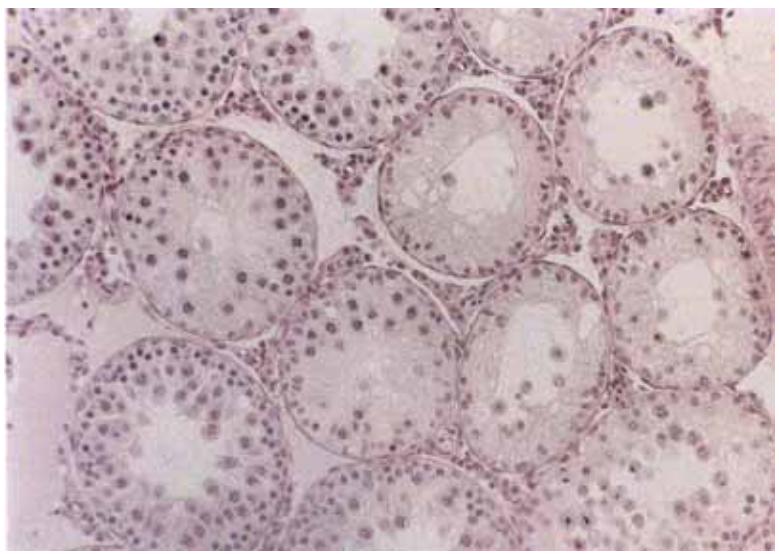
Control



Johnsen's score: 10

Normal seminiferous tubules with full differentiation.

2%DEHP

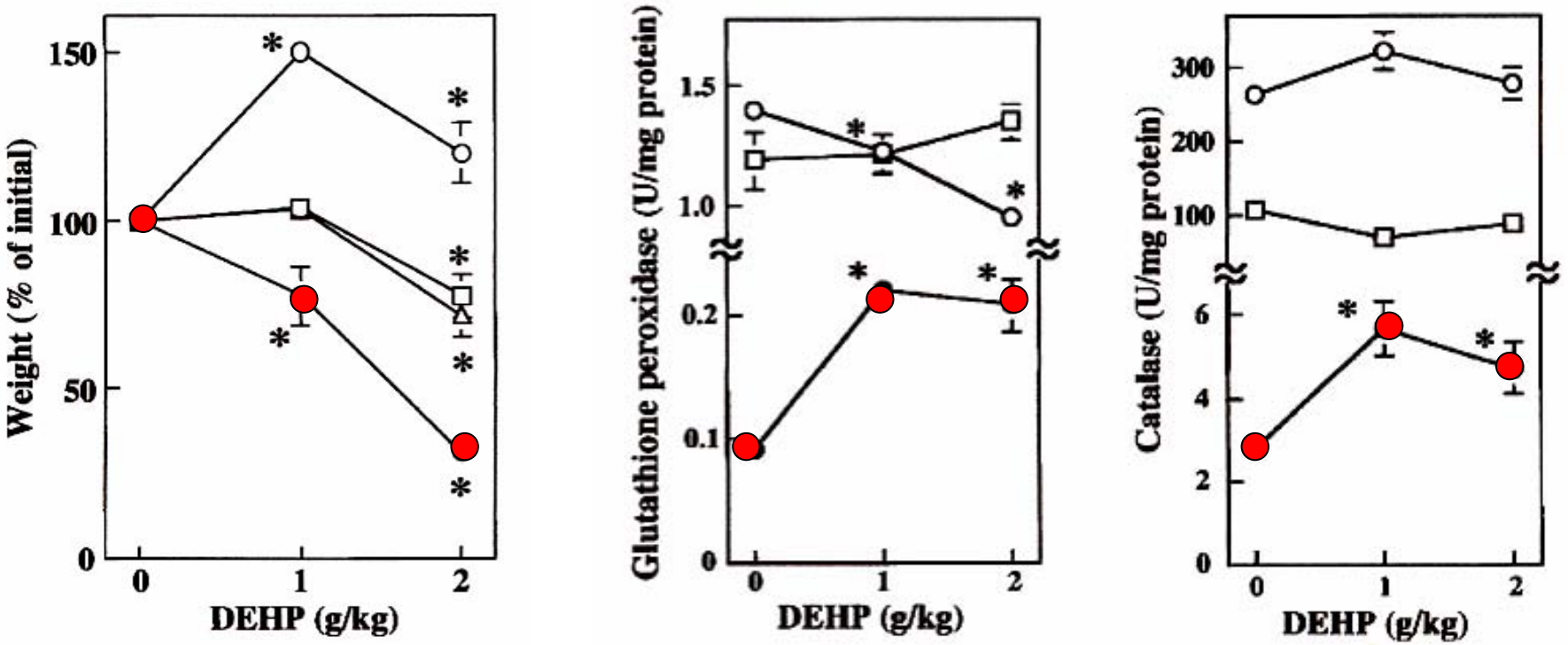


Johnsen's score: 3～4

- no spermatids,
- very few spermatocytes,
- arrest of spermatogenesis at the primary spermatocyte stage

Role of oxidative stress in germ cell apoptosis induced by di(2-ethylhexyl)phthalate.

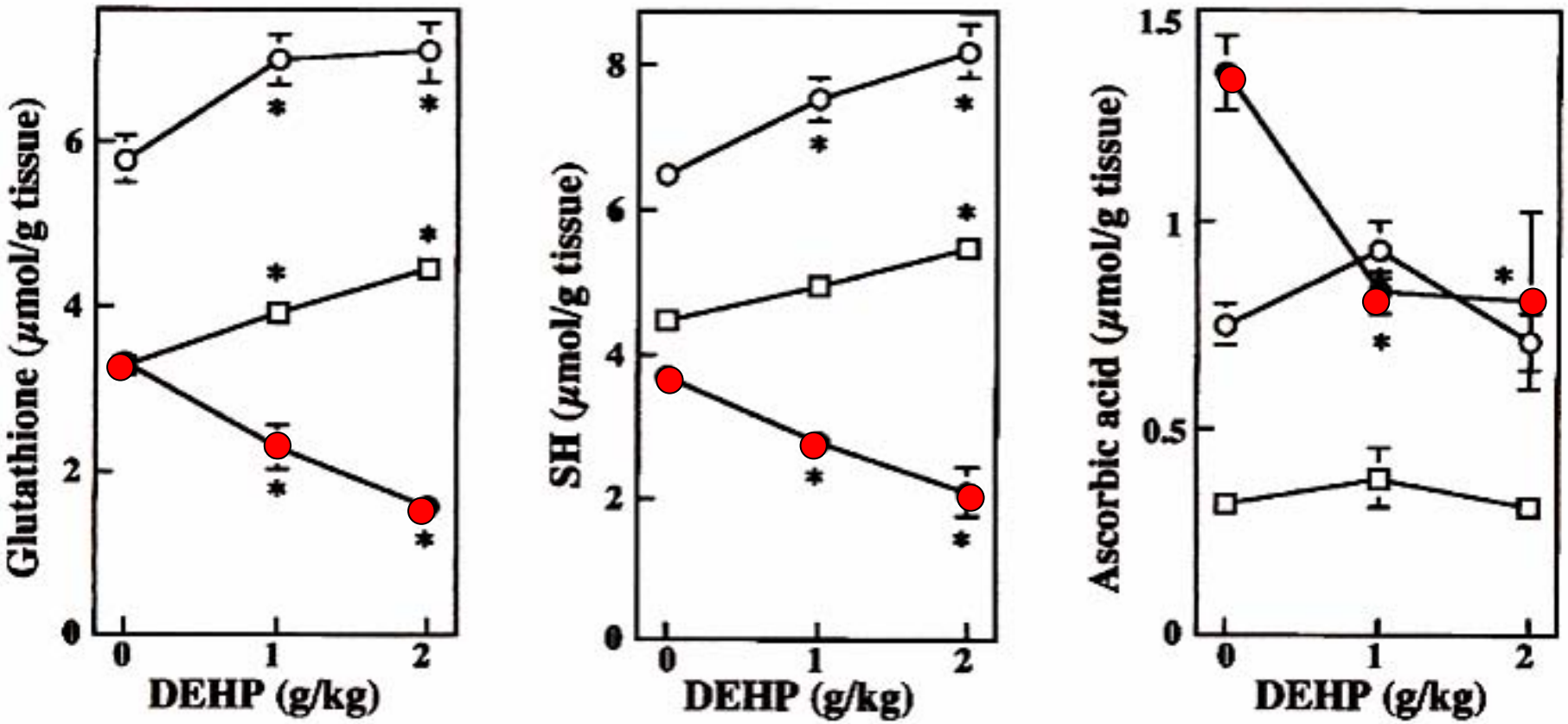
Biochem. J. 2002; 365: 849–856



△ Body weight ○ Liver □ Kidney ● Testis

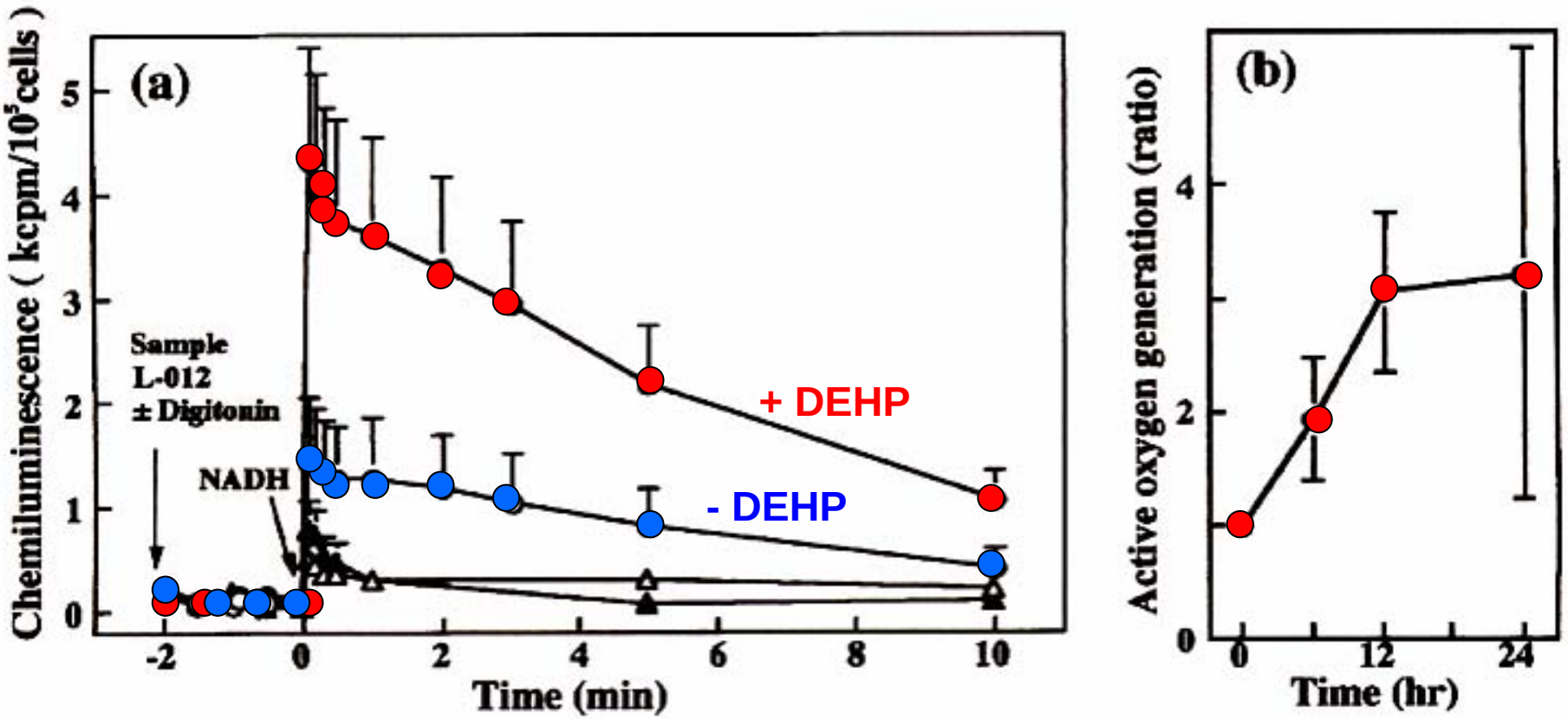
Oral administration of DEHP for 7 days induced atrophy of the testis and hypertrophy of the liver without affecting body weight.
Increase in the activity of glutathione peroxidase and catalase was found in the testis.

Decrease of antioxidant levels in the testis



DEHP significantly induces decrease in the concentration of glutathione, free thiols (SH) and ascorbic acid in the testis.

Effect of DEHP on the generation of radical oxygen species (ROS) in the testis



Generation of ROS occurred significantly higher in the testicular cells from DEHP-treated animals than those from control group.
ROS generation increased in a time-dependent manner after administration of DEHP.