Fluctuation of Lipid Peroxides and Related Enzyme Activities in SHRSP and WKY upon the Administration of CCl₄ or Triglyceride Hydroperoxide

Mitsuaki Sano, Reiko Kojima, Mutsumi Kawashima and Isao Tomita. Shizuoka College of Pharmaceutical Sciences, Shizuoka 422

The analysis of expired gases and TBA reacting substances (TBARS) in the liver has demonstrated that SHRSP degraded triglyceride hydroperoxide (TG-P) more slowly, suffering from severe hepatic lesion in comparison with WKY (Kojima et al., Jpn., Heart J., 23, 389(1981)).

In the present investigation, the fluctuations of TBARS, the activities of glutathione peroxidase (GSH-Px) and glutathione reductase (GSSG-R) were compared in the liver of SHRSP and WKY after the single P.O. administration of CCl₄ (60 µl /100g BW) or I.V. administration of TG-P (0.4 µmoles as MDA/100g BW). The changes of the enzyme activities were also examined in SHRSP whose blood pressure were lowered to the level of that of WKY by means of free access to the feed containing antihypertensive drugs.

Methods

Rats (SHRSP, WKY 4 or 7 months old) were sacrificed 3 and 15 hrs after the single administration of CCl₄ or 24 hrs after the single administration of TG-P. TBARS and the enzyme activities (GSH-Px and GSSG-R) in the liver were determined as previously described (Kojima et al., Jpn., Heart J., 23, 389(1981)). The lipid composition in the liver was analyzed according to the method of I. Kupke (J. Chromato., 146, 261, 1978). TG-P was prepared from linseed oil by lipoygenase oxidation (37°C for 30 min) followed by purification with TLC. CMF diet (Oriental Yeast Co.) containing reserpine (7mg/2kg), methyclothiazide (250mg/2kg) or hydralazine (500mg/2kg) were given ad libitum to SHRSP (5 weeks old) for 11 weeks to lower their blood pressure.

Results and discussion

No significant changes in the activities of the hepatic GSH-Px and GSSG-R were observed in WKY upon the CCl₄ administration. In SHRSP, however, the GSH-Px activity decreased to 94%, 85% and the activity of GSSG-R also decreased to 90%, 75% of the normal level, 3 and 15 hrs after the CCl₄ administration respectively.

The level of TBARS in the liver rose much higher in SHRSP (288% in 3 hrs and 496% in 15 hrs) than in WKY (134% and 174% respectively) and the concomitant increase of hepatic TG level was observed (278% and 471% in SHRSP, while 211% and 297% in WKY, 3 and 15 hrs after the CCl₄ administration respectively). The increase in the serum GPT was greater in SHRSP (1002% in 15 hrs) than in WKY (407% in 15 hrs). The administration of TG-P to SHRSP and WKY gave similar results. All these observations suggest that SHRSP with high blood pressure are more susceptible to CCl₄ or TG-P than WKY.

In order to examine the correlation between blood pressure and susceptibility to peroxide, the enzyme activities of SHRSP with blood pressure lowered from 217.6±14.16 mmHg to 142.0±6.22 mmHg were compared to those of WKY with 138.7±6.26 mmHg of blood pressure.

The activities of GSH-Px and GSSG-R in SHRSP with decreased blood pressure were 102.7±7.31, 69.58±1.90 units/mg prot. respectively while those in SHRSP with high blood pressure were 107.00±5.88 and 63.12±4.50 units/mg prot. respectively. As the former values in SHRSP were still different from those of WKY (132.0±19.83 and 54.7±2.54 units/mg prot. respectively), the enzyme activities do not appear to be related to blood pressure but regulated genetically.

(This work was supported in part by a Grant-in-Aid for Medical Research from the Ministry of Health and Welfare of Japan)