Note

Degeneration of Lymphoid Tissues in Mice with the Oral Intake of Low Molecular Weight Compounds Formed during Oil Autoxidation

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Several studies have been reported on the toxicity and nutritive problems associated with lipid peroxides produced during the autoxidation of food oils.^{1,2)} Low molecular weight (LMW) compounds, one type of autoxidation product of oils, are thought to be more toxic than the hydroperoxides to rats and mice.³⁾ The main components of LMW compounds are short-chain aldehydes such as 4-hydroxy nonenal.³⁾ The effect of these aldehydes on the animals have already been studied in detail.⁴⁾ For instance, it has been shown that 4-hydroxy nonenal inactivated glucose-6-phosphatase,⁵⁾ and that 2-alkenals readily reacted with biochemically important groups such as sulphhydryl, amino and hydroxyl.⁴⁾ However, it has not been shown whether the LMW compounds affect the lymphoid tissues. The present paper reports the degenerative effects on such lymphoid tissues as the thymus, spleen and Peyer's patches in mice by the oral intubation of LMW compounds.

LMW compounds were prepared as described previously.³⁾ Of the LMW compounds, 4-hydroxy-2-nonenal, 8-hydroxy methyl octanoate and 10-formyl methyl-9-decenoate were identified as the major constituents by gas chromatography-mass spectrometry.³⁾

Male C57 BL/6 mice (6-week old) were purchased from Funabashi Farms Co. (Chiba, Japan). To investigate the toxicity of LMW compounds as components of autoxidized oils and to give the mice an exact amount of LMW compounds, the LMW compounds were quantitatively diluted with fresh methyl linoleate (ML), which dose not cause lymphocyte necrosis. Graded amounts (30, 40, 45 and 50 mg) of LMW compounds with 100 mg of ML were given once orally to the mice of each group using a stomach tube. 150 mg of ML was administered alone as a standard. Twenty four hours after administering the

LMW compounds of ML, the mice were killed and prepared for light microscopy by the hematoxylin eosin and periodic acid-schiff staining methods.

Remarkable necrosis of lymphocytes in the thymus and the Peyer's patches, which were scattered on the ileum, was observed after the LMW compounds treatment (Figs. 1 and 2). As shown in Table 1, lymphocyte necrosis was not found when 30 mg of LMW compounds was administered. However, when 40, 45 or 50 mg of LMW compounds were dosed, 50%, 38% and 55%, respectively, of the mice examined showed lymphocyte necrosis in their thymus. In the Peyer's patches, necrosis appeared in 25%, 25% and 45% of the mice to which 40, 45 and 50 mg, respectively, of LMW compounds had been administered, (Table I). In the spleen, lymphocyte necrosis was not particularly apparent from the LMW compounds, compared with that in the thymus and Peyer's patches. Before the dose of LMW compounds (40 mg) with ML (100 mg), the body weight of the mice was 22.1 ± 1.1 g (mean $\pm$ S.D. of 4 mice). At one day after the administration, the body weight was 21.9 ± 0.6 g, indicating that the body weight had not been affected by the LMW compounds treatment.

This study shows that an oral intake of the LMW

FIG. 1. Thymus from a Mouse Treated with 45 mg of LMW Compounds.

There are numerous lymphocytic debris in the cortical and medullar zones. ($\times 700$)

FIG. 2. Peyer's Patch from a Mouse Treated with 45 mg of LMW Compounds.

There are numerous lymphocytic debris in the lymphoid tissue of the Peyer's patch. The thick arrow indicates the muscle layer of the ileum. ($\times 700$)

compounds produced in the autoxidation of oils caused significant damage to lymphocytes in the thymus and Peyer's patches. The authors have already reported that an oral intake of lipid hydroperoxides caused lymphocyte damage in the thymus of mice.⁶⁾ When 190 mg of methyl linoleate hydroperoxides (MLHPO) was administered, 29% of the mice showed lymphocyte necrosis in the thymus, and the incidence ratio was increased to 43% and 50% in mice to which 270 and 310 mg of MLHPO had been administered, respectively. The present results suggest that LMW compounds damage the lymphocytes more markedly than do the hydroperoxides. This characteristic of LMW compounds may account for their high toxicity.

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TABLE I. APPEARANCE OF NECROSIS IN THYMUS AND PEYER'S PATCHES AFTER ORAL ADMINISTRATION OF LMW COMPOUNDS TO MICE

	Thymus necrosis	Peyer's patches necrosis
[mg/22 g mouse]	[%] ^a	[%]
LMW 30 mg + ML 100 mg	0 (0/7)	0 (0/7)
LMW 40 mg + ML 100 mg	50 (4/8)	25 (2/8)
LMW 45 mg + ML 100 mg	38 (3/8)	25 (2/8)
LMW 50 mg + ML 100 mg	55 (6/11)	45 (5/11)
Untreated	0 (0/7)	0 (0/7)
ML 150 mg	0 (0/7)	0 (0/7)

^a Percentages of mice which showed the thymus or Peyer's patches necrosis to the total mice examined. Figures in parenthesis indicate the incident number of mice.

LMW compounds, low molecular weight compounds.

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