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Effect of Dietary Protein Levels on the Manifestation of Gramoxone Toxicity in Rat Liver

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Abstract

Effects of dietary protein levels on the manifestations of the toxicity of gramoxone, a bipyridine herbicide, in the liver of rats were investigated. The addition of gramoxone, with regard to the body weight and feed efficiency ratio of rats, had a more dramatic effect on animals fed a low or intermediate protein diet than for those similarly treated among rats fed a relatively high protein diet. Lipid content in the rat liver tended to increase with the addition of gramoxone into each protein diet, with the exception of the high protein-gramoxone diet. The addition of gramoxone tended to increase hepatic TBA value significantly in rats, especially among those fed the low protein-gramoxone diet or the control-gramoxone diet. Significant morphological changes, including fat changes of hepatic cells and increases in the number of Kupffer cells, were found both in rats fed the low protein diet and those fed any of the gramoxone-treated diets. Fat changes within hepatic cells were found to be especially severe in rats fed the low protein-gramoxone diet. Distributions of glycogen in rat liver appeared to increase in rats fed any of the diets to which gramoxone had been added.

Key words : dietary protein levels, gramoxone toxicity, rat liver

INTRODUCTION

Recently, there has been a heightened risk of exposure to foreign compounds, such as pesticides, solvents, food additives, various forms of dust, gases, metals, and some drugs, etc[1]. Foreign compounds can be toxic *per se*, or be metabolized within living organisms to products that cause toxic effects[2]. Among the several factors which affect the metabolic rate of foreign compounds, the nutritional status of a living organism is deemed to be the more important factor in representing the toxicity of foreign compounds. Marasmic diet, kwashiorkoric diet, and vitamin deficiency are found to increase the toxicity of foreign compounds[2-5].

According to Boyd and Krupa[6], oral administration of diuron, a herbicide, caused serious toxic changes in both the liver and kidneys of protein deficient rats. Reduction of relative spleen weight and liver necrosis were observed among the BHT-treated rats fed a 4% casein diet[7]. Madhavan and Gopalan[8] reported that the liver damage caused by aflatoxin increased markedly among protein deficient rats. Additionally, Tanaka et al.[9] showed that the absorption of paraquat in the small intestine was higher among rats fed a 5% casein diet than in those fed a 45% casein diet. Webb et al.[10] reported that rats fed 5% casein diets were more susceptible to malathion and parathion acute toxicity compared with either those rats pair-fed a 20% casein diet, or with those fed a 20% casein diet *ad libitum* .

The production and use of herbicides for destruction of noxious weeds have increased markedly. Because plants differ significantly from animals, both

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in their morphology and physiology, it might be expected that herbicides would provide little hazard of toxicity to man. There are, however, a great number of highly toxic chemicals capable of causing fatal poisonings in man and animals[11]. They permeate the soil, thus causing the soil and water to become contaminated. Of herbicides most commonly used, gramoxone (paraquat ; 1,1′-4,4′-bipyridium dichloride) has been reported to cause necrotic effects in animal lung, liver, and kidney[11]. It has been also proposed that the suggested mechanism of gramoxone toxicity is mediated by free radical reactions, and involves the damage to cell membrane[12-14].

Because the manifestations of chemical toxicity are significantly related to the nutritional status of individuals, this study is designed to determine the effects of dietary protein levels on the manifestation of gramoxone toxicity in rats′ livers. The purpose of the present study is to define how the toxicity of gramoxone is manifested in rats in relation to varied dietary protein levels, and also to show whether the toxicity of gramoxone can be modified by increasing dietary protein levels or not.

MATERIALS AND METHODS

Feeding experiment

In order to determine the effects of dietary protein levels on the manifestations of gramoxone toxicity, 36 Wistar-strained male rats, aged 6 to 7 weeks, were divided into 6 dietary groups and fed experimental diets for 2 weeks. The 6 experimental diets used were 18% casein diet as a control diet, 18% casein-0.04% gramoxone diet, 5% casein diet as a low protein diet, 5% casein-0.04% gramoxone diet, 36% casein diet as a high protein diet, and 36% casein-0.04% gramoxone diet. Each diet, prepared according to the composition shown in Table 1, was kept refrigerated and given fresh to each rat in the corresponding group every other day. Food intakes and body weight changes were recorded every other day. After 2 weeks, the rats were anesthetized with ether. The liver was obtained in order to determine the combined effects of dietary protein levels and gramoxone on the rat′s liver.

Table 1. Composition of the experimental diets

Constituents (%)	C	CG	L	LG	H	HG
Casein	18	18	5	5	36	36
Corn starch	72	72	85	85	54	54
Corn oil	5	5	5	5	5	5
Salt mixture[1]	4	4	4	4	4	4
Vitamin mixture[2]	1	1	1	1	1	1
Total	100	100	100	100	100	100

Abbreviations : C, 18% casein diet, control diet ; CG, 18% casein-0.04% gramoxone diet ; L, 5% casein diet. low protein diet ; LG,5% casein-0.04% gramoxone diet ; H,36% casein diet, high protein diet ; HG,36% casein-0.04% gramoxone diet

[1]Salt mixture : purchased from Nutritional Biochemicals Corp., Cleveland, Ohio, U.S.A.

[2]Vitamin mixture : Vitamin Diet Fortification mixture; purchased from Nutritional Biochemicals Corp., Cleveland, Ohio, U.S.A.

Analysis of lipid and TBA value in the rat liver

The rat liver was homogenized in a glass homogenizer using extracting solution (chloroform/methanol, 2/1,v/v). Total lipid was extracted with an extracting solution for one and half hours using a Soxtec system HT 2-1045 extraction unit 1 and a Soxtec system 1044 service unit 1. For hepatic TBA value, the absorbances of the sample were determined at 532 nm.

Histochemical examination of the rat liver tissue

Three millimeter squares of rat liver tissue were prepared immediately after excising. The samples were fixed in a 10% neutral formalin solution for 24 hours. The fixed and dehydrated samples were embedded in paraffin (m.p. 56~58°C). The embedded samples were then sectioned to 5~6 μm in width using a microtome (American Optical 820, U.S.A.). The hematoxylin-eosin (H-E) staining method and the periodic acid Schiff (PAS) staining method were employed to examine the histochemical characteristics of the rat liver tissue and to determine glycogen distributions in the rat liver[15], respectively. In PAS

staining, glycogen in the liver colors red.

Statistical analysis

To detect significant differences in the results of the feeding experiment, lipid content in the rat liver, and hepatic TBA value, data were treated statistically using SPSS[16]. The Subprogram, ONEWAY[16], which was specifically designed for a one-way analysis of variance, was employed using a significance level of 0.05. If significant differences were present, the LSD procedure was used at a significance level of 0.05 in order to determine the pattern of difference.

RESULTS AND DISCUSSION

Total weight gain and feed efficiency ratio of rats

Weight gain and feed efficiency ratio of rats fed high (36% casein diet), control (18% casein diet), and low (5% casein diet) proteins with or without gramoxone for 2 weeks are shown in Table 2. The highest mean weight gain (78.25 ± 3.86 g) and the highest mean feed efficiency ratio (33.87 ± 3.78 %) were obtained in rats fed the high protein diet. On the other hand, the lowest mean weight gain (-7.00 ± 3.27 g) and the lowest mean feed efficiency ratio (-4.91 ± 2.22 %) were obtained in rats fed the low protein-gramoxone diet.

Table 2. Total weight gain and feed efficiency ratio of rats fed the experimental diets

Dietary group	Total weight gain		Feed efficiency ratio	
	Mean	SD	Mean	SD
	g		%	
C	76.00	± 8.67	33.72	± 2.84
CG	40.25[b]	±18.73	22.14[b]	± 8.44
L	0.50[a]	± 3.87	0.33[a]	± 2.96
LG	-7.00[a]	± 3.27	-4.91[a]	± 2.22
H	78.25	± 3.86	33.87	± 3.78
HG	70.75	± 9.64	30.13	± 3.55

Abbreviations are the same as those in Table 1

[a]Mean scores are not different from each other, but significantly different from the other mean scores in the same column ($p<0.05$)

[b]Mean scores are significantly different from the other mean scores in the same column ($p<0.05$)

Results of a one-way analysis of variance indicated that no significant differences existed in the weight gain or in the feed efficiency ratio of rats fed the control diet, the high protein diet and the high protein-gramoxone diet. There were no significant differences either in the weight gain or in the feed efficiency ratio among those rats fed the low protein diet and those on the low protein-gramoxone diet. Significant differences ($p<0.05$) were, however, found both in the weight gain and in the feed efficiency ratio of rats fed the low protein diet, and the low protein-gramoxone diet, and those rats fed the other diet. There were significant differences in the weight gain and feed efficiency ratio of rats fed the control-gramoxone diet as compared with those rats fed the other diet ($p<0.05$).

The results were consistent with those found by other researchers who reported that the body weight of experimental animals fed low protein diets increased much more slowly than those fed control or high protein level diets[17,18]. Mathur et al.[17] reported that rats fed 3% casein diet stopped growing within 3 to 4 days after being placed on the diet, while rats fed 16% casein diet grew well. Peters and Harper[18] showed that although the 11-day cumulative weight gains observed in rats which had consumed 20%, 25%, 30%, or 35% casein diet had not differed significantly from one another, rats fed 5% casein diet gained significantly less weight than those rats in any of the other dietary groups.

With regard to the addition of foreign compounds, several researchers reported that the administration of specific foreign compounds resulted in a decrease in the body weight of the experimental animals[5,19~23]. The addition of 0.1% PCB into the diets containing 10%, 20%, and 30% casein was shown to have caused a subsequent decrease in the body weight of rats as compared with rats fed each of the corresponding control diets. Additionally, a significantly lower growth rate was evidenced in the case of those rats fed the 10% casein diet[5]. Rao and Wong[19] demonstrated that significant reductions in body weight resulted in rats fed either 4% casein or

8% casein diet as compared with other rats which were fed 24% casein diet when BHT was administered intragastrically. According to Ando[20], the growth rate and feed efficiency ratio of rats fed 5% casein diet was significantly lower than the respective rates and ratios for rats fed 10%,.20%, 30% and 40% casein diet when DDT had been injected intraperitoneally. The growth rate of rats fed a low protein diet containing aflatoxin also decreased dramatically as compared with the rates of rats which were fed a high protein diet containing aflatoxin[21,22]. Kari et al.[23] showed that both the 14-day weight changes as well as the feed efficiency ratios of mice which were injected with methylazoxymetanol were markedly dependent upon dietary protein levels.

The addition of gramoxone into the rats' diets was shown to affect significant reduction in the body weight of those fed diets containing decreasing levels of protein. The feed efficiency ratio for each diet group proved to be of a tendency quite similar to those results recorded in body weight.

Lipid content in the liver of rats

Hepatic lipid contents of those rats fed the six experimental diets are presented in Table 3. The highest mean lipid content (5.54±1.73%) occurred in the liver of rats fed the low protein-gramoxone diet, while the lowest such content (3.13±0.21%) was shown to be present in the liver of those rats which had been fed the high protein diet. The addition of gramoxone resulted in a slight increase of lipid content in the liver of all rats, regardless of the dietary protein level administered.

Table 3. Lipid content in the liver of rats fed the experimental diets (%)

Dietary group	Mean	SD
C	3.23	± 0.72
CG	4.04	± 0.26
L	4.92[b]	± 1.51
LG	5.54[a]	± 1.73
H	3.13[b]	± 0.21
HG	3.59	± 0.65

Abbreviations are the same as those used in Table 1
[a]Mean score is significantly different from the mean score of either C, H, or HG ($p<0.05$)
[b]Mean scores are significantly different from each other ($p<0.05$)

Results of a one-way analysis of variance indicated that significant differences ($p<0.05$) existed in lipid content between those rats fed the low protein-gramoxone diet and those levels of rats which were fed either the control, the high protein and/or the high protein-gramoxone diets. There were significant differences in the liver lipid levels between those rats fed the low protein diet and those in the high protein diet group ($p<0.05$). There were, however, no significant differences in the lipid levels among rats fed the control, the control-gramoxone, the high protein, and the high protein-gramoxone diets. These results indicated that the low protein diet seemed to have exerted more influence, or to have greater bearing upon the build up of lipid levels in the liver of rats than did the high levels of protein in the corresponding diets. Moreover, the addition of gramoxone caused a subsequent increase of lipid content in the liver of such treated rats.

According to Yeh and Leveille[24], hepatic lipogenesis was depressed through elevation of dietary protein intake levels. Furthermore, Innami[5] reported that fatty liver was observed to occur in the liver of rats which had PCB added to their diets. The materials detected were identified as triglyceride, cholesterol, and phospholipid. Plaa[25] described that the accumulation of lipids in the liver of rats resulted from a blockage of the secretion of hepatic triglyceride into the plasma, and that this phenomena was induced through introduction of such foreign compounds as carbon tetrachloride, ethionine, phosphorus, puromycin,and tetracycline. According to Lombardi[26], the blockage of hepatic triglyceride usage resulted from a reduction in the synthesis of VLDL in the liver of rats. Lee and Sung[27] have additionally demonstrated that there were significant increase of total cholesterol and triglyceride content in rats which had been administered inhalation anesthetics.

TBA values in the liver of rats

Hepatic TBA values of rats fed experimental diets

are presented in Table 4. The lowest TBA value (0.09±0.02) was seen in those rats fed a low protein diet, while the highest such value (0.28±0.08) was obtained in those rats fed the control-gramoxone diet. Results of a one-way analysis of variance indicated that there were no significant differences in the hepatic TBA values from among those rats fed either the control, the low protein, the high protein, and/or the high protein-gramoxone diet. Additionally, no significant differences were shown to exist in the hepatic TBA values of those rats fed either the control-gramoxone diet or those fed the low protein-gramoxone diet and the corresponding values for those rats fed any of the other diets ($p<0.05$). The addition of gramoxone tended to increase hepatic TBA value significantly in rats, especially among those fed the low protein-gramoxone diet or the control-gramoxone diet. These results indicated that there were no significant differences in the hepatic TBA values of rats with respect to dietary protein levels. However, the addition of gramoxone exerted to increase the hepatic TBA value of rats, especially among rats fed the control-gramoxone and/or those fed the low protein-gramoxone diet.

According to Innami[5], hepatic TBA values tended to increase rather remarkably in rats which had been administered PCB. He reported that the addition of PCB into their diet resulted in fat content changes, formation of lipid peroxidation, and increased the unsaturated fatty acid levels in the liver of rats. Additionally, he suggested that this increase in unsaturated fatty acid could act as substrates for lipid peroxidation.

Because TBA value is related to the formation of lipid-peroxidation, it might be suggested that the formation of lipid-peroxidation could start in rats fed the control-gramoxone diet or the low protein-gramoxone diet.

Table 4. TBA values in the liver of rats fed the experimental diets (μg MA/g)

Dietary group	Mean	SD
C	0.11	± 0.02
CG	0.28[a)]	± 0.08
L	0.09	± 0.02
LG	0.20[a)]	± 0.06
H	0.14	± 0.07
HG	0.15	± 0.01

Abbreviations are the same as those used in Table 1
[a)]Mean scores are not significantly different from each other, but significantly different from the other mean scores in the same column ($p<0.05$)

Morphological properties of hepatic tissue and glycogen distribution in the liver of rats

Histological findings and glycogen distribution in the liver of rats fed the experimental diets are presented in Tables 5 and 6, respectively. No stromatic changes were seen to have occurred in the liver of rats fed any of the experimental diets. There were, however, severe epithelial changes in the liver of those rats fed each experimental diet, even though

Table 5. Histological findings of the liver of rats fed the experimental diets

Dietary group	Epithelial change			Stromatic change		
	CS	FC	KC	ICI	F	PC
C	-	±	±	-	-	-
CG	±	+	+,++	-	-	-
L	±	++	+,++	-	-	-
LG	++	++++	+++	-	-	-
H	-	±	±,+	-	-	-
HG	±	±	+++	-	-	-

Abbreviation: : CS, cloudy swelling ; FC, fat change ; KC, Kupffer cell ; ICI, inflammatory cells infiltration ; F, fibrosis ; PC, passive congestion ; others are the same as those used in Table 1
-,absent ; ±,trace ; +,weak ; ++,moderate ; +++,intensive ; ++++, very intensive

Table 6. Glycogen distribution in the liver of rats fed the experimental diets

Cells	Dietary group					
	C	CG	L	LG	H	HG
Zone 1[1)]	±〉+	±-+	±〉+	+++,±	++-+++〉±	+++-++++〉+-++
Zone 2[2)]	±	±,+	±	++,±	++〉±	++-+++〉±,+
Zone 3[3)]	±〉+	+-±	±〉+	++〉±	+-++,±	+++〉+,++

Abbreviations are the same as those used in Table 1
[1)]Zone 1, periportal region ; [2)]Zone 2, midlobular region ; [3)]Zone 3, centrolobular region
±, trace ; +, weak ; ++, moderate ; +++, intensive ; ++++,very intensive ; 〉, most marked

slight differences existed. Liver biopsy examination of hepatic tissue from rats fed the control diet and the high protein diet indicated uniformly stained cells extending from the central vein to the periphery of the liver lobule. Slight, cloudy swelling occurred in the liver of rats fed the control-gramoxone diet. An increase in the size and number of lipid droplets was manifest in a few hepatic cells, and the number of Kupffer cells, cells of the macrophage system, also tended to increase in the hepatic tissue of rats of the same diet. The basic structure of the hepatic cells, however, appeared unchanged and normal here. Similar changes were noticed in rats fed the low protein group; both the slight, cloudy gross swelling of the liver existed and the tendency of fat droplets to increase in a few hepatic cells was observed. Both moderate fat changes in the hepatic cells and an increase in the number of Kupffer cells were noticed in rats fed the control-gramoxone diet. Moderate, cloudy swelling and severe increases in the number of lipid droplets in the hepatic cells of rats fed the low protein-gramoxone diet were observed. Histologic examination of rats livers in this dietary grouping showed both the existence of severe fat changes in the hepatic cells and also an increased number of Kupffer cells. Epithelial changes in the liver of rats fed the high protein diet were similar to those changes seen in rats fed the control diet. In the case of the high protein-gramoxone dietary group, a slight cloudy swelling of the liver was evident as there was change observed in the fatty make-up of the hepatic cells of rats in the group. No significant changes, however, were seen to exist. A dramatic increase in the number of Kupffer cells existed in the liver of rats of this diet group. The results were consistent with the reports of other researchers[5,8,25,28].

According to Enwonwu and Sreebny[28], the usual richness characteristic of both the endoplasmic reticulum membrane and the cytoplasmic ribosomes was observed in the liver of well-fed rats. They also reported that conspicuous dilations of the membrane cisternae, well-defined lipid inclusions, and abnormal accumulation of glycogen were observed in the liver of rats fed low protein diets. Moreover, cloudy swelling of the centrilobular region, fatty degeneration, and early necrosis of the liver occurred in rats which had been both fed protein deficient diets and had been administered diuron[6]. Similar results were observed in the liver of rats which had also been fed a protein deficient diet, but administered DDT[25]. Madhavan and Gopalan[8] showed that lesions of the liver occurred more weakly in rats fed 20% casein diet and treated with aflatoxin than among those rats fed 4% casein diet and similarly treated. They suggested that a high level of dietary protein had some correlating, protective effects against such aflatoxin injury.

Glycogen distributions in the liver of rats derived from PAS staining method are shown in Table 6. According to Park[29], the distribution of hepatic glycogen was marked, during the infancy of rats, though seen to become depressed after rats had reached 6 weeks of age. Dietary protein levels appeared to have little effect on the glycogen distributions in the liver of rats. Nevertheless, slight increases in glycogen levels were observed in the liver of rats fed the high protein diet.

Generally, the administration of gramoxone resulted in a prominent increase of glycogen distributions in the liver of rats. These results were found to be in agreement with the results of Corrin and Aterman[30]. They reported that the administration of various levels of cortisone for 4 days caused an increase in hepatic glycogen levels, particularly and most prominently in the periportal region. According to Hong et al.[31], the introduction of a rodenticide, especially RH 787, resulted in the destruction of Langerhans' islets in the pancreas of rats. Judging from those results, one can deduce that the aforementioned heightened distribution levels of glycogen found to be present in the liver of gramoxone-treated rats might most likely be attributed to interferential reactions of the pancreas. Tables showing the morphologic changes and glycogen distribution in the livers of rats fed the experimental diets, are given in Figs.1, 2, 3 and 4.

REFERENCES

1. Klaassen, C. D. and Doull, J. : Evaluation of safety:

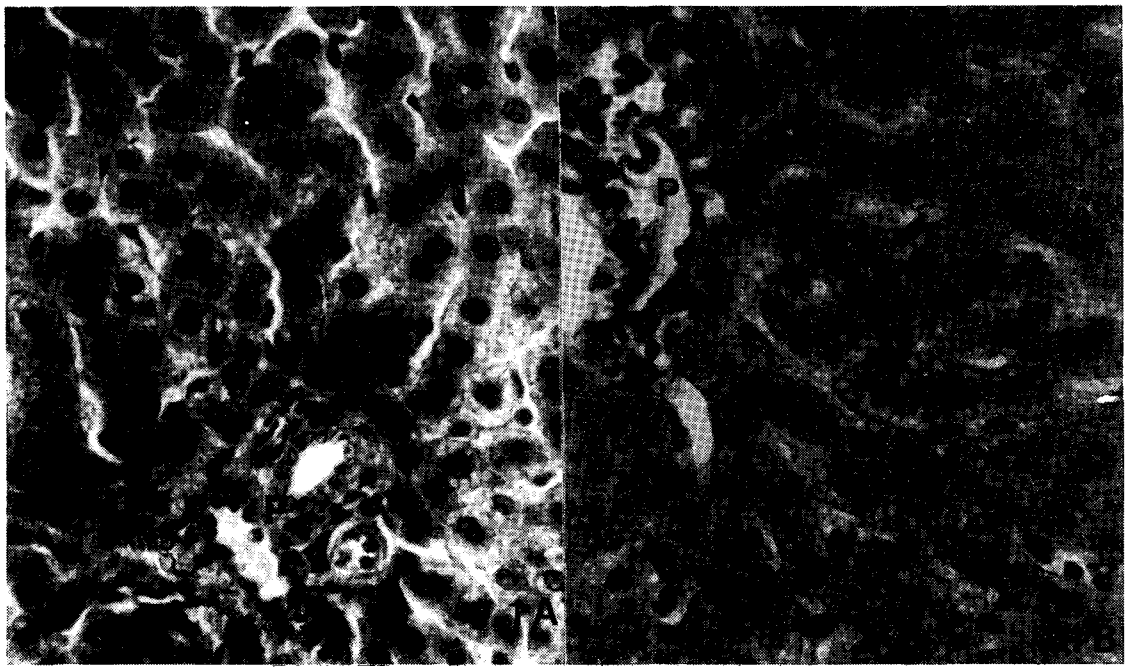

Fig. 1. Hepatic cells in periportal regions of rat liver with PAS stain. The red granules in the cytoplasm are glycogen. Lipid droplets occurred in both 1A and 1B, but they were not changed severely. An increase in the number of Kupffer cells was noticed in rats fed 1B. 1A, 18% casein diet group ; 1B, 18% casein-0.04% gramoxone group ; p, portal area. X400.

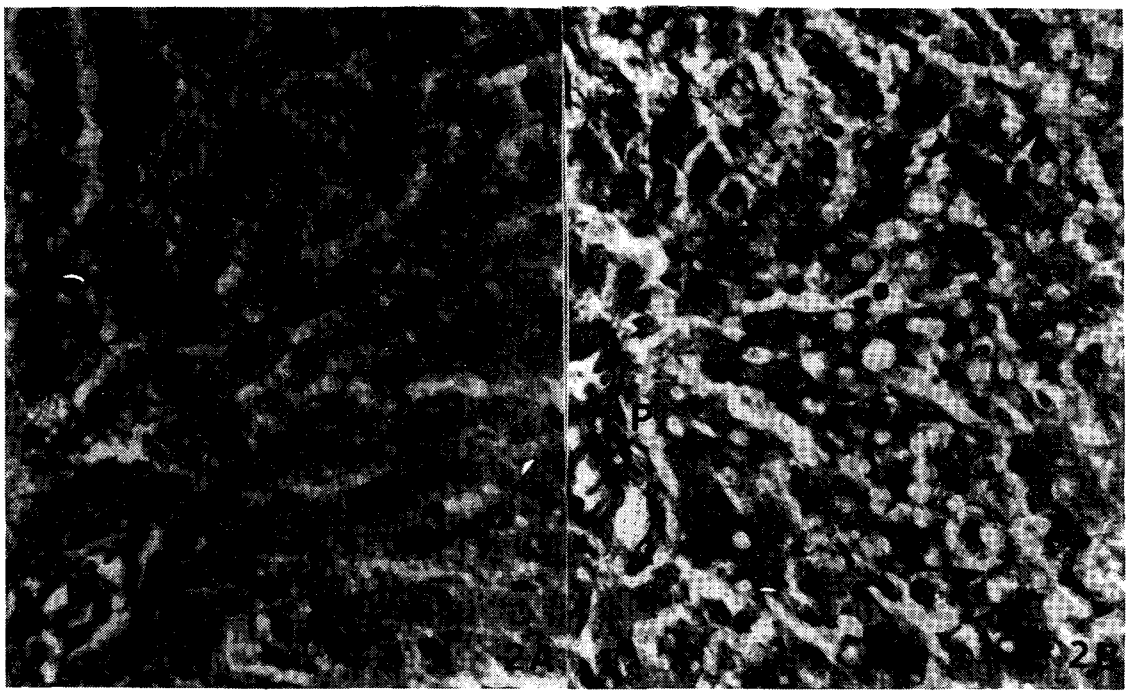

Fig. 2. Hepatic cells in periportal regions of rat liver with PAS stain. The intense red granules in the cytoplasm of 2B are glycogen, and fat changes occurred more severely in 2B than in 2A. Both the slight, cloudy gross swelling existed and lipid droplets in a few hepatic cells were observed in 2A. Moderate, cloudy swelling and severe increases in the number of lipid droplets and Kupffer cells were observed in 2B. 2A, 5% casein diet group ; 2B, 5% casein-0.04% gramoxone group ; P, portal area. X400.

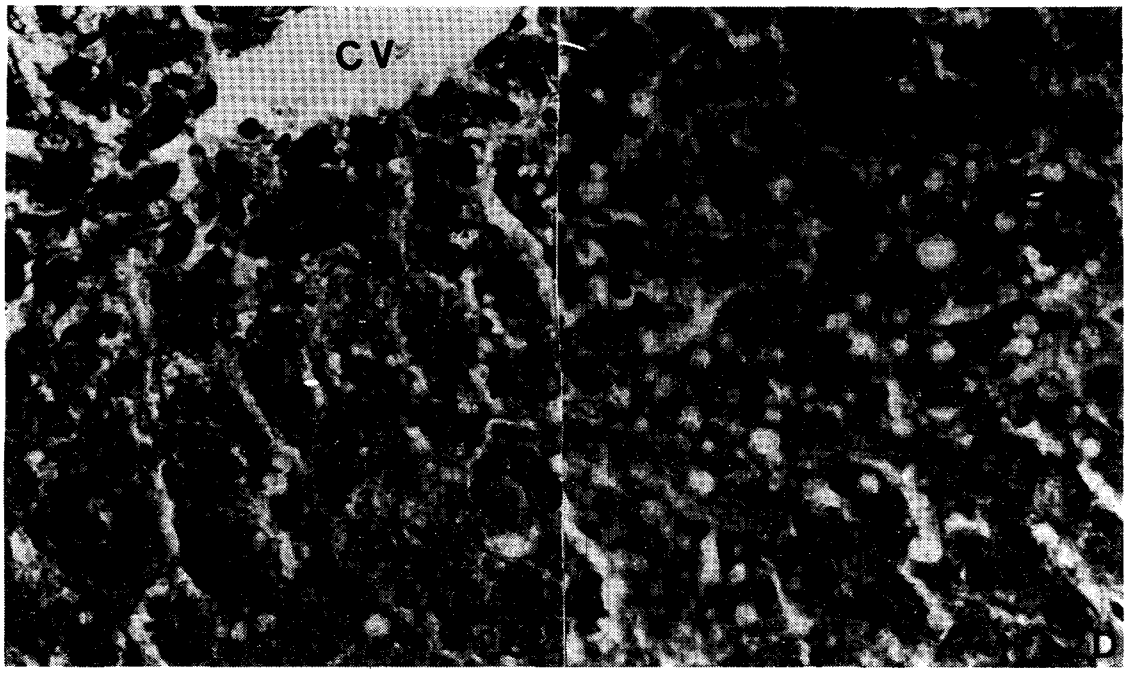

Fig. 3. Hepatic cells in centrolobular (left) and midlobular regions (right) of rat liver with PAS stain. The moderate red granules in the cytoplasm of 2C and 2D are glycogen, and fat changes appeared severely in both of them. 2C and 2D, 5% casein-0.04 gramoxone ; CV, central vein. X400.

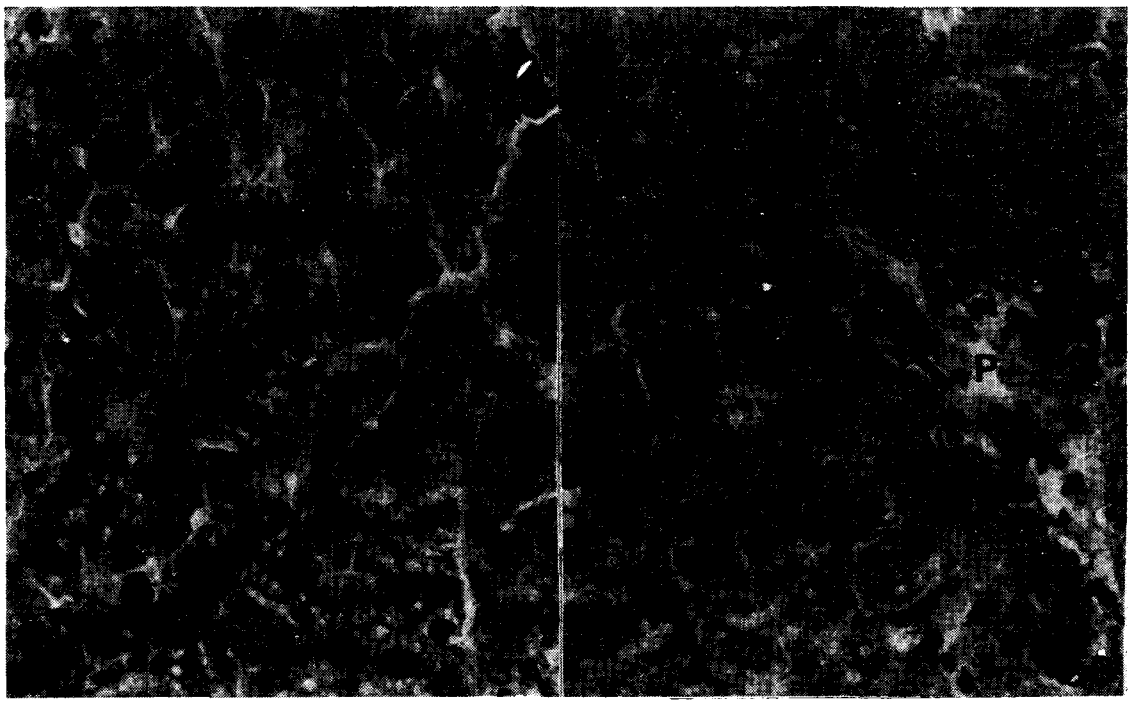

Fig. 4. Hepatic cells in midloubular (left) and periportal regions (right) of rat liver with PAS stain. The intense red granules in the cytoplasm of 3A and 3B are glycogen. Fat changes did not occur severely in both of them. Slight cloudy swelling was shown in 3B, but it was not serious. An increase in the number of Kupffer cells existed in 3B. 3A, 36% casein diet group ; 3B, 36% casein-0.04% gramoxone group; ; P, portal area. X400.

Toxicologic evaluation. In "*Toxicology*". 2nd ed., Doull, J., Klaassen, C. D. and Amdur, M. O. (eds.), Macmillan publishing Co., Inc., New York. p. 11 (1980)
2. Neal, R. A. : Metabolism of toxic substances. In "*Toxicology*". 2nd ed., Doull, J., Klaassen, C. D. and Amdur, M. O. (eds.), Macmillan publishing Co., Inc., New York. p. 56 (1980)
3. Doull, J. : Factors influencing toxicology. In "*Toxicology*". 2nd ed., Doull, J., Klaassin, C. D. and Amdur , M. O. (eds.), Macmillan publishing Co., Inc., New York. p. 70(1980)
4. Campbell, T. C. and Hayes, J. R. : Role of nutrition in the drug metabolizing enzyme system. *Pharmacol. Rev.*, **26**, 171(1974)
5. Innami, S. : Interaction between toxicity of pollutants and nutrition. *J. Jap. Soc. Food Nutr.*, **38**, 1(1985)
6. Boyd, E. M. and Krupa, V. : Protein deficient diet and diuron toxicity. *J. Agr. Food Chem.*, **18**, 1104(1970)
7. Wong, G. K. K. and Rao, A. V. : Effects of dietary protein on the subacute toxicity of butylated hydroxytoluene (BHT) in rats. *Drug Nutr. Interact.*, **2**, 57 (1983)
8. Madhavan, T. V. and Gopalan, C. : Effect of dietary protein on aflatoxin liver injury in weanling rats. *Arch. Path.*, **80**, 123(1965)
9. Tanaka, R., Fujisawa, S. and Nakai, K. : Study on the absorption and protein binding cabaryl, dieldrin and paraquat in rats fed on protein diet. *J. Toxicol. Sci.*, **6**, 1(1981)
10. Webb, R. E., Bloomer, C. C. and Miranda, C. L. : Effect of casein diets on the toxicity of malathion and parathion and their oxygen. *Bull. Environ. Contam. Toxicol.*, **9**, 102(1973)
11. Murphy, S. D. : Pesticides. In "*Toxicology*". 2nd ed., Doull, J., Klaassen, C. D. and Amdur, M. O. (eds.), Macmilan publishing Co., Inc., New York. p. 357 (1980)
12. Bus, J. S., Cagen, S. Z., Olgaard, M. and Gibson, J. E. : A mechanism of paraquat toxicity in mice and rats. *Toxicol. Appl. Pharmac.*, **35**, 501(1976)
13. Barabas, K., Szubo, L., and Matkovics, B. : The search for ideal antidote treatment in gramoxone intoxication. *Gen. Pharmac.*, **18**, 129(1987)
14. Gage, J. C. : The action of paraquat and diquat on the respiration of liver cell fractions. *Biochem. J.*, **109**, 757(1968)
15. McManus, J. F. A. : Histological and histochemical uses of periodic acid. *Stain Technol.*, **23**, 99(1948)
16. Nie, N. H., Hu, C. H., Jenkins, J. G., Steinbrenner, K. and Bent, D. H. : *Statistical package for the social sciences*. 2nd ed., McGraw-Hill Book Co., New York. p. 675(1975)
17. Mathur, M., Ramalingaswami, V. and Deo, M. G. : Influence of protein deficiency on 19S antibody-forming cells in rats and mice. *J. Nutr.*, **102**, 841 (1972)
18. Peters, J. C. and Harper, A. E. : Adaptation of rats to diets containing different levels of protein : Effects on food intake, plasma and brain amino acid concentrations and brain neurotransmitter metabolism. *J. Nutr.*, **115**, 382(1985)
19. Rao, A. V. and Wong, G. K. K. : Effects of dietary protein on the pharmacokinetics of butylated hydroxytoluene (BHT) in rats. *Drug Nutr. Interact.*, **2**, 69 (1983)
20. Ando, M. : Studies on the effect of dietary protein and fat content upon DDT metabolism in rat liver. *J. Toxicol. Environ. Health*, **10**, 11(1982)
21. Mainigi, K. D. and Campbell, T. C. : Effects of low dietary protein and dietary aflatoxin on hepatic glutathione levels in F-344 rats. *Toxicol. Appl. Pharmacol.*, **59**, 196(1981)
22. Princen, L. O. and Campbell, T. C. : Effects of sex difference and dietary protein level on the binding of aflatoxin B_1 to rat liver chromatin proteins *in vivo*. *Cancer Res.*, **42**, 5053(1982)
23. Kari, F. W., Johnston, J. B., Truex, C. R. and Visek, W. J. : Effect of dietary protein concentration on yield of mutagenic metabolites from 1,2-dimethylhydrazine in mice. *Cancer Res.*, **43**, 3674(1983)
24. Yeh, Y. Y. and Leveille, G. A. : Effect of dietary protein on hepatic lipogenesis in the growing chick. *J. Nutr.*, **98**, 356(1969)
25. Plaa, G. L. : Toxic responses of the liver. In "*Toxicology*". 2nd ed., Doull, J., Klaassen, C. D. and Amdur, M. O. (eds.), Macmillan publishing Co., Inc., New York. p.206(1980)
26. Lombardi, B. : Fatty liver: Considerations on the pathogenesis of fatty liver. *Lab. Invest.*, **15**, 1(1966)
27. Lee, Y. J. and Sung, N. E. : Effects of various anesthetics on the hepatic microsomal cytochrome system and the lipid contents of albino rats. *Ewha Med. J.*, **5**, 147(1982)
28. Enwonwu, C. O. and Sreebny, L. M. : Studies of hepatic lesions of experimental protein-calorie malnurition in rats and immediate effects of refeeding an adequate protein diets. *J. Nutr.*, **101**, 501(1971)
29. Park, H. C. : Histochemical studies on the distribution of glycogen and some enzymes in the hepatic tissue of rats during postnatal growth. *J. Busan Med. Coll.*, **16**, 11(1976)
30. Corrin, B. and Aterman, K. : The pattern of glycogen distribution in the liver. *Amer. J. Anat.*, **122**, 57(1962)
31. Hong, K. W., Yang, O. S. and Park, H. C. : Clinical and experimental studies on the rodenticide RH-787 toxicity damage of pancreatic B cells. *J. Kor. Med. Assoc.*, **20**, 223(1977)

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Gramoxone이 단백질 level에 따라 흰쥐 간에 미치는 독성에 관한 연구

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요 약

식이속의 단백질농도가 피리딘계 제초제인 gramoxone의 독성발현에 어떤 영향을 미치는가를 알기 위해 Wistar계 흰쥐 숫놈 36마리 (6~7주령)를 6개의 실험사료군으로 나누어 2주간 사육하며 그 미치는 영향을 조사하였다. 체중증가 상황은 각단백-gramoxone군들의 경우 각 정상단백군에 비해 저조하였으며 저단백-gramoxone군에서 제일 심하였고 고단백-gramoxone군에서는 유의한 차가 없었다. 간의 지질함량변화는 각단백-gramoxone군들의 경우, 고단백-gramoxone군을 제외하고 각 단백군에 비해 증가하는 경향을 나타내었으며 특히 저단백-gramoxone군에서 가장 심하였다. 간장내 TBA가는 정상단백군, 저단백군, 고단백군 및 고단백-gramoxone군 사이에는 유의차가 없었으나 정상단백-gramoxone군과 저단백-gramoxone군의 경우 전자의 실험군들에 비해 매우 높았다. 정상단백군 및 고단백군의 간에서는 유의한 형태적인 변화가 없었으나 저단백군과 각단백-gramoxone군들에서는 정도의 차이는 있었으나 간조직의 변화가 나타났으며 간세포 지방변화 및 Kupffer세포의 숫적인 증가가 관찰되었다. 특히 간세포 지방변화는 저단백-gramoxone군에서 심하였고 고단백-gramoxone군에서는 현저하지않았다. 간세포의 glycogen함량은 각단백-gramoxone군들에서 타군들에 비해 증가하는 경향을 보였으며 저단백-gramoxone군에서 제일 심하였다.