DIETARY TAURINE REDUCES OXIDIZED FISH OIL AND VITAMIN A INDUCED TOXICITY IN MALE WISTAR RATS

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Attempts are made to investigate the effects of taurine and oxidized fish oil on vitamin A. Thirty male wistar rats were divided five groups of male Wistar rats were fed a mega dose (50,000 IU) of retinyl palmitate either with or without supplement of taurine and oxidized fish oil at the same time for 6 weeks. After 2, 4 and 6 weeks of treatment, each group of six rats were killed and examined. It was found that oxidized fish oil significantly elevated the symptoms of vitamin A, which includes the decrease of body weight and the concentration of glutathione (GSH) in liver and increase the ratios of liver and kidney weight to body weight, the activities of AST, ALT and ALP in plasma, the level of TBARS in liver and plasma, the levels of BUN and creatinine in the plasma, the level of vitamin A in the plasma (P<0.05). However, taurine significantly ameliorated the toxicity of vitamin A with oxidized fish oil. It increases body weight and reduces the concentration of WBC and HCT in blood, the levels of vitamin A in the liver and kidney, the level of TBARS in liver, the ratios of liver and kidney weight to body weight, the activities of AST, ALT and ALP in plasma, and the levels of cholesterol, triglyceride, calcium and phosphorus in plasma (P<0.05). Therefore, oxidized fish oil elevated the toxicity of vitamin A, while taurine prevented the toxicity of vitamin A and oxidized fish oil.

Key words: taurine, oxidized fish oil, toxicity, rats, vitamin A

Abbreviations: AIN=American Institute of Nutrition; ALP=alkaline phosphatase; ALT=alanine transaminase; AST=aspartate transaminase; AV=acid value; BHT=butylated hydroxytoluene; DTNB=5, 5'-dithiobis (2-nitrobenzoic acid); GR=glutathione reductase; GSH=glutathione; GSSG=glutathione disulfide; HPLC=high performance liquid chromatography; MDA=malondialdehyde; NADPH=nicotinamide adenine dinucleotide; PUFA =polyunsaturated fatty acid; TBA=thiobarbituric acid; TBARS=thiobarbituric acid-reactive substances; TNB=2-nitro-5-thiobenzoic acid; RBC=red blood cell; HCT=hematocrit; WBC=white blood cell; HGB=hemoglobin; BUN=blood urea nitrogen; EPA = eicosapentaenoic acid; DHA=dicosahexaenoic acid; POV=peroxide value.

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Introduction

Vitamin A is an essential nutrient for human beings because it cannot be synthesized de novo within the body. It is necessary for vision, reproduction, membrane structure, growth, and development[1]. Although the incidence of vitamin A excess is a very minor problem compared with that of vitamin A deficiency, it is estimated that 200 cases of vitamin A poisoning occur annually in the world[1]. Typical symptoms of acute vitamin A include headache, nausea, vomiting, occasional fever, vertigo and visual disorientation[2, 3]. Peeling of the skin may also occur[4]. All of these symptoms are usually reversible on cessation of overdosing. Liver enlargement and high level of triglyceride in plasma are the most usable clinical indicators of vitamin A[5, 6].

Food poisoning of vitamin A induced from ingesting fish liver has sporadically occurred in Taiwan[7, 8]. The typical symptoms of acute vitamin A induced from taking excess pure vitamin A have been reported to be different from those taking fish liver[9]. It is well known that marine fish livers are rich in ω-3 polyunsaturated fatty acids (ω-3 PUFA) and taurine (2-aminoethanethanesulfonic acid)[10, 11]. The symptoms of vitamin A induced from the fish liver may be affected by fish oil and taurine. We have found that PUFA in non-oxidized fish oil inhibited the acute induction of hypertriglyceridemia and liver enlargement by a single excess dose of retinyl palmitate in rats[12].

However, PUFA in fish oil are easily oxidized when fish livers are cooked in the air. So the symptoms of vitamin A induced from fish liver may be also altered by oxidized fish oil. The oxidized oil is a hazardous substance to human beings and animals[13-15]. Meanwhile, taurine is a special amino acid, which possesses an amino group and a sulfonate group that conjugates with bile acids in the liver[16]. It has been reported that taurine might possess a protective action against drug induced injuries[17, 18]. It is well known that marine foods, especially mollusks, contain high amounts of taurine[19, 20], taurine has been reported to possess a protective function against chemical-induced injuries by drugs such as doxorubicin and streptoxotocin[21-23] and heavy metals[24, 25]. Recently, we reported that taurine played an important role in lowering the toxic effect of oxidized fish oil in rats[26]. The toxicity of fish liver containing vitamin A might exhibit a mixed function of vitamin A, oxidized fish oil and taurine. To investigate the interaction of taurine, oxidized fish oil and vitamin A, a study of the toxicological character of these factors in the vitamin A incident was undertaken.

Materials and Methods

Reagents

Standard vitamin A (retinyl palmitate) was purchased from Sigma Chemical Company (ST. Louis, MO). Taurine was purchased from Dokui Chemical Company (Taiwan), purity of 99.5% to add of 5% in the feed. The corn oil was supplied by President Co. (Taiwan).

Preparation of oxidized fish oil

Fish oil was obtained from Kozein Company (Taiwan), 1 g fish oil contents of 30% (EPA＝180 mg; DHA=120 mg; vitamin E=1 mg). Fish oil was heated at 60±2℃ for 12 hr in a water-bath with air pumping into it to produce oxidized fish oil[27]. The oxidized fish oil was characterized as follows: POV

302.8 meq/kg oil, AV 9.13 mg/g oil and TBA 11.63 mg/kg oil. The fresh fish oil was characterized as follows: POV 14.8 mg/kg oil, AV 0.35 mg/g oil and TBA 0.24 mg/kg oil. The value of POV, AV and TBA in the oil was determined by AOAC method[28].

Animals

Male weanling Wistar rats were purchased from the National Taiwan University Hospital. They were kept in an air-conditioned room (23±1℃, 50-60% humidity) lit for 12 hr/day (07.00 to 19.00 hr). Experimental protocol was approved by the institutional animal care and use committee of Toko University. After acclimating for 2 weeks with a commercial non-purified diet (Rodent Laboratory Chow 5001, Pruida Co., USA), 30 rats were divided into five groups. Six rats in each group were assigned to receive 6-week course of one of five formulated diets (Table 1). The diets were formulated as described previously by AIN[29] because this formula is still commonly used in spite of new one recommended by AIN in 1993. Water and food were always available. After feeding, all rats were weighed. The blood of the rats was taken at 2 and 4 weeks interval from the tail vein. Then, the blood samples were analyzed for blood characteristics including RBC, WBC, HGB and HCT by using a Cell Hematology Analyzer (DYN 500, Sequoi-Turner, USA). The plasma of blood samples was collected by centrifugation (2,000 ***g*** for 15 min) from blood and examined for levels of cholesterol, triglyceride, calcium, phosphorus, activities of AST, ALT, ALP, BUN and creatinine by a Vitalab Selectra Biochemical Autoanalyzer (E. Merck, Germany) with enzymatic kits. After 6 week of treatment, the rats from each group were weighed and euthanized after anesthetizing with diethyl ether. The liver and kidney of rats were

Table 1. Composition of the experimental diet in each group for test oxidized fish oil, vitamin A, oxidized fish oil+vitamin A, and oxidized fish oil+vitamin A+taurine

Ingredient (%)	Diets[a]				
	Control	Oxidized fish oil	Vitamin A	Oxidized fish oil+Vitamin A	Oxidized fish oil+Vitamin A +Taurine
Surcose	20	20	20	20	20
Casein	35	35	35	35	35
Corn starch	30	27	30	27	22
Cellulose	5	5	5	5	5
Corn oil	5	5	5	5	5
Methionine	0.3	0.3	0.3	0.3	0.3
Choline	0.2	0.2	0.2	0.2	0.2
AIN Mineral mix	3.5	3.5	3.5	3.5	3.5
AIN vitamin mix	1	1	1	1	1
Taurine	0	0	0	0	5
Oxidized fish oil	0	3	0	3	3
Vitamin A (IU)	0	0	50,000	50,000	50,000

[a] Oxidized fish oil: 3% oxidized fish oil in diet; vitamin A: 50000 (IU) vitamin A in diet; Oxidized fish oil+vitamin A: 3% oxidized fish oil and 50000 (IU) vitamin A in diet; Oxidized fish oil+vitamin A+Taurine: 3% oxidized fish oil and 5% taurine and 50000 (IU) vitamin A in diet.

quickly excised without perfusion and weighed. Both ratios of liver and kidney weight to body weight were obtained. Then, the liver and kidney samples were stored at -40℃ for GSH and TBARS determinations. The plasma was analyzed for AST, ALT, ALP, cholesterol, triglyceride, calcium and phosphorus were also assayed by a Vitalab Selectra with using enzymatic kit.

TBARS production

Lipid peroxidation activities in the liver were assayed by measurement of MDA, an end-product of peroxidized fatty acids, and TBA reaction product. The sample of 20% liver homogenate was mixed with 1.0 ml of 0.4% TBA in 0.2 N HCl and 0.15 ml of 0.2% BHT in 95% ethanol. The samples were incubated in a 90℃ water-bath for 45 min. After incubation, the TBAMDA adduct was extracted with isobutanol. The isobutanol extract was mixed with methanol (2:1) prior to injection into the system of HPLC. The supernatant was examined by using the HPLC system at an excitation 515 nm and an emission 550 nm on a Hitachi Fluorescence Detector (Japan)[30].

GSH measurement

GSH reacts non-enzymatically with DTNB to yield GSSG and TNB. GSSG is then reduced enzymatically by NADPH and GR to regenerate GSH. Concentrations of DTNB, NADPH and GR are chosen such that the rate of the overall reaction is linearly proportional to the concentration of total GSH. The rate of formation of TNB is followed spectrophotometrically, and assay is calibrated using standards. GSH is derivatized if the sample is reacted with 2-vinylpyridine. Only GSSG is detected during subsequent assay[31].

Vitamin A analyses in liver, kidney and serum

Vitamin A in liver and kidney homogenates (20% w/v in water) were extracted using diisopropyl ether, essentially according to Nilsson et al.[32] and separated on a Nucleosil C-18 5 μm high performance liquid chromatography (HPLC) column using an ethanol: water gradient elution. Retinol, retinyl acetate and retinyl palmitate were detected with a fluorescence detector with an excitation wavelength of 325 nm and emission wavelength of 475 nm (Model 821-FP, Jasco). Internal (retinyl acetate) and external (retinol and retinyl palmitate) standards were used for quantification. Serum analyses of retinoic acid and retinyl esters were done by AS Vitas (Oslo, Norway) on material shielded from light. Briefly, 200 μl of serum or standard solutions was mixed with 600 μl of 2-propanol and centrifuged at 4000 × ***g***. The supernatant was analyzed by liquid chromatography on an HP-1100 HPLC system furnished with a Supersphere 100 RP-18 column (Agilent Technologies, Palo Alto, CA) and detected at 325 nm with an ultraviolet detector. The mobile phase consisted of methanol-dichloromethane and the injection volume was 100 μl. A threepoint calibration curve, constructed with albumin solutions enriched with different concentrations of retinyl palmitate, was used to quantify all retinyl esters. The intra-assay variation was 5.1%.

Histopathology

Liver and kidney samples were fixed in 10% formalin phosphate-buffer, dehydrated, paraffin-embedded and archived. Sections of 2-4 μm of all zones of hepatic lobule and median part of kidney were sagitally cut and mounted on aminopropyltriethoxysilane-coated slides (APTS, A-3648, Sigma). Following

deparaffinization in xylene, sections were rehydrated, stained with hematoxylin and eosin (H&E) and examine for light microscopy[33].

Statistical methods

The Statistical Package for the Social Sciences (SPSS, version 13.0, SPSS Inc, Chicago, Ill), was used for all data analysis. Analysis of variance was applied to detect differences in the means of variables at baseline and the end of each 6 wk treatment intervention period. Paired t tests were used to examine differences in measurements and percentage changes over time for each of the biochemical markers[34]. Data are presented as the mean ± SEM. Statistical significance was indicated by $P \leqq 0.05$.

Results

In clinical plasma examination, the indicators concerning blood characters, liver function and kidney function have been determined in the toxicity. Activities of AST, ALT and ALP in plasma are generally tested as indicators for liver functions, and the levels of creatinine, plasma urea nitrogen are tested as indicators for kidney functions.

The effects of taurine, oxidized fish oil and vitamin A on the body weight of rats are shown in Fig. 1. After 6 weeks of treatment, oxidized fish oil did not affect the growth of rats, while the vitamin A significantly reduced the body weights of rats. As for the reducing of the body weight, oxidized fish oil elevated the toxicity of vitamin A, but taurine ameliorated the toxicity of vitamin A+oxidized fish oil. The effects of taurine, oxidized fish oil and vitamin A on the weight ratios of liver to body and kidney to body are shown in Fig. 1. After 6 weeks of treatment, oxidized fish oil did not affect the two ratios, while the vitamin A significantly increased them (93% and 33 % up for liver and kidney, respectively), while taurine reduced the toxicity of both vitamin A and oxidized fish oil. In the reducing of the body weight of rats and the increasing of the weight ratios of liver to body and kidney to body, oxidized fish oil and vitamin A showed synergistic effects.

The effects of taurine, oxidized fish oil and vitamin A on the blood of rats are shown in Fig. 2. Only concentrations of WBC and HCT were increased by vitamin A after 2 week of treatment. They became normal after 4 weeks of treatment. Although oxidized fish oil might not affect the toxic effect of vitamin A, taurine significantly reduced them. The effects of taurine, oxidized fish oil and vitamin A on the activities of AST, ALT and ALP in the plasma are shown in Fig. 3. It was found that the activities of AST, ALT and ALP in the plasma of rats fed with the supplement of oxidized fish oil+vitamin A were gradually increased with the feeding time course. The activities of AST, ALT and ALP in the plasma of rats are increased with the increasing of oxidized fish oil+vitamin A. The activities of AST, ALT and ALP in those rats fed diet with supplement of taurine were significantly to reduce the toxicity of vitamin A and oxidized fish oil ($\boldsymbol{P}<0.05$), indicating taurine might play protective effect on oxidized fish oil+vitamin A toxicity in rats.

The effects of taurine, oxidized fish oil and vitamin A on the levels of cholesterol, triglyceride, calcium and phosphorus in the plasma of rats are shown in Fig. 4. After 6 week feeding, it was found that vitamin A significantly increased the levels of these indicators. The oxidized fish oil was found having no effect on these indicators. Although

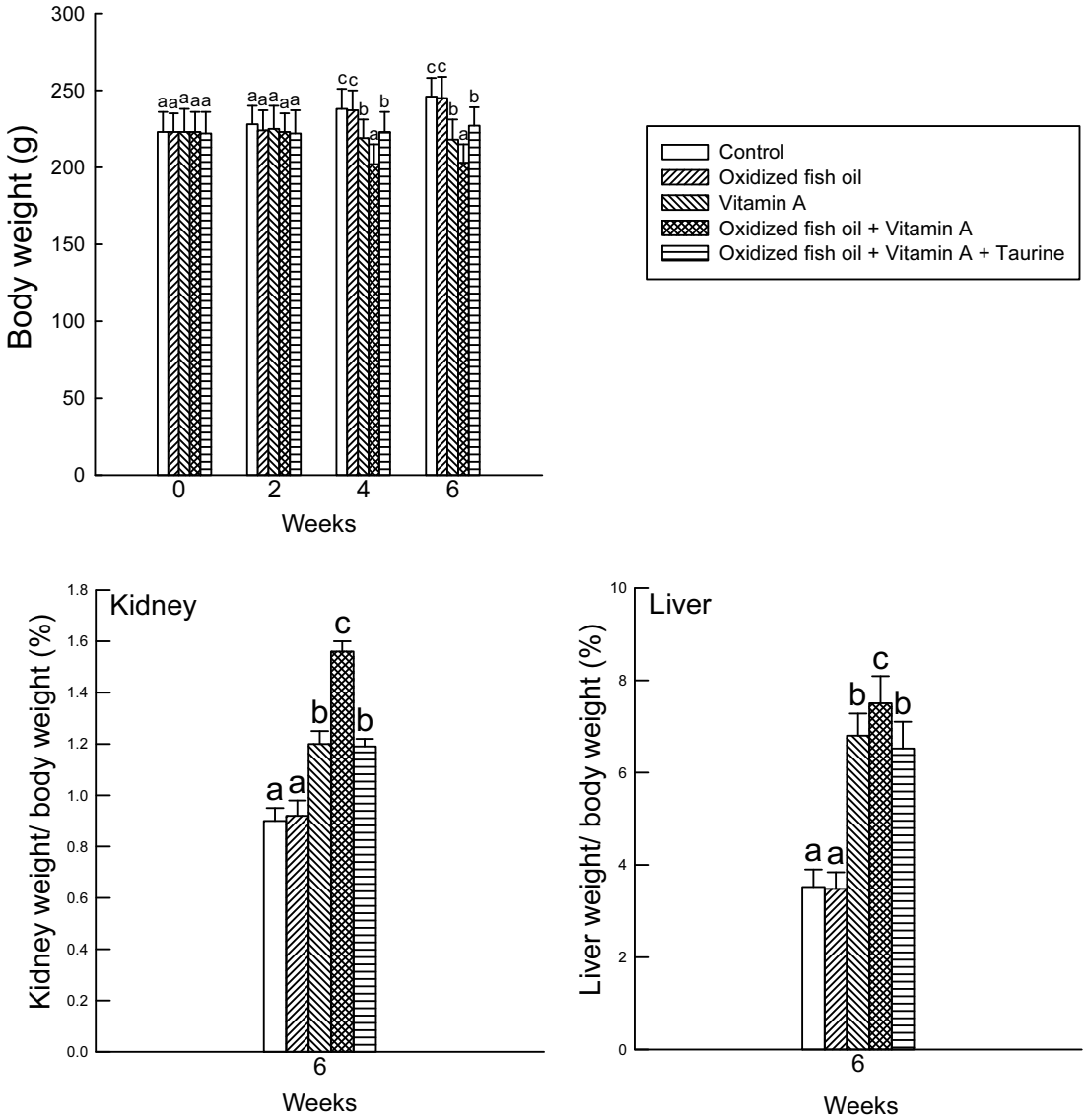

Fig. 1. Effects of taurine, oxidized fish oil and vitamin A on the body weight of rats at 0, 2, 4 and 6 weeks. a-c: values in the same week with different superscript are significantly different (P<0.05) (n=6).

oxidized fish oil did not elevate the levels of cholesterol, calcium and phosphorus in the plasma of rats induced by vitamin A, it significantly inhibited the level of triglyceride. Taurine showed significant effects in reducing the levels of cholesterol, calcium and phosphorus, but triglyceride as compared with the oxidized fish oil+vitamin A, but not as compared with the control group.

The effects of taurine, oxidized fish oil and vitamin A on the concentrations of TBARS and GSH in the liver of rats are shown in Fig. 5. After 2 week of treatment, the level of GSH in the oxidized fish oil+vitamin A. A group (reduced the most. Both vitamin A and oxidized fish oil reduced the level of GSH, while taurine ameliorated the decrease of GSH caused by vitamin A and oxidized fish oil. The level of GSH was soon recovered after 4 weeks of treatment when the rats were treated once with vitamin A and

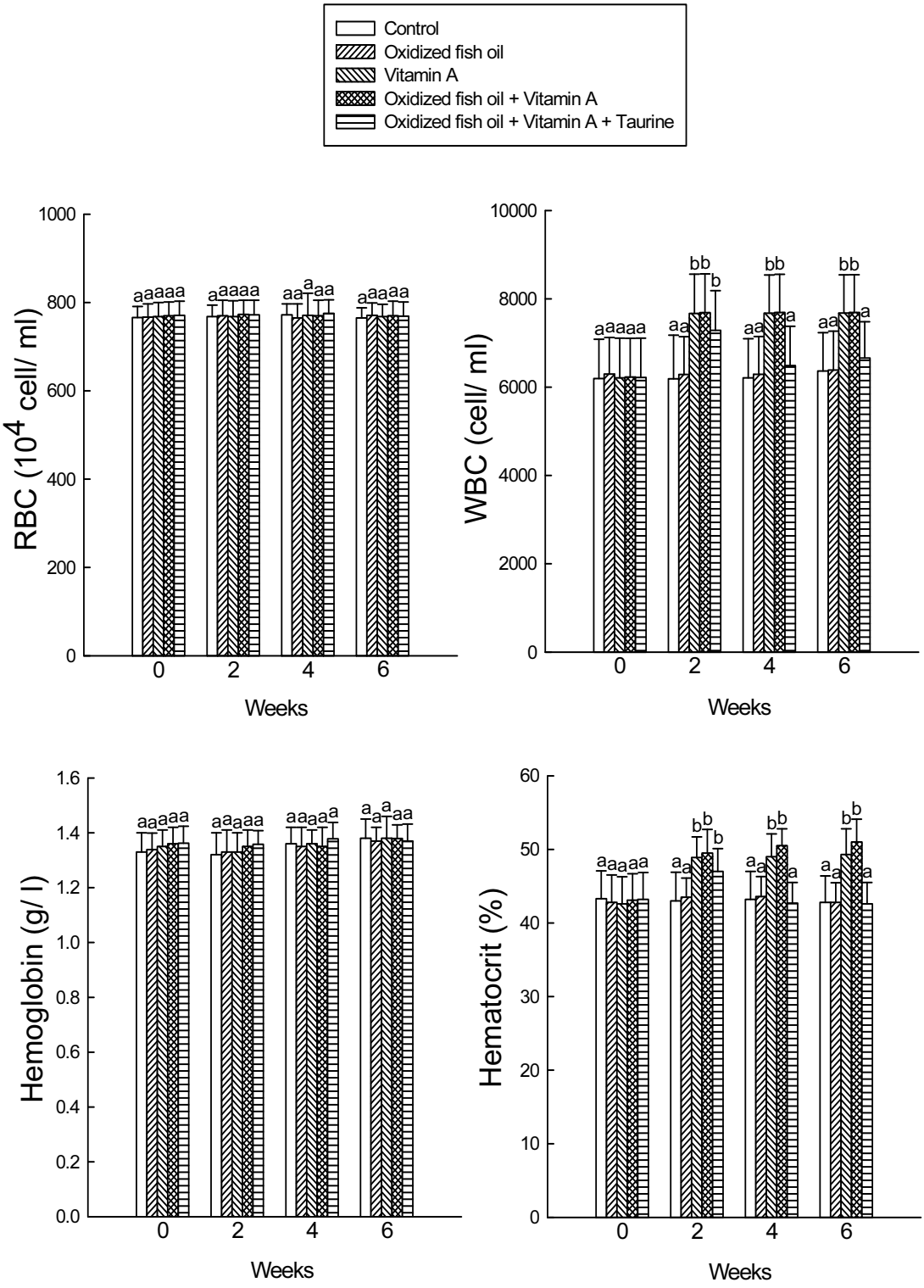

Fig. 2. Effects of taurine, oxidized fish oil and vitamin A on the weight ratios of liver to body and kidney to body of rats at 6 weeks. a-c: values in the same week with different superscript are significantly different (P<0.05) (n=6).

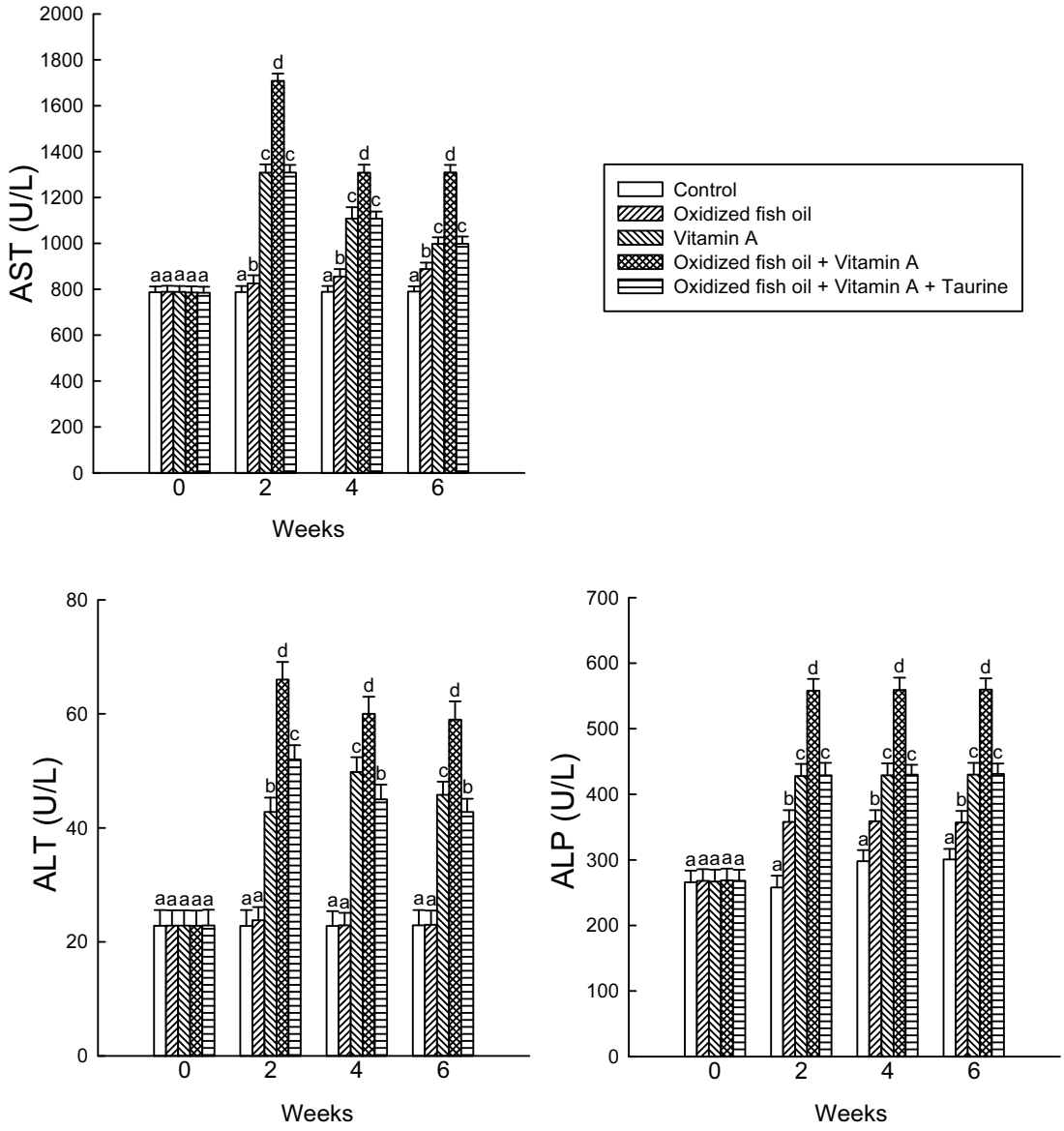

Fig. 3. Effects of taurine, oxidized fish oil and vitamin A on the activities of RBC, WBC, HGB and HCT of serum plasma of rats at 2, 4 and 6 weeks. a-b: values in the same week with different superscript are significantly different (P<0.05) (n=6).

oxidized fish oil. On the contrast, the level of TBARS in the liver of rats induced by vitamin A with or without oxidized fish oil was not recovered even after 6 weeks of treatment. Meanwhile, both vitamin A and oxidized fish oil significantly increased the level of TBARS and exhibited the synergistic effect in increasing the level of TBARS. Taurine showed the effect of ameliorating the toxicity of vitamin A and oxidized fish oil in increasing the level of TBARS.

The effects of taurine, oxidized fish oil and vitamin A on the level of BUN and creatinine in the plasma of rats are also shown in Fig. 5. After 6 week feeding, the level of BUN and creatinine in the plasma was higher in the groups fed diet with supplement of oxidized fish oil+vitamin A than in vitamin A, oxidized fish oil and control group. When the diet

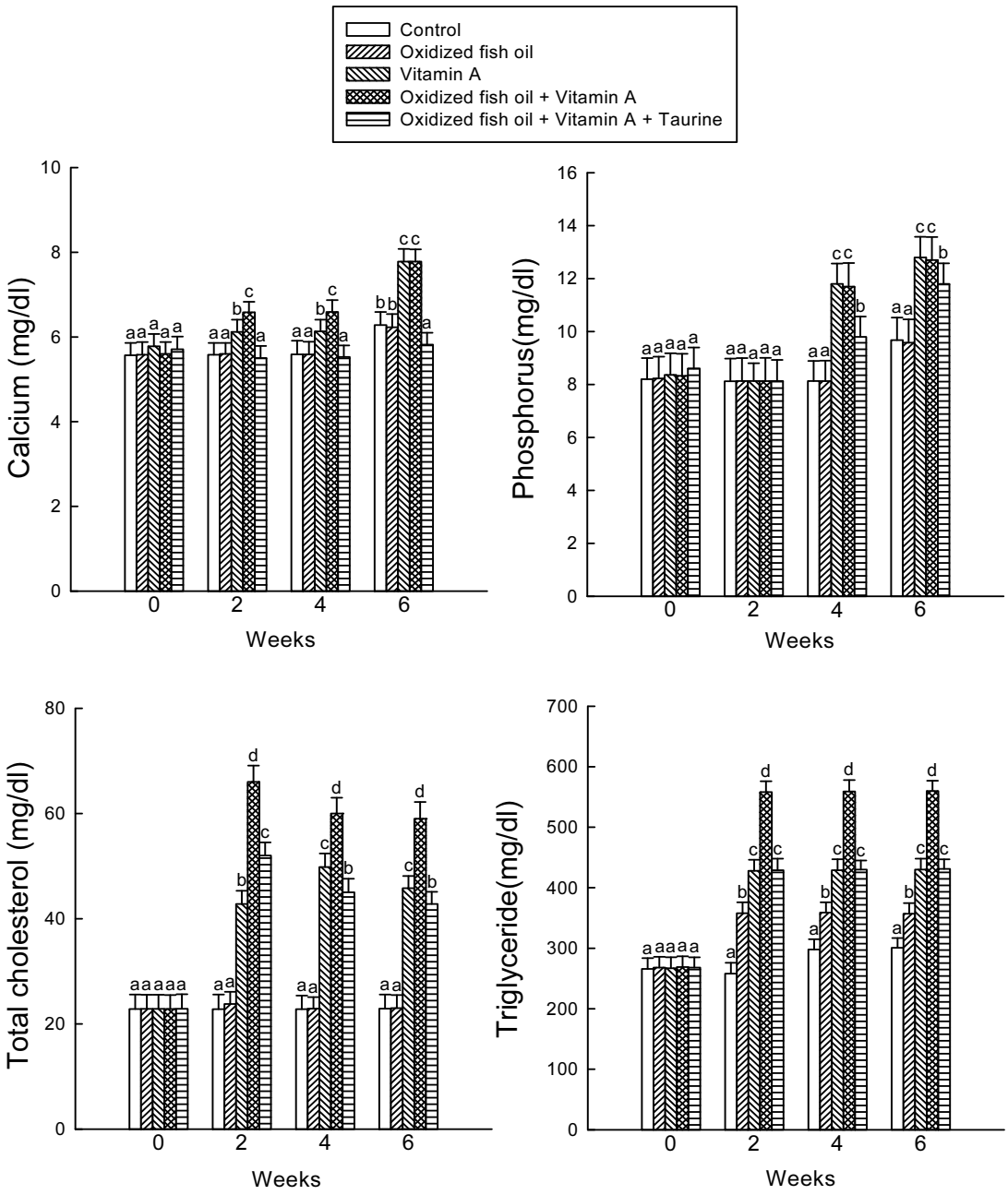

Fig. 4. Effects of taurine, oxidized fish oil and vitamin A on the activities of AST, ALT, and ALP of serum plasma of rats at 2, 4 and 6 weeks. a-d: values in the same week with different superscript are significantly different (P<0.05) (n=6).

was supplemented with taurine, the level of BUN and creatinine was significantly reduced (P<0.05).

The effects of taurine, oxidized fish oil and vitamin A on the TBARS production in the plasma in rats are shown in Fig. 6. After 6 week feeding, the level of TBARS in the plasma of rats fed with supplement of oxidized fish oil+vitamin A was higher than that of control group (P<0.05). When the diet was supplemented with taurine, the level of TBARS was significantly reduced (P<0.05).

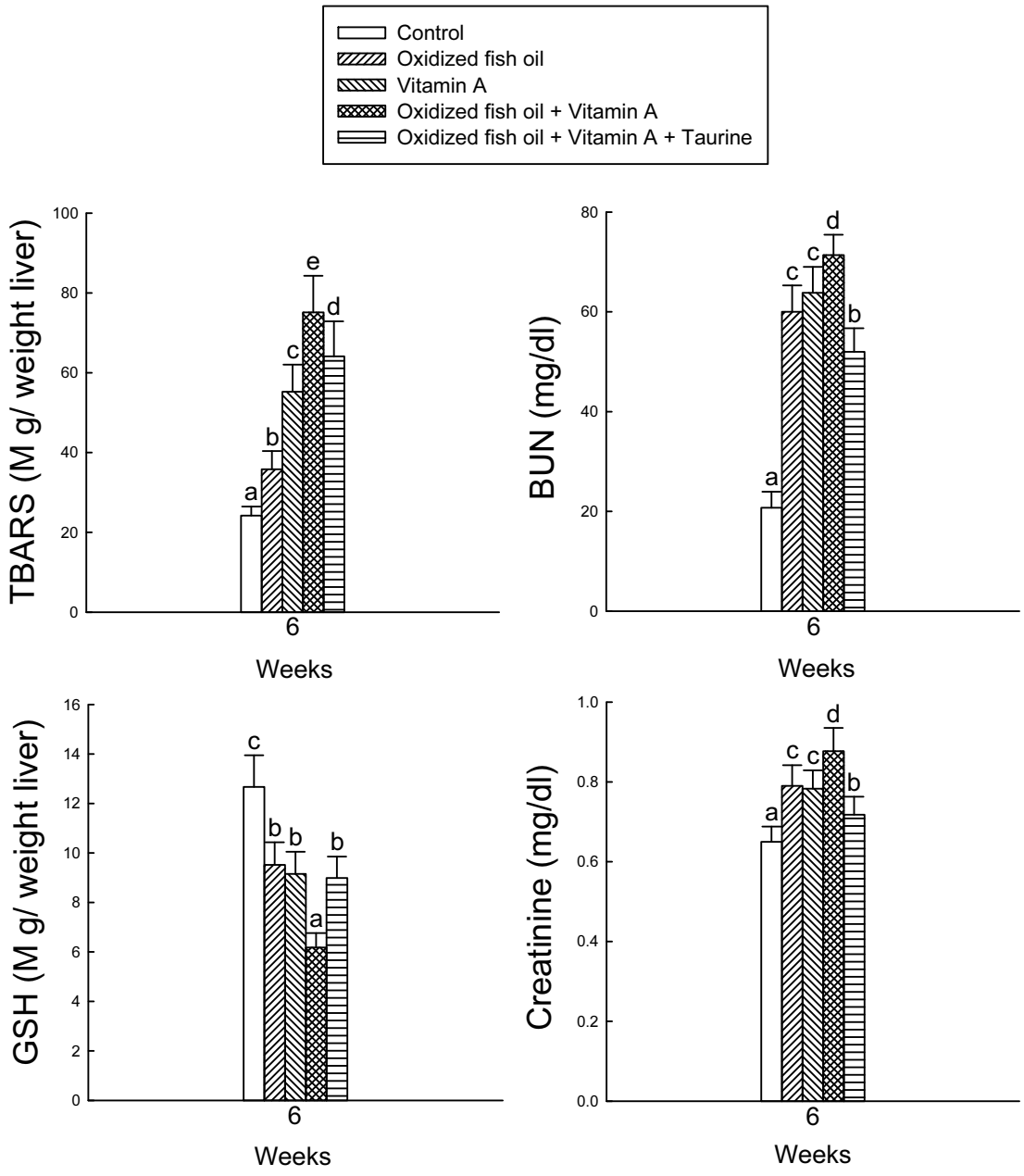

Fig. 5. Effects of taurine, oxidized fish oil and vitamin A on the levels of cholesterol, triglyceride, calcium, and phosphorus of serum plasma of rats at 2, 4 and 6 weeks. a-d: values in the same week with different superscript are significantly different (P<0.05) (n=6).

The effects of taurine and vitamin A on the level of vitamin A in the liver, kidney and serum of rats are shown in Fig. 7. After 6 week feeding, the level of vitamin A in the liver, kidney and serum was obviously higher in the groups fed diet with supplement of vitamin A than in control group. The level of vitamin A in the liver, kidney and serum was increased with the increasing dose of vitamin A in the diet. When the diet was supplemented with taurine, the level of vitamin A in the liver and kidney was significantly reduced, and the level of vitamin A in the serum was slightly increased (P<0.05).

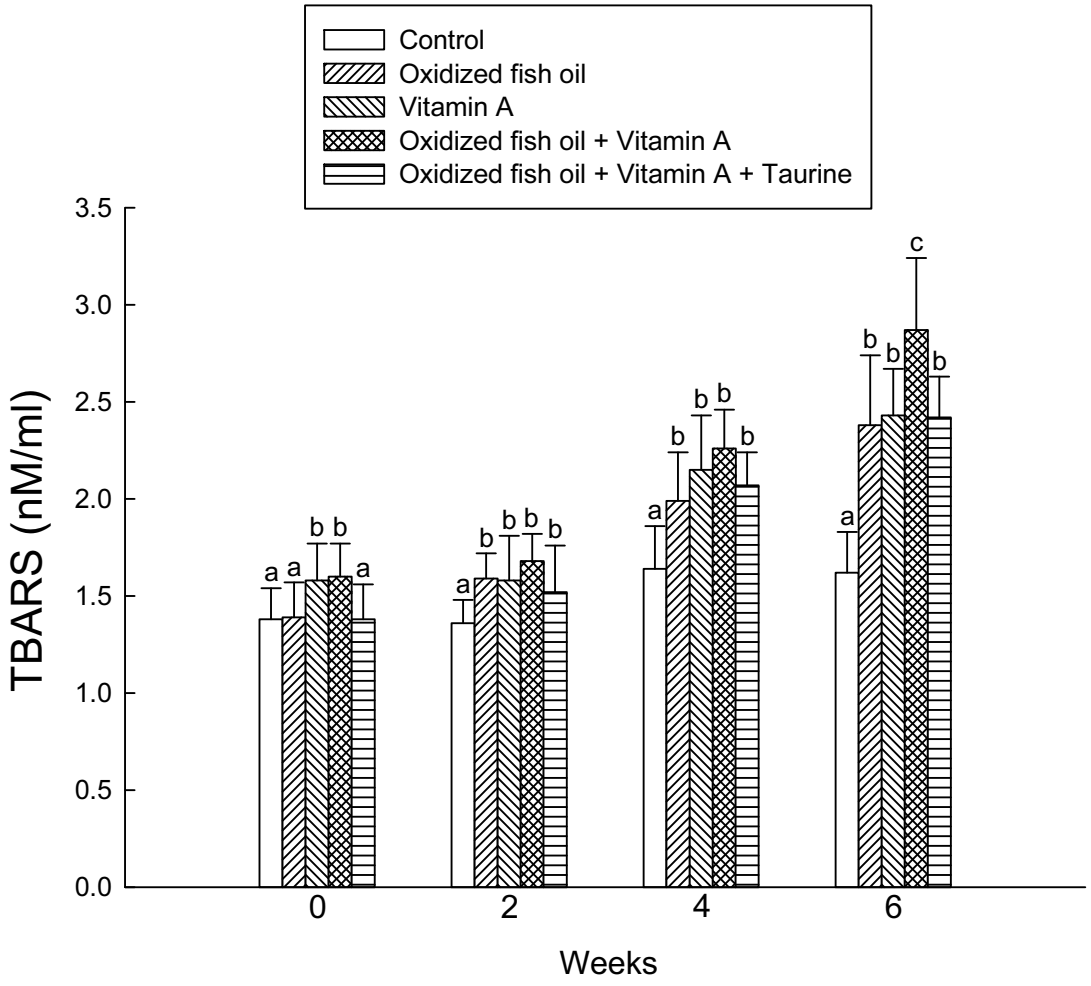

Fig. 6. Effects of taurine, oxidized fish oil and vitamin A on the levels of TBARS and GSH in the liver and BUN and creatinine in the plasma of rats at 6 weeks. a-e: values in the same week with different superscript are significantly different (P<0.05) (n=6).

Histopathological changes were assessed by observing in the kidney and liver section for necrotic and swollen hepatocytes. Referring to the histological finding is shown in Figs. 8, 9. Swollen cells are identified by enlargement and ruptured plasma membrane. Morphological alterations involving all zones of hepatic lobule were observed in the vitamin A and oxidized fish oil+vitamin A treatment revealed necrosis or degeneration and enlargement of the tubular or peritubular tissues.

Discussion

Typical symptoms of acute vitamin A in rats were the liver and kidney enlargement and high level of triglyceride in plasma[5]. In this study, the symptoms of vitamin A caused by acute excess retinyl palmitate were as follows: 1. The body weight and the concentration of GSH in the liver were reduced. 2. The ratios of liver and kidney weights to body weight, the activities of AST, ALT and ALP in plasma, the levels of cholesterol, triglyceride, calcium, and phos-

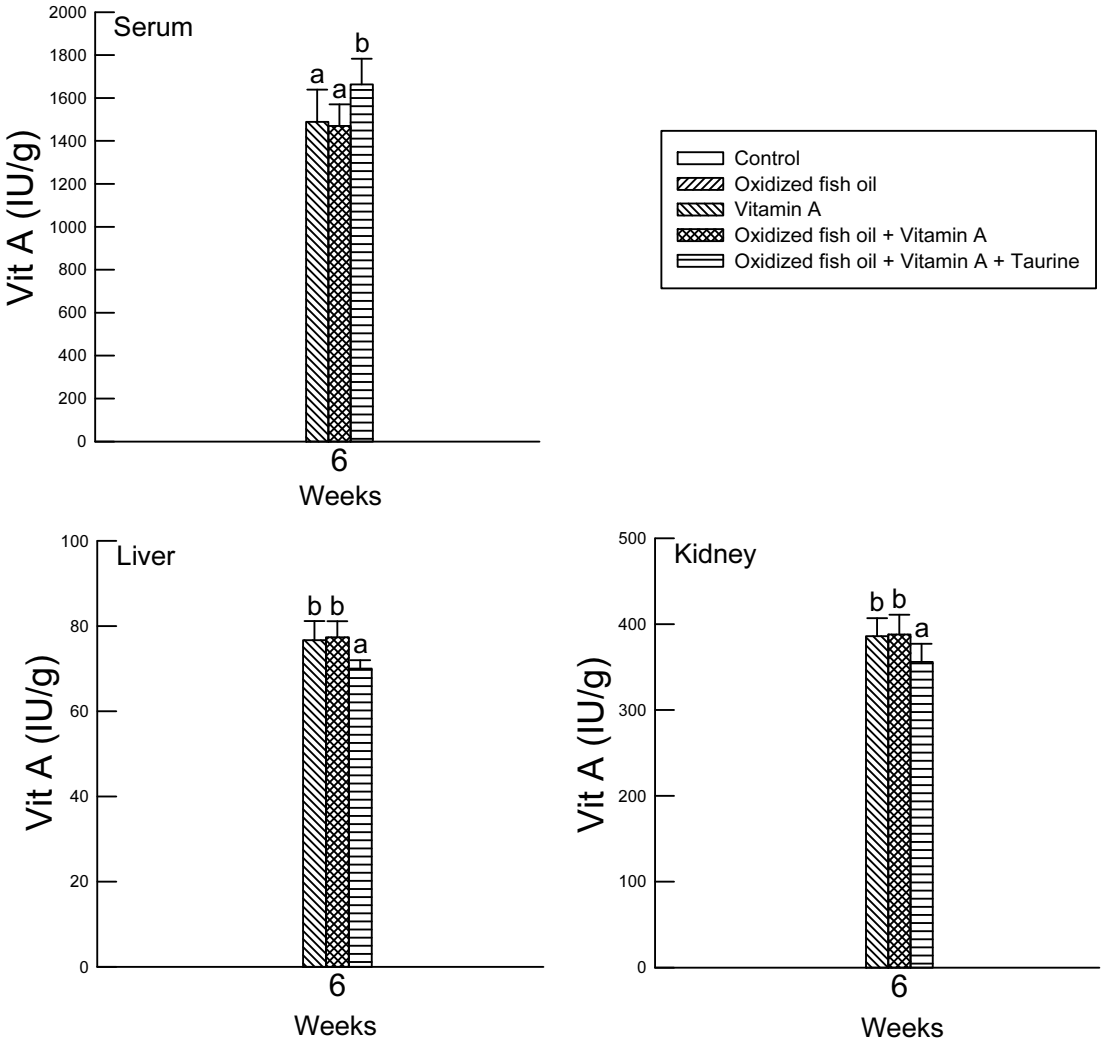

Fig. 7. Effect of taurine, oxidized fish oil and vitamin A on the level of TBARS in the plasma of rats at 2, 4 and 6 weeks. a-c: values in the same week with different superscript are significantly different (P<0.05) (n=6).

phorus in plasma, the level of TBARS in liver and the concentration of WBC and HCT in blood were increased. Among them, blood parameters, GSH and triglyceride recovered normal after 4 or 6 weeks of treatment. In some papers, retinol has been reported to reduce GSH depletion following a toxicant challenge and therefore protect from injury[35-37]. Bray et al.[38] indicated that retinol could not affect the level of GSH nor induce any activity of cytochrome P450 enzymes in the mice. However, retinol supplementation had the effect of decreasing GSH stored in the lung[39]. It indicates that retinal acting as an antioxidant or xenobiotic role depends on species, tissues, dose and other factors. In this study, high dose of retinol in rats might act as a xenobiotic role because it reduced the level of GSH in liver. The reason might be the vitamin A, which induces the expression of cytochrome P450 enzymes and then depletes GSH. The mechanism still needs to be studied.

Oxidized fish oil significantly elevated the tox-

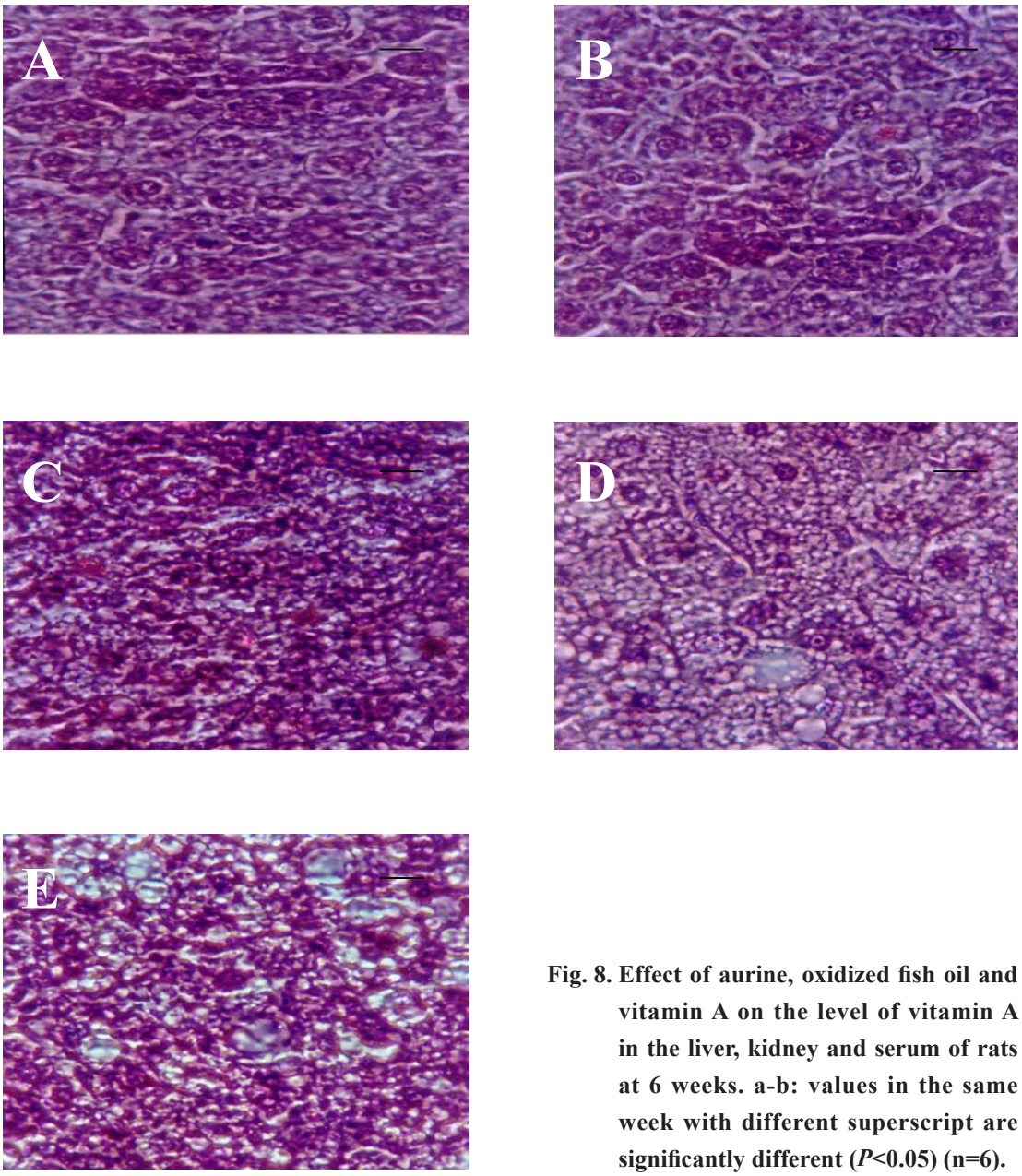

Fig. 8. Effect of aurine, oxidized fish oil and vitamin A on the level of vitamin A in the liver, kidney and serum of rats at 6 weeks. a-b: values in the same week with different superscript are significantly different (P<0.05) (n=6).

icity of vitamin A, including to reduce body weight and the concentration of GSH in liver and to increase the ratios of liver and kidney weight to body weight, the activities of AST, ALT and ALP in plasma, the levels of BUN and creatinine in the plasma, and the level of TBARS in liver. Furthermore, oxidized fish oil exhibited the reducing effect on the level of triglyceride due to retaining PUFA in oxidized fish oil[7]. Contrastly, taurine significantly ameliorated the toxicity of vitamin A and oxidized fish oil, including to increase body weight and to reduce the concentration of WBC and HCT in blood, the level of TBARS in liver and plasma, the ratios of liver and kidney weight to body weight, the activities of AST, ALT

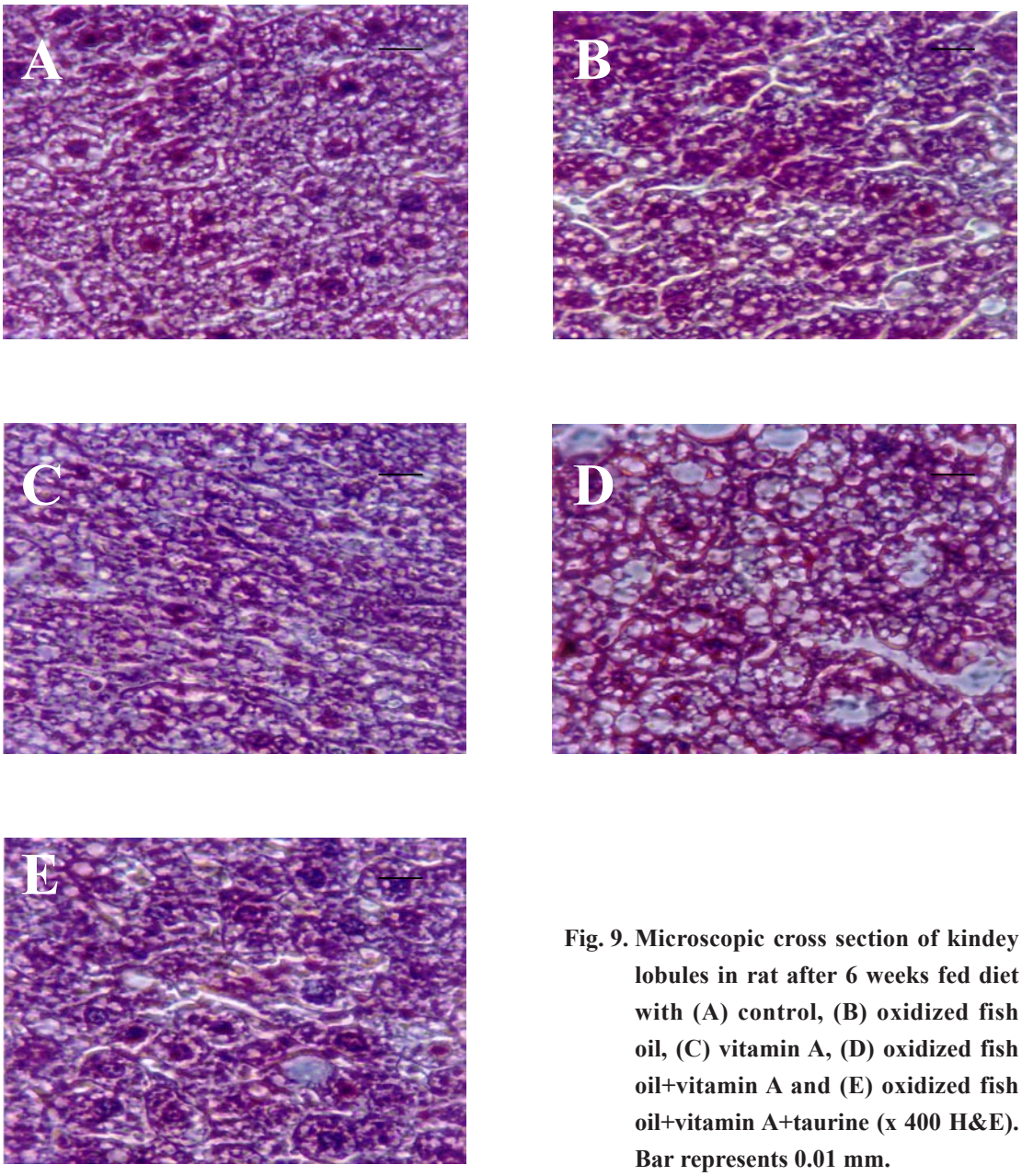

Fig. 9. Microscopic cross section of kindey lobules in rat after 6 weeks fed diet with (A) control, (B) oxidized fish oil, (C) vitamin A, (D) oxidized fish oil+vitamin A and (E) oxidized fish oil+vitamin A+taurine (x 400 H&E). Bar represents 0.01 mm.

and ALP in plasma, the levels of BUN and creatinine in the plasma and the levels of cholesterol, calcium, and phosphorus in plasma. Therefore, oxidized fish oil elevated the toxicity of vitamin A, while taurine prevented the toxicity of vitamin A and oxidized fish oil. Taurine may play an important role in preventing the toxicity of vitamin A because the levels of cholesterol, calcium and phosphorus in plasma of rat were induced by vitamin A was affected by taurine only.

Although the long-term toxicity of oxidized fish oil in rats was found serious[26], the toxicity of the dose (POV 6.6 meq) in this study was not. The oxidized fish oil revealed to increase the activity of AST, ALT and ALP in plasma and the level of TBARS in liver and plasma, and to decrease the concentration of GSH in liver. It showed a strong synergistic effect on

the toxicity of vitamin A. The activities of AST, ALT and ALP in plasma were significantly affected by vitamin A in oxidized fish oil. Taurine significantly reduced the enzymatic activities of AST, ALT and ALP in plasma, indicating that the toxicity of vitamin A and oxidized fish oil could be ameliorated by taurine. In the previous paper[7], taurine was proved to play an important role in preventing the toxicity of oxidized fish oil. In this study, taurine also showed itself important in preventing the toxicity of vitamin A either with or without oxidized fish oil.

TBARS is an end product of lipid peroxidation. The level of TBARS in the liver and plasma increased when vitamin A and/or oxidized fish oil were fed to the rats. This means that the toxicity of vitamin A either with or without oxidized fish oil was caused by lipid peroxidation. The level of TBARS in liver and plasma decreased significantly when the rats were treated with taurine. The result is the same as those reported previously[24, 25, 40, 41]. Therefore, it is reasonable to assume that taurine may act as a good scavenger for the products of lipid peroxidation induced by drugs[40], heavy metal[24, 25] and oxidized oil[26]. The function of GSH for protecting biological organisms from xenobiotic injuries is well known[42-45]. The level of GSH in liver was raised significantly when the rats were treated with the supplement of taurine. It suggests that taurine may play an important role in the metabolism of GSH. The related mechanism should be studied further.

On the other hand, the levels of BUN and creatinine in the plasma of rats are tested as indicators for kidney functions[46, 47]. Judging from both indicators and the ratio of kidney weight to body weight, vitamin A and oxidized fish oil significantly induced the dysfunction of kidney. Although supplementing with taurine in diet did not ameliorate the ratio of kidney weight to body weight, the levels of BUN and creatinine in the plasma of rats were significantly reduced when the rats were fed diet with supplement of taurine. The accumulated amount of vitamin A was higher in the kidney than in the liver, which was the same as previous report[48]. Accumulation of vitamin A is the net consequence of uptake, biotransformation and elimination processes within an individual. Once vitamin A is absorbed, taurine exert synergistic actions in scavenging it may be transformed into vitamin-thionein. Although the half-life of vitamin-thionein in the liver and kidney is not known exactly, it is many years[49] with continued retention, there is progressive accumulation in these tissues. The accumulated amount of vitamin A in the tissue was effectively reduced by taurine. Taurine is a special amino acid, which possesses an amino group and a sulfonate group. These functional groups might bind with vitamin A, and then stimulated the excretion of such compounds. In this study, it was also found that the amount of vitamin A in the serum of rats fed with supplement of taurine was slightly increased. There is no evidence that taurine directly reduces the production of free radicals but it may well operate by binding vitamin A which is then not absorbed or is more rapidly excreted. In other words it may act by reducing the overall bioavailability of vitamin A or the intracellular availability of absorbed vitamin A. Hence, dietary taurine may play a role to reduce the toxic effect of vitamin A in the liver and kidney of rats. In this study, it was also found that the amount of oxidized fish oil and vitamin A in the serum of rats fed with the supplement of taurine was slightly increased. There is no evidence that taurine directly reduces the production of free radicals but it may well

operate by binding oxidized fish oil and vitamin A which is then not absorbed or is more rapidly excreted. In other words it may act by reducing the overall bioavailability of oxidized fish oil and vitamin A or the intracellular availability of absorbed oxidized fish oil and vitamin A. Hence, dietary taurine may play a role to reduce the toxic effect of oxidized fish oil and vitamin A in the liver and kidney of rats.

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攝食牛磺酸降低雄性鼠攝食氧化魚油和維生素A所產生的毒性影響

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為了解牛磺酸對於大鼠攝食氧化魚油和維生素A所產生的毒性影響，乃將30隻雄性Wistar系大鼠分成5個組別，分別為控制組、餵食氧化的魚油（3%）、維生素A（50,000 IU）、氧化的魚油（3%）和幼兒用藥小冊子(中英文)封面(1116)（50,000 IU）、添加牛磺酸（5%）在氧化的魚油（3%）和維生素A（50,000 IU）的大鼠分別飼養6週，並在第2、4和6週分析大鼠的血液中之生化指標等，實驗發現，攝食氧化魚油會提高攝食維生素A所產生的毒性影響，會造成大鼠的體重的降低，肝臟中的glutathione（GSH） 減少（P<0.05），肝體比和腎體比增加（P<0.05），asparate transferase（AST）、alanine transaminase（ALT）、alkaline phosphatase（ALP）、肝臟中的thiobarbituric acid-relative substances（TBARS）、blood urea nitrogen（BUN）和creatinine之指數上升（P<0.05），在餵食添加牛磺酸在氧化魚油和維生素A的組別發現體重增加，並且可降低大鼠血液中white blood cell（WBC）、hematocrit（HCT）、肝臟及腎臟中的維生素A、肝臟中的TBARS、肝體比和腎體比、AST、ALT、ALP、cholesterol、triglyceride、calcium、phosphorus（P<0.05），因此，氧化魚油會升高維生素A的毒性，由此顯示食物中添加牛磺酸在大鼠的飲食中可預防和降低氧化魚油和維生素A所產生的毒性作用。

關鍵字：維生素A、氧化魚油、牛磺酸、毒性影響、大鼠

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