Influence of Oryzanol and Ferulic Acid on the Lipid Metabolism and Antioxidative Status in High Fat-Fed Mice

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Summary The comparative effects of oryzanol and ferulic acid on the lipid metabolism and antioxidative status of high fat-fed mice were investigated. The mice were given a diet containing 17% fat (HF), supplemented with oryzanol (HF-O) or ferulic acid for 7 weeks. The control mice (NC) were fed with normal diet. The HF mice exhibited increased body weight gain, plasma and hepatic total cholesterol and triglyceride concentrations, and lipid peroxidation rate, and reduced high-density lipoprotein cholesterol level. In general, they also showed lower hepatic antioxidant and higher lipid-regulating enzymes activities relative to that of NC group. Addition of oryzanol or ferulic acid in the diet counteracted these high fat-induced hyperlipemia and oxidative stress via increased faecal lipid excretion and regulation of antioxidant and lipogenic enzymes activities. This study illustrates that oryzanol and ferulic acid have relatively similar hypolipidemic actions and could be effective in lowering the risk of high fat diet-induced obesity.

Key Words: oryzanol, ferulic acid, lipid metabolism, antioxidant enzyme, obesity

Introduction

Scientific studies have shown that high dietary fat intake promotes the development of obesity in humans and rodents as a result of an imbalance between energy intake and energy expenditure [1]. Characterized by the accumulation of excess adipose tissue, obesity is considered the leading metabolic disease in the world due to its rapidly increasing prevalence in both developed and developing countries [2]. The progression of obesity has been associated with a higher risk for type II diabetes mellitus, cardiovascular disease, and dyslipidemia [2, 3]. Moreover, obese people were also found to have respiratory disorders such as obstructive sleep apnea and obesity hypoventilation syndrome [2].

Recently, a number of studies have focused on the prevention and treatment of obesity and its associated health risks using naturally-occurring antioxidants. Phenolics, in particular, exhibit a wide range of pharmacological properties including anti-inflammatory, anti-cancer, and hypolipidemic [4]. They are widely distributed in plants and therefore a basic part of the human diet. Oryzanol and ferulic acid, the major phenolic compounds in rice bran oil, were reported to have strong antioxidant activities [5, 6]. They possess various physiological properties, such as inhibition of tumor promotion, reduction of serum cholesterol levels, and protective action against liver injury [6–8].

Oryzanol is a mixture of ferulic acid (4-hydroxy-3-methoxycinnamic acid) esters of triterpene alcohols [9] and primarily extracted from rice bran oil. On the other hand, aside from cereal grains, ferulic acid is also abundantly present in various fruits and vegetables, such as banana, citrus fruits, bamboo shoots, eggplant, cabbage, and broccoli [10]. Wilson et al. reported that oryzanol has a greater effect on lowering plasma lipid and lipoprotein cholesterol concentrations in hypercholesterolemic hamsters [7]. However, they also suggested that ferulic acid may have a greater antioxidant capacity compared with oryzanol.

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While the health aspects of oryzanol and ferulic acid have been studied extensively in the past, there have been few reports on the physiological functions of these phenolic compounds in relation to obesity. Furthermore, the comparative effects of these phytochemicals on the lipid metabolism and antioxidative status remain unclear. Thus, this study was conducted to evaluate and compare the effects of dietary feeding of oryzanol and ferulic acid on the lipid metabolism and antioxidant enzyme activity in mice fed with high fat diet.

Materials and Methods

Animals and diet

Thirty-two male C57BL/6 mice of 4 weeks of age, weighing 12 g, were obtained from Orient Inc. (Seoul, Korea). They were individually housed in stainless steel cages in a room maintained at 25°C with 50% relative humidity and 12/12 h light/dark cycle and fed with a pelletized chow diet for 2 weeks after arrival. The mice were then randomly divided into 4 dietary groups \((n = 8)\). The first and second groups were fed with a normal (NC) and high fat (HF, 17% w/w) diets, respectively, while the other two groups were fed with high fat diet supplemented with either oryzanol (HF-O) or ferulic acid (HF-FA, >98% pure, Tsuno, Osaka, Japan). The composition of the experimental diet (Table 1) was based on the AIN-76 semisynthetic diet. The mice were fed for 7 weeks and allowed free access to food and water during the experimental period. The food consumption and weight gain were measured daily and weekly, respectively. Faeces were collected during the final week to measure the level of faecal cholesterol and glyceride excretion. At the end of the experimental period, the mice were anaesthetized and sacrificed. Blood samples were collected and centrifuged at 1,000 \(\times g\) for 15 min at 4°C to obtain the plasma. The livers were removed, rinsed with physiological saline, and stored at −70°C until analysis. The current study protocol was approved by the Ethics Committee of Kyungpook National University for animal studies.

Measurement of plasma, hepatic, and faecal lipids

The plasma total cholesterol (TC), total triglyceride (TG), and high-density lipoprotein (HDL) cholesterol were determined using a commercial kit (Asan Pharmaceutical, Seoul, Korea). The liver and faecal lipids for TC and TG analyses were extracted and purified using the method described by Folch et al. [11].

Determination of lipid peroxidation

The erythrocyte and plasma thiobarbituric acid reactive substances (TBARS) were measured according to the method of Ohkawa et al. [12]. Trichloroacetic acid (5%, v/v) and 0.06 M thiobarbituric acid were added to 50 μL of plasma and red blood cell preparation and incubated at 80°C for 90 min. After cooling at room temperature, the mixtures were centrifuged at 2,000 rpm for 25 min and the absorbance of the resulting supernatant was determined at 535 nm. A malondialdehyde (MDA) solution was used as standard. The results were calculated and expressed as nmol MDA/mL plasma or g Hb.

Determination of hepatic lipid-regulating enzyme activities

The glucose-6-phosphate dehydrogenase G6PD activity was measured based on the reduction of 6 mM NADP⁺ by

| Table 1. Composition of the experimental diets (%) | \(\text{Component} \) | \(\text{Dietary group}\) | NC | HF | HF-O | HF-FA |
|---|---|---|---|---|---|---|
| Casein | 20 | 20 | 20 | 20 |
| DL-Methionine | 0.3 | 0.3 | 0.3 | 0.3 |
| Sucrose | 50 | 49.5 | 49.5 | 49.5 |
| Corn starch | 15 | 5 | 5 | 5 |
| Cellulose | 5 | 5 | 5 | 5 |
| Corn oil | 5 | 3 | 3 | 3 |
| Cholinebitartrate | 0.2 | 0.2 | 0.2 | 0.2 |
| Mineral mixture\(^1\) | 3.5 | 3.5 | 3.5 | 3.5 |
| Vitamin mixture\(^2\) | 1 | 1 | 1 | 1 |
| Lard | 17 | 17 | 17 | 17 |
| \(\gamma\)-oryzanol | 0.5 | 0.5 | 0.5 | 0.5 |
| Ferulic acid | | | | |
| Total (%) | 100 | 100 | 100 | 100 |

\(^1\)NC, normal diet; HF, high fat diet; HF-O, high fat diet + oryzanol; HF-FA, high fat diet + ferulic acid. \(^2\)AIN-76 mineral mixture. \(^3\)AIN-76 vitamin mixture.
G6PD in the presence of glucose-6-phosphate [13]. The enzyme activity was determined by monitoring the increase in absorption of the reaction mixture at 340 nm at 37°C. The activity was expressed as the reduction of 1 nmol of NADPH/min.

The malic enzyme (ME) activity was determined using the method of Ochoa [14]. The reaction mixture contained 125 mM potassium phosphate buffer (pH 7.4), 10 mM EDTA, 10 mM β-mercaptoethanol, 33 μM acetyl-CoA, 100 μM malonyl-CoA, and 100 μM NADPH. The mixture was added with malonyl CoA and the change in absorbance at 340 nm at 30°C was recorded. The initial rate of activity was expressed as the rate of utilization of NADPH in nmol/min/mg protein.

The catalase (CAT) activity was measured using the method of Aebi [17]. The activity was determined using the method of Paglia and Valentine [19]. The catalase was measured spectrophotometrically according to the method developed by Mackness et al. [20]. Briefly, 50 μL of serum was added to 1 ml Tris/HCl buffer (100 mM, pH 8.0) containing 2 mM CaCl₂ and 5.5 mM paraoxon. The absorbance of the mixture was measured at 340 nm. A molar extinction coefficient of 0.041/mM/cm was used to determine the activity, which was expressed as nmol oxidized NADPH/min/mg protein.

The glutathione reductase (GR) activity was determined using the method of Mize and Langdon [15]. The reaction mixture contained 1 mM EDTA and 1 mM GSSG in a 0.1 M potassium phosphate buffer (pH 7.4). The oxidation of NADPH was monitored at 340 nm and the activity was expressed as nmol oxidized NADPH/min/mg protein.

The superoxide dismutase (SOD) activity was spectrophotometrically measured according to the method described by Marklund and Marklund [16]. The SOD was detected on the basis of its ability to inhibit superoxide-mediated reduction. The activity was expressed as unit/mg protein, wherein one unit represents the amount of enzyme that inhibited the oxidation of pyrogallol by 50%.

The glutathione peroxidase (GSH-Px) activity was determined based from the method described by Gibson and Hubbard [15]. The assay mixture contained 125 mM potassium phosphate buffer (pH 7.0), 10 mM EDTA, 10 mM β-mercaptoethanol, 33 μM acetyl-CoA, 100 μM malonyl-CoA, and 100 μM NADPH. The mixture was added with malonyl CoA and the change in absorbance at 340 nm at 30°C was recorded. The initial rate of activity was expressed as the rate of utilization of NADPH in nmol/min/mg protein.

### Determination of hepatic antioxidant enzyme activities

The superoxide dismutase (SOD) activity was spectrophotometrically measured according to the method developed by Marklund and Marklund [16]. The SOD was detected on the basis of its ability to inhibit superoxide-mediated reduction. The activity was expressed as unit/mg protein, wherein one unit represents the amount of enzyme that inhibited the oxidation of pyrogallol by 50%.

The catalase (CAT) activity was measured using the method of Aebi [17]. The disappearance of hydrogen peroxide was monitored spectrophotometrically at 240 nm for 5 min. A molar extinction coefficient of 0.041/mM/cm was used to determine the CAT activity. The activity was defined as the μmol decreased H₂O₂/min/mg protein.

The glutathione peroxidase (GSH-Px) activity was measured according to the method of Paglia and Valentine with slight modifications [18]. The cytosolic supernatant was added to the reaction mixture (6 mM glutathione, 1.2 mM NADPH, and 1.25 um H₂O₂: in 20 mM Tris-HCl, pH 7.0), which was pre-warmed at 25°C for 5 min. The mixture was further incubated at 25°C for 5 min and the absorbance was measured at 340 nm. A molar extinction coefficient of 6.22/mM/cm was used to determine the activity, which was expressed as nmol oxidized NADPH /min/mg protein.

The glutathione reductase (GR) activity was determined using the method of Mize and Langdon [19]. The reaction mixture contained 1 mM EDTA and 1 mM GSSG in a 0.1 M potassium phosphate buffer (pH 7.4). The oxidation of NADPH was monitored at 340 nm and the activity was expressed as nmol oxidized NADPH/min/mg protein.

The paraoxonase (PON1) activity was determined based from the method described by Mackness et al. [20]. Briefly, 50 μL of serum was added to 1 ml Tris/HCl buffer (100 mM, pH 8.0) containing 2 mM CaCl₂ and 5.5 mM paraoxon. The absorbance of the mixture was measured at 340 nm to determine the generation rate of 4-nitrophenol. The enzymatic activity was calculated using the molar extinction coefficient 17100/M/cm.

### Statistical Analysis

All data are presented as the mean ± SE. The data was evaluated by one-way ANOVA using a Statistical Package for Social Sciences software program (SPSS Inc., Chicago, IL) and the differences between the means were assessed using Duncan’s multiple range test. Statistical significance was considered at p<0.05.

### Results and Discussion

#### Body weight gain

Prior to feeding the mice with the experimental diets, there was no significant difference in the body weight among the mice groups (Table 2). The daily food intake did not differ among the animal groups and was constant (3 g/day) throughout the study. At the end of the experimental period, a substantially higher body weight was observed in mice fed with high fat diet (HF group) than that of the normal control mice (NC group). Previous studies have also shown a significant increase in the body weight of rats after a high fat-diet feeding relative to that of the normal diet-fed ones [21]. While the mice fed with high fat in

| Dietary group | Initial weight (g) | Final weight (g) | Weight gain (g) |
|---------------|--------------------|-----------------|----------------|
| NC            | 20.43 ± 0.20      | 23.34 ± 0.54    | 2.90 ± 0.50    |
| HF            | 20.40 ± 0.19      | 31.02 ± 0.50    | 10.61 ± 0.19   |
| HF-O          | 20.34 ± 0.19      | 28.13 ± 0.45    | 7.78 ± 0.57    |
| HF-FA         | 20.24 ± 0.19      | 25.81 ± 0.25    | 5.57 ± 0.37    |

\(^{1}\) Values are means ± SE (n = 8). Means in the same column not sharing a common superscript are significantly different at p<0.05. \(^{2}\) NC, normal diet; HF, high fat diet; HF-O, high fat diet + oryzanol; HF-FA, high fat diet + ferulic acid.

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combination with oryzanol (HF-O group) or ferulic acid (HF-FA group) also exhibited higher final body weight compared with that of the control ones, their body weight was considerably lower than that of the HF group. This indicates that dietary feeding of oryzanol or ferulic acid significantly suppressed the weight gain of the high fat diet-induced obesity in mice. Moreover, it was also observed that the weight gain of HF-FA group was significantly lower than that of the HF-O group, suggesting that ferulic acid is more effective than oryzanol in controlling the increase in body weight of mice under a high fat diet.

Plasma, hepatic, and faecal lipid profiles

The effect of high fat diet supplemented with oryzanol or ferulic acid on the plasma, liver, and faecal lipids of mice is presented in Table 3. The HF mice exhibited considerably higher total cholesterol and triglyceride contents in the blood plasma and liver than that of the NC group. A high fat diet was reported to induce oxidative injury and lipid abnormalities in rats [22]. Earlier researches also revealed elevated levels of plasma and hepatic total cholesterol and triglycerides in rats fed with a high fat diet [21]. In the present study, the plasma and liver total cholesterol levels in HF-O and HF-FA mice did not significantly differ with that of the NC group, indicating that both oryzanol and ferulic acid were able to prevent the increase in cholesterol level in high fat-fed mice. Furthermore, significantly higher plasma HDL-cholesterol contents were found in HF-O and HF-FA groups compared with that of the NC and HF ones. The mice fed with ferulic acid exhibited the lowest plasma triglyceride content, while the HF-O mice showed similar triglyceride level with the NC group. These findings are in accordance with the results obtained by other researchers, wherein oryzanol and ferulic acid also lowered the plasma total cholesterol and triglyceride levels and increased the HDL-cholesterol concentrations in hypercholesterolemic rats and hamsters [7, 23]. Although the hepatic triglyceride levels in HF-O and HF-FA groups were higher in comparison with that of the control mice, they were still significantly lower than that of the HF group. It was also noted that supplementation of oryzanol and ferulic acid resulted in an increased faecal excretion of cholesterol and triglyceride, respectively. It appears that these phytochemicals were able to improve the plasma and hepatic lipid profile in mice under a high fat diet by significantly increasing the faecal lipid excretion.

Table 3. Plasma, hepatic, and faecal lipid profiles in mice fed with high fat diet supplemented with oryzanol and ferulic acid

| Dietary Group | Plasma Lipids | Liver Lipids | Faecal Lipids |
|--------------|--------------|--------------|---------------|
|              | Triglyceride | Total Cholesterol | HDL-Cholesterol | Triglyceride | Total Cholesterol |
| NC           | 108.21 ± 1.78 | 134.89 ± 7.14 | 66.01 ± 2.88 | 22.59 ± 3.01 | 4.60 ± 0.30 |
| HF           | 121.25 ± 1.80 | 170.18 ± 4.21 | 73.13 ± 5.47 | 51.88 ± 3.25 | 6.53 ± 0.25 |
| HF-O         | 112.38 ± 1.75 | 138.37 ± 2.29 | 85.46 ± 2.98 | 38.15 ± 2.94 | 11.94 ± 0.60 |
| HF-FA        | 96.95 ± 2.05  | 135.36 ± 2.84 | 87.74 ± 1.78 | 39.05 ± 2.19 | 87.74 ± 1.78 |

Values are means ± SE (n = 8). Means in the same row not sharing a common superscript are significantly different at p<0.05.

Plasma and erythrocyte lipid peroxides

High consumption of dietary fat has been shown to induce the formation of free radicals and reactive oxygen species, resulting in lipid peroxidation and oxidative stress [24], which in turn play an important role on the pathogenesis of obesity-associated diseases such as atherosclerosis and diabetes mellitus [25]. Measurement of TBARS concentration is widely used as an indicator of lipid peroxidation process and oxidative stress in laboratory animals [25]. In the present study, both the plasma and erythrocyte lipid peroxides of obesity-induced mice on high fat and high fat diet + oryzanol or ferulic acid were higher than that of the NC group. These findings are in accordance with the results obtained by other researchers, wherein oryzanol and ferulic acid also lowered the plasma total cholesterol and triglyceride levels and increased the HDL-cholesterol concentrations in hypercholesterolemic rats and hamsters [7, 23]. Although the hepatic triglyceride levels in HF-O and HF-FA groups were higher in comparison with that of the control mice, they were still significantly lower than that of the HF group. It was also noted that supplementation of oryzanol and ferulic acid resulted in an increased faecal excretion of cholesterol and triglyceride, respectively. It appears that these phytochemicals were able to improve the plasma and hepatic lipid profile in mice under a high fat diet by significantly increasing the faecal lipid excretion.

Table 4. Plasma and erythrocyte TBARS level in mice fed with high fat diet supplemented with oryzanol and ferulic acid

| Dietary Group | Plasma TBARS (nmol/mL) | Erythrocyte TBARS (nmol/g Hb) |
|--------------|------------------------|-------------------------------|
| NC           | 6.81 ± 0.67abc         | 2.81 ± 0.13abc               |
| HF           | 8.92 ± 1.21abc         | 3.07 ± 0.13abc               |
| HF-O         | 5.02 ± 0.98abc         | 2.50 ± 0.43abc               |
| HF-FA        | 5.16 ± 0.27abc         | 2.52 ± 0.11abc               |

Values are means ± SE (n = 8). Means in the same column not sharing a common superscript are significantly different at p<0.05.

1 Values are means ± SE (n = 8). Means in the same row not sharing a common superscript are significantly different at p<0.05. 2 NC, normal diet; HF, high fat diet; HF-O, high fat diet + oryzanol; HF-FA, high fat diet + ferulic acid.
TBARS levels were found highest in HF group (Table 4). However, dietary feeding of oryzanol and ferulic acid suppressed the increased rate of lipid peroxidation in high fat-fed mice, as manifested by the significantly lower plasma and erythrocyte TBARS concentrations in HF-O and HF-FA mice than that of the HF ones. This illustrates that both oryzanol and ferulic acid inhibit oxidative stress by possibly scavenging excessive high fat diet-induced free radicals. Previous studies have shown that both oryzanol and ferulic acid possess antioxidant activity [7]. It was reported that oryzanol is a powerful inhibitor of iron-driven hydroxyl radical formation [26]. The antioxidant properties of ferulic acid, on the other hand, could be attributed to its aromatic phenolic ring that stabilizes and delocalizes the unpaired electron within its aromatic ring [6, 27], thereby acting as free-radical scavengers.

Hepatic lipid-regulating enzymes activity

Hepatic lipogenic enzymes, such as G6PD, ME, and FAS, are involved in the generation of cellular NADPH, which is essential for the biosynthesis of fatty acid and cholesterol [28]. Thus, lower activities of these enzymes could limit the availability of fatty acids required for the synthesis of hepatic triglycerides. A high fat diet was reported to increase the activities of FAS and other hepatic lipid-regulating enzymes in mice [29]. Park et al. also found increased G6PD activity in obese animals [28]. Results of the present study showed that a high fat diet did not significantly affect the activities of G6PD and FAS (Table 5). However, both oryzanol and ferulic acid exhibited lower FAS activity than that of the NC and HF groups. Only oryzanol-fed mice showed significantly lower G6PD activity relative to that of HF mice. The ME activity considerably decreased in mice as a consequence of high fat diet, but addition of oryzanol and ferulic acid in the diet restored the normal activity level of the enzyme. ME was the mostly activated among the three lipid regulatory enzymes analyzed, indicating that it plays a central role in the reduction of triglyceride level in oryzanol- and ferulic acid-fed mice. These findings illustrate that oryzanol and ferulic acid could reduce triglyceride and cholesterol levels in high fat-fed mice by suppressing hepatic lipogenesis via regulation of the activities of NADPH-generating enzymes.

Hepatic antioxidant enzymes activity

In order to control the destructive potential of free radicals, the cells have developed a highly complex antioxidant protection system, which include antioxidant enzymes that catalyze free radicals-quenching reactions. A high fat diet resulted in a marked decrease in the activities of GSH-Px, CAT, and PON1 in mice (Table 6), indicating that high consumption of dietary fat could be detrimental to the intrinsic antioxidant defense system in mice. GSH-Px and CAT utilize and degrade hydrogen peroxides, which could form into highly reactive hydroxyl radicals, to non-toxic products [30]. PON1 hydrolyzes biologically active oxidized phospholipids and destroys lipid hydroperoxides [31]. Addition of oryzanol and ferulic acid in the diet significantly counteracted the decline in the activity of these enzymes in high fat-fed mice. HF-FA group exhibited the highest GSH-Px and CAT activities. Although the high fat diet did not significantly change the SOD and GR activities in mice,

Table 5. Hepatic lipid-regulating enzyme activity1 in mice fed with high fat diet supplemented with oryzanol and ferulic acid

| Lipid-regulating enzyme | NC2 | NF | HF-O | HF-FA |
|-------------------------|-----|----|------|-------|
| G6PD (nmol/min/mg protein) | 10.32 ± 1.62ab | 13.75 ± 1.02b | 9.94 ± 0.96c | 11.05 ± 0.78ab |
| ME (nmol/min/mg protein) | 90.59 ± 8.63a | 114.01 ± 11.20b | 86.30 ± 3.95c | 102.73 ± 10.20a |
| FAS (nmol/min/mg protein) | 55.01 ± 3.01b | 58.93 ± 3.72b | 38.72 ± 3.12e | 44.41 ± 1.71e |

1 Values are means ± SE (n = 8). Means in the same row not sharing a common superscript are significantly different at p<0.05. 2 NC, normal diet; HF, high fat diet; HF-O, high fat diet + oryzanol; HF-FA, high fat diet + ferulic acid.

Table 6. Hepatic antioxidant enzyme activity1 in mice fed with high fat diet supplemented with oryzanol and ferulic acid

| Hepatic antioxidant enzyme | NC2 | HF | HF-O | HF-FA |
|---------------------------|-----|----|------|-------|
| SOD (unit/mg protein) | 1.93 ± 0.04ab | 1.64 ± 0.03a | 2.12 ± 0.16b | 1.76 ± 0.08a |
| GSH-Px (nm/min/mg protein) | 14.55 ± 0.25a | 12.70 ± 0.29b | 15.14 ± 0.31b | 19.46 ± 0.21c |
| CAT (μmol/min/mg protein) | 1.50 ± 0.06a | 1.02 ± 0.05a | 1.44 ± 0.05b | 1.78 ± 0.13c |
| GR (nmol/min/mg protein) | 9.59 ± 1.21a | 12.27 ± 1.59b | 28.97 ± 1.79a | 24.73 ± 2.41b |
| PON1 (μmol/min/mg protein) | 3.74 ± 0.28b | 1.68 ± 0.50a | 3.57 ± 0.37b | 3.93 ± 0.31b |

1 Values are means ± SE (n = 8). Means in the same row not sharing a common superscript are significantly different at p<0.05. 2 NC, normal diet; HF, high fat diet; HF-O, high fat diet + oryzanol; HF-FA, high fat diet + ferulic acid.
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dietary feeding of oryzanol resulted in a substantial increase in the enzyme activities. The mice fed with ferulic acid also exhibited significantly higher GR activity than that of the NC and HF groups. Among the antioxidant enzymes analyzed in this study, GR appeared to be the most actively induced in mice fed with oryzanol and ferulic acid under high-fat condition. This suggests that GR, which also scavenges reactive oxygen species, is an integral component of the antioxidant defense mechanism against obesity-induced oxidative stress. The substantial increase in GR activity relative to that of the other enzymes implies that GR might be the major hepatic antioxidant enzyme responsible for the decreased rate of lipid peroxidation in obese mice fed with oryzanol and ferulic acid.

Conclusion

In general, oryzanol and ferulic acid have relatively similar effects on the lipid metabolism and antioxidative status in high fat-fed mice. Both could suppress high fat-induced hyperlipidemia in mice via increased faecal excretion of cholesterol and triglyceride and inhibition of fatty acid biosynthesis. In addition, the high fat-induced oxidative stress was prevented through enhancement of the antioxidant enzyme activities in the liver. These hypolipidemic effect and antioxidant-status improving ability of oryzanol and ferulic acid show that these phenolic compounds may be useful for the treatment of obesity and possibly reduce the risk of obesity-related diseases.

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