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# Anti-Obesity Effect of a New Dietary Supplement Consisting of Hydroxycitrate, Carnitine and Red Pepper (3D-Relax Diet) in High-Fat Fed Rats

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## Abstract

**Anti-obesity effect of a new dietary supplement (3D-relax) in high-fat fed rats. The aim of this study was to assess the effects of 3D-relax; a proprietary formulation containing hydroxycitrate (233 mg/g), carnitine (150 mg/g) and red pepper (150 mg/g); on body weight, body fat, and serum lipids levels in rats fed a high-fat diet. Male SD 7-wk-old rats (n=8) were fed a high fat diet [52% total dietary energy (E%) from fat, 15.4 E% protein, 32.6E% carbohydrate] with or without 3D-relax administration (1 g/kg body weight/day) for 3 weeks. Administration of 3D-relax significantly reduced the increase in body weight compared to the group fed high fat without 3D-relax. Food efficiency ratio (FER) tended to be decreased with administration of 3D-relax, but was not significant. The perirenal and epididymal fat pad weights of rats administered 3D-relax were significantly lower than those of the high fat group that did not ingest 3D-relax during the 3 weeks. The oral administration of 3D-relax significantly increased HDL-cholesterol level and lowered total cholesterol level compared to those of high fat alone group. These results suggest that 3D-relax reduced body weight and fat gains, and those effects are presumably linked to its inhibitory effects on lipogenesis.**

**Key words:** hydroxycitrate, carnitine, red pepper, anti-obesity, body fat, serum lipid, high-fat diet

## INTRODUCTION

The increasing incidence of obesity is a recognized medical problem in developed countries (1). However, treatment of obesity is often unsuccessful. Obesity is defined as an excess of body weight that is mainly attributable to an increased body fat accumulation and induced by an imbalance of energy intake and expenditure. Many studies have shown that a high body fat deposition is associated with metabolic complications such as insulin resistance, hypertension, diabetes, and ischaemic heart disease, particularly when the excess body fat is stored in the deep abdominal area (2-4).

Weight loss can usually be achieved with dieting, behavioral modification, and exercise (5), as well as by pharmacotherapy or surgery. Pharmacologic agents designed to suppress hunger have promoted weight loss, but are often accompanied by unacceptable side effects. The most recent introduction in this class of drugs, Sibutramine may increase blood pressure and heart rate in some patients (6). The limited success and potential complications of those pharmacologic weight loss aids has led to a large and growing market for alternative therapies such as herbal products. Hydroxycitrate (HCA) is an active ingredient that is extracted from the rind of the fruit *Garcinia cambogia*, a native species to India, and promotes weight reduction by inhibiting or limiting the capacity for de novo lipogenesis (7). Furthermore, HCA might induce weight loss through increased satiety by increasing fatty acid oxidation (8). Several studies found a positive effect of HCA administration alone or in combination with other ingredients on appetite, energy intake, body weight loss or energy expenditure (9-11).

Carnitine has also been recently used as a component of dietary supplements, and has considerable potential as part of a weight-loss strategy. Carnitine (β-hydroxy-γ-trimethylaminobutyric acid) has an essential role in lipid catabolism as an essential cofactor of CPT-1 (carnitine palmitoyl transferase 1) activity for fatty acid transport into mitochondria. Administration of carnitine has been demonstrated to reduce blood and tissue lipid accumulation (12) and is effective at lowering tissue fat content. Recently, carnitine was shown to be the determinant of lipogenesis in animals and has been demonstrated to increase lipid

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utilization in humans (13). The joint administration of HCA and carnitine may be clinically useful as a strategy for disinhibiting and activating CPT-1. Although numerous supplements are purported to increase fat oxidation (carnitine) or inhibit hepatic lipogenesis (HCA), and all of these compounds are currently marketed in supplemental form to increase weight loss, few have actually been shown to be effective in scientific studies.

Several studies have shown the effects of capsaicin, a pungent principle of hot red pepper, on body weight, body fat gain and serum lipid values in rats fed a high-fat diet. Kawada et al. (14) investigated the effect of a high fat diet containing 0.014% capsaicin on body fat and serum lipid levels in rats. These results suggested that capsaicin stimulates lipid mobilization from adipose tissue and lowers the perirenal adipose tissue weight and serum triglyceride concentrations in rats fed a high-fat (30% lard) diet. Furthermore, Choo and Shin (15) reported that administration of capsaicin in the diet completely prevented the increase in body weight and fat gain induced by a high-fat diet in rats.

These findings led us to speculate that the 3D-relax dietary supplement consisting of HCA, carnitine and red pepper, ingredients widely used in weight loss supplements, might have efficacy in reducing body weight and fat gain. Therefore, we investigated the effect of 3D-relax on reducing body weight and fat gain as well as serum lipid levels in rats fed a high fat diet.

## MATERIALS AND METHODS

### Animals and diets

Male SD rats aged 7 weeks (Daehan-BioLink Co., Chungbuk, Korea) were acclimatized for 3 days under conditions of controlled temperature (24±1°C), relative humidity (55%) and lighting (dark from 20 : 00~08 : 00 hours) in a room with low background noise. In the preliminary periods, they were given access to water and a commercial diet (Samyang Co., Seoul, Korea) containing the following (g/kg diet): moisture, 80; protein, 230; fat, 35; fiber, 50; carbohydrate, 600, and water *ad libitum*. After an adaptation period, the rats were divided into two groups (8 rats/group), and fed high-fat diets (52 E% fat, 15.4 E% protein, 32.6 E% carbohydrate) (Table 1), with or without oral administration of the 3D-relax supplement, for 3 weeks. The rats were daily-administered 3D-relax diet supplement (1 g/kg body weight) or a placebo solution in saline via a stomach tube during the experiment period. The composition of the 3D-relax diet used this experiment was: 23.3% (233 mg/g) hydroxycitrate, 15% (150 mg/g) carnitine, 15% (150 mg/g) red pepper and 46.7% (467 mg/g) polydextrose.

**Table 1.** Composition of the experimental diets

| Nutrient | High-fat diet (g/100 g diet) |
|---|---|
| Casein | 20 |
| Corn starch | 32.3 |
| Sucrose | 10 |
| Lard | 20 |
| Soybean oil | 10 |
| Mineral mixture[1)] | 3.5 |
| Vitamin mixture[2)] | 1 |
| Cellulose | 3 |
| DL-methionine | 0.2 |

[1)]Composition of mineral mixture was as follows (g/kg): $CaPO_4$ $2H_2O$,145.6; $KH_2PO_4$ 257.2; $NaH_2PO_4$, 93.5; NaCl, 46.6; calcium lactate, 350.9; ferric citrate, 31.8; $MgSO_4$, 71.7; $ZnCO_3$, 1.1; $MnSO_4 \cdot 4H_2O$, 1.2; $CuSO_4 \cdot 5H_2O$, 0.3; KI, 0.1.
[2)]Vitamin mixture: ICN vitamin mixture (No 904654,1999).

### Measurement and analyses

Food intake and body weight were monitored every other day for 3 weeks. Food was withheld for 4 h before death. Blood was collected from the arota ventralis into tubes containing EDTA under ether anesthesia, and the epididymal and perirenal fat pad were immediately surgically removed and weighed. Plasma was separated by centrifugation at 1,900×g for 15 min at 4°C and frozen at -20°C until analyzed. Blood plasma levels of total cholesterol (TC), HDL cholesterol and TG were measured using enzymatic kits (Wako Chemical Co., Osaka, Japan).

### Statistical analysis

The data were subjected to analysis of variance and expressed as mean±SE. The significance of differences were compared using Student's *t*-test. Values of $p<0.05$ were considered to indicate statistical significance

## RESULTS AND DISCUSSION

### Body weight, food intake, food efficiency ratio

Body weight gains during the experimental period are shown in Fig. 1. The weight gain was consistently less in the group administered 3D-relax (3D-relax group) from day 8 onward, and was statistically significant on days 8, 12 and 24 d. Consequently, weight gain in the high-fat group was significantly greater than the weight gain in 3D-relax group (162.3±8.16 vs 139.7±7.14 g, $p<0.05$ at 24 day). Blanchard et al. (16) reported that dietary L-carnitine supplementation (1 g/kg body weight/day) significantly reduced the food intake and body weight in obese cats. This result is similar to our results in rats administrated 3D-relax containing 150 mg carnitine per 1 g of 3D-relax. On the otherhand, Leonhardt et al. (17) have investigated whether HCA, which inhibits lipogenesis, reduces food intake and body weight regain in rats. They demonstrated that HCA (3%w/w) reduces body weight

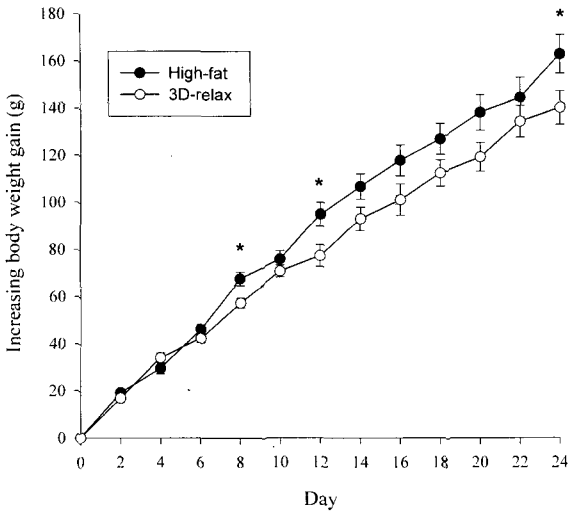


**Fig. 1.** Effect of 3D-relax on body weight gain of rats fed a high-fat diet.
High-fat: high-fat fed rats, 3D-relax: high-fat fed rats administered 3D-relax (1 g/kg body weight/day). Values are mean±SE for 8 rats. Significantly different from the corresponding value for the high-fat group by Student's *t*-test (*$p<0.05$).

regain, and that the effect is linked to its inhibition of lipogenesis. As shown in Table 2, the feed intake and FER were not significantly different between the 3D-relax and high fat groups.

### Effect of 3D-relax administration on body fat content

As shown in Fig. 2, the wet weights of the epididymal and the perirenal fat pads relative to body weight were lower in 3D-relax group than in the high fat group ($p<0.05$, $p<0.01$, respectively), which is consistent with Kawada's study (14), indicating that absorbed capsaicin, a pungent material of red pepper, induces a rapid mobilization of body fat for fuel use rather than storing it in adipose tissues in high-fat fed mice. Choo and Shin (15) reported that the administration of capsaicin (0.02% of diet) significantly reduced body fat gain compared to high-fat fed rats without capsaicin.

HCA/carnitine has been recommended as a diet aid for rapid fat loss on the basis of its presumed ability to promote the transport of free fatty acid (FFA) into hepatic mitochondria. McCarty and Gustin (18) has indicated that joint administration of HCA and carnitine to obese subjects was associated with a remarkable rate of body fat loss and thermogenesis, strongly suggestive of uncoupled fatty-acid oxidation.

**Table 2.** Effect of 3D-relax on feed intake, body weight gain and feed efficiency ratio of high-fat fed rats

| Group[1)] | Food intake (g/day) | Body weight gain (g/day) | FER[2)] |
|---|---|---|---|
| High-fat | 17.36±0.46[3)] | 7.28±0.76 | 0.42±0.04 |
| 3D-relax | 17.21±0.60 | 5.63±0.63* | 0.33±0.04 |

[1)]High-fat: high-fat fed rats.
3D-relax: high-fat fed rats administered 3D-relax (1 g/kg body weight/day).
[2)]FER: feed efficiency ratio=body weight (g/day) / feed intake (g/day).
[3)]Values are mean±SE for 8 rats.
Significantly different from the corresponding value for the high-fat group by Student's *t*-test (*$p<0.05$).

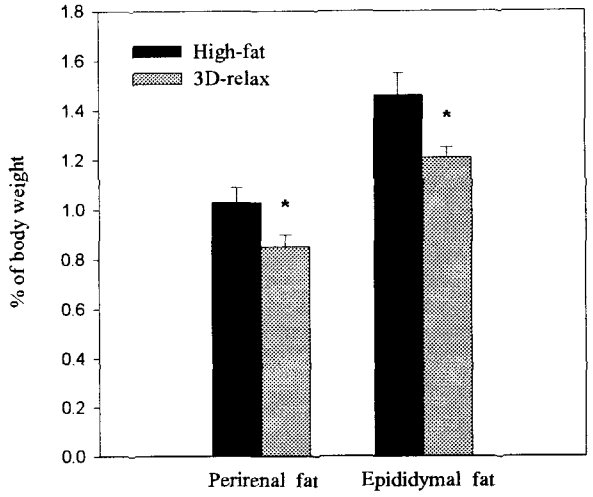


**Fig. 2.** Effect of 3D-relax on relative body fat weight of rats fed a high-fat diet.
High-fat: high-fat fed rats, 3D-relax: high-fat fed rats administered 3D-relax (1 g/kg body weight/day). Values are mean±SE for 8 rats. Significantly different from the corresponding value for the high-fat group by Student's *t*-test (*$p<0.05$).

### Effect of 3D-relax administration on plasma lipids

The changes in plasma lipid levels in the control and 3D-relax groups are summarized in Table 3. The plasma total cholesterol level was significantly reduced in the 3D-relax group compared with that of the high fat group ($p<$

**Table 3.** Effect of 3D-relax on TG, total cholesterol, HDL cholesterol, and HTR

| Group[1)] | Triglyceride (mg/dL) | Total cholesterol (mg/dL) | HDL cholesterol (mg/dL) | HTR[2)] |
|---|---|---|---|---|
| High-fat | 96.28±11.31[3)] | 102.45±4.94 | 56.42±2.62 | 0.58±0.04 |
| 3D-relax | 80.07±9.98 | 86.87±5.11* | 75.70±2.79** | 0.85±0.04** |

[1)]High-fat: high-fat fed rats.
3D-relax: high-fat fed rats administered 3D-relax (1 g/kg body weight/day).
[2)]HTR = HDL cholesterol / total cholesterol.
[3)]Values are mean±SE for 8 rats.
Significantly different from the corresponding value for the high-fat group by Student's *t*-test (*$p<0.05$, **$p<0.01$).

0.05), while HDL cholesterol level and HTR (HDL cholesterol/total cholesterol) of 3D-relax group were significantly increased ($p<0.01$). The triglyceride levels between groups were not significantly different. The lowered plasma cholesterol concentration may be a consequence of reduced absorption of cholesterol and fat, and therefore closely associated with the reduction in body-fat accumulation. 3D-relax appeared to affect lipid metabolism, and its major ingredients, HCA, carnitine and capsaicin, are regarded as the principal components responsible for lowering plasma total cholesterol and triglyceride.

There is considerable evidence that carnitine administration causes a decrease in lipid accumulation in humans and animals. For example, oral administration of carnitine decreased plasma triglycerides in hyperlipidmic subjects (12,19). L-carnitine administration is involved in the decrease of total plasma cholesterol and triglyceride in rat fed with a cholesterol enriched diet (20). Heo et al. (21) have shown that L-carnitine administration (50 mg/kg/48 h) for four weeks significantly decreases plasma triglycerides. Brady et al. (22) reported in obese rat that the administration of L-carnitine (250~2000 mg/kg/day) significantly decreased plasma triglycerides and the mechanism of action appeared to be via decreased secretion of triglycerides by liver in obese rats. Our study, in high-fat fed rats administered 3D-relax containing carnitine (150 mg/g), showed similar results as those of Brady et al. (22), although the content of carnitine used in our study was lower than was used by Brady et al. (22)

From these results, it is evident that 3D-relax has an anti-obesity effect through reducing of body weight gain and accumulated body fat weight. These effects might be resultant from the inhibition of lipogenesis by carnitine/HCA and the stimulation of lipid metabolism by capsaicin, a pungent component of hot red pepper. Therefore, the 3D-relax appeared to affect lipid metabolism, since HCA, carnitine, and capsaicin of 3D-relax are regarded as the principal components responsible for lowering plasma total cholesterol and triglyceride. These hypolipidemic effects may be related to the reduction of body fat. In conclusion, the present results indicate that 3D-relax reduces body weight gain and body fat in high-fat fed rats, and that it accelerates lipid energy metabolism, suggesting that it has efficacy as an anti-obesity supplement for obese people. Therefore, the 3D-relax may be recommended as an anti-obesity functional food.

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