YAM (DIOSCOREA ALATA) INHIBITS HYPERTRIGLYCERIDEMIA AND LIVER ENLARGEMENT IN RATS WITH HYPERCHOLESTEROL DIET

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Attempts were made to elucidate the effect of yam (Dioscorea alata) on the hypercholesterol diet. Twenty-four male Wistar rats were used and treated with corn oil, high dose of cholesterol (10%) and yam (40%). It was found that excess cholesterol and yam resulted in a stimulatory effect on the growth of rats. The enlargement of liver increased after 2 weeks with treatment of excess cholesterol ($p<0.05$). Such symptom was prevented in the group supplemented with yam. The level of triglyceride and cholesterol in the plasma of rats was significantly reduced by yam, even when rats were treated with excess cholesterol at the same time. The activity of plasma aspartate transaminase (AST) and alanine transaminase (ALT) were significantly increased as soon as rats were treated with excess cholesterol and yam in the 1-2 weeks. However, such activity was not observed when the rats were only treated with excess cholesterol for 4-8 weeks. These data demonstrated that yam might inhibit the acute induction of hypertriglyceridemia and liver enlargement in hypercholesterol diet rats.

Key words: Yam, Cholesterol, Triglyceride, Hypercholesterolemia, Liver function.

INTRODUCTION

Yams are major food crops in West Africa, the Caribbean, islands of the south Pacific, South-East Asia, India and parts of Brazil[1-5]. Nutritionally, yam constitutes a better source of ascorbic acid and protein than cassava[6].

It is estimated that there are more than 600 species in the world, 93 of which are found in China and 14 of those in Taiwan[7]. Yam tubers provide much of the carbohydrates in many tropical countries. In addition, it is used

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in Chinese herbal medicine and was first described in the *Shennong Benchao Jing* as the "Chinese yam." Chinese yam is commonly used in Chinese medicine to strengthen stomach function, improve anorexia, and eliminate diarrhea[8]. In Taiwan, yam is also used as tonic nourishment and is considered a potential functional food. Effects of Taiwanese yam on upper gut structure and physiologic function have not been investigated. Although the mechanisms by which yams modulate gastrointestinal function have not been elucidated, yams may stimulate the proliferation of gastric epithelial cells and enhance digestive enzyme activities in the small intestine. Therefore, we hypothesized that consumption of yams would modulate the physiologic function of the upper gut. hypercholesterolemia has become a major cause of mortality throughout the world[9]. Hypercholesterolemia due to high levels of low-density lipoprotein (LDL) cholesterol (C), hypertriglyceridemia often associated with low values of high-density lipoprotein (HDL)-C, and especially combined hyperlipidemia are all associated with increased risk factors in the develop of atherosclerosis, cardiovascular diseases and thrombotic diseases.

Yam tuber contains viscous mucilage composed of soluble glycoprotein, dietary fiber[10] and plant saponins (diosgenin) that may modulate lipid metabolism[11-13]. Soluble polysaccharides, especially viscous fiber, have consistently been shown to reduce serum total and low-density lipoprotein (LDL) cholesterol levels in hyperlipidemic models but not always in healthy subjects[11]. Therefore, the effects of diets enriched with Taiwanese yam on lipid metabolism in a high cholesterol model remain to be investigated. To investigate the effect of yam on hypercholesterol diet, a study of the hypercholesterolemia character of pure cholesterol with or without supplement of yam was undertaken by using male wistar rats.

MATERIALS AND METHODS

Animals

Male weanling Wistar rats were purchased from National Taiwan University Hospital. They were kept in an air-conditioned room (23±1℃, 50–60% humidity) lit for 12 h per day (07:00–19:00 h). After acclimating for 2 weeks with a commercial non-purified diet (Rodent Laboratory Chow 5001, Pruida Co., USA), 24 rats were divided into four groups. Six rats in each group were assigned to receive an 8-week course of one of four formulated diets (Table 1). The diets were formulated as described previously by American Institute of Nutrition (AIN)[14] because this formula is still commonly used in spite of new one recommended by AIN in 1993. The lyophilized uncooked yam (*Dioscorea alata*) powder prepared from Keelung yam (Keelung, Taiwan). The form of cholesterol (99.9% purity) was supplied by Wako Chemical (Osaka, Japan). Water and food were always available. After treatment for 1, 2, 4 and 8 weeks, 6 rats from each group were weight and sacrified after anesthetizing with diethyl ether. The blood was obtained from the abdominal aorta. The liver was cut out, weight and divided by body weight to get the percentage of ratio as the hepatosomatic index. Plasma was collected by centrifugation (1,000 x g for 15 min). plasma cholesterol, triglyceride, aspartate transaminase (AST) and alanine transaminase (ALT) activities were determined by a Microprocessor Clinical Chemistry Analyser (Cobas Mira, Switzerland) with enzymatic kits (E. Merck, Germany).

Table 1. Composition of the experimental diets for animal diet of yam and cholesterol

Ingredient	Diets			
	Basel diet (%)	Yam diet (%)	Cholesterol diet (%)	Yam+Cholesterol diet (%)
Casein	20	20	20	20
Methionine	0.3	0.3	0.3	0.3
Cellulose	5	5	5	5
Corn oil	2	2	2	2
Cholesterol	0	0	10	10
Yam power	0	40	0	40
Choline	0.2	0.2	0.2	0.2
AIN Mineral mix	3.5	3.5	3.5	3.5
AIN vitamin mix	1	1	1	1
Corn starch	68	28	58	18

Statistical analysis

Statistical analysis for differences among rats in the experimental groups was performed by the 2-way analysis of variance procedure and Duncan's new multiple range tests[15]. A P value<0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The effects of excess cholesterol and yam on the body weight of rats are shown in Fig. 1. After 8 weeks of treatment, the body weight of rats in yam+cholesterol group was significantly heavier than that of control and yam groups ($p<0.05$). It means that excess cholesterol and yam showed stimulating effect on the body weight of rats. The effects of excess cholesterol and yam on the hepatosomatic index of rats are shown in Fig. 2. The hepatosomatic index of rats in cholesterol group was significantly greater than the other groups after treatment for 2 weeks ($p<0.05$), but it became normal was increased after 2 weeks of treatment with excess cholesterol, and yam could inhibit the effect of excess cholesterol on the enlargement of liver[16] also pointed out that the high dose of cholesterol caused liver enlargement in rats. Fig 3 shows the effects of excess cholesterol and yam on triglyceride levels of plasma in rats. Excess cholesterol induced increase of triglyceride concentration in rats of cholesterol group. Similar results were also reported by other groups[17,18]. As shown in Fig. 3, yam could effectively reduce the level of triglyceride in the plasma of rats even when excess cholesterol was added at the same time. The reducing effect of yam on the level of triglycerides in the plasma of rats was also reported as previously described[19, 20]. From this result, the hypertriglyceridemia induced by hypercholesterol diet is obviously interfered with by yam intake.

Excess cholesterol did not increase the cholesterol level in the plasma of rats (Fig. 4.). Yam significantly reduced the cholesterol level in the plasma of rats, even when the rats were treated with excess cholesterol at the same time. This result was also reported by several other groups[21, 22], but it was not found and quality of yam or the difference in experimental conditions. The effects of excess cholesterol and yam on the AST and ALT

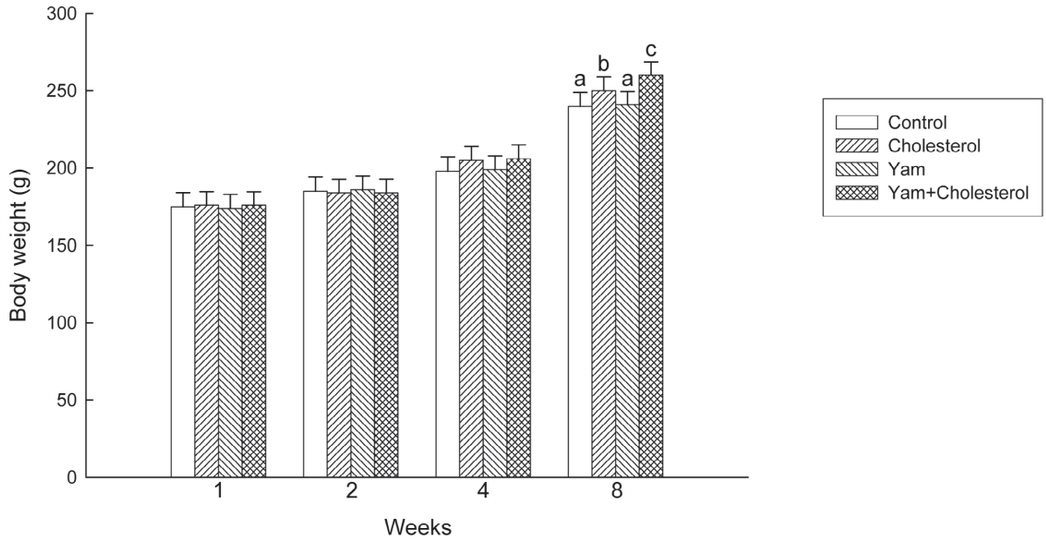

Fig 1. Effects of cholesterol and yam on the body weight of rats at 1, 2, 4 and 8 weeks. a-c: values in the same week with different superscript are significantly different (P< 0.05).

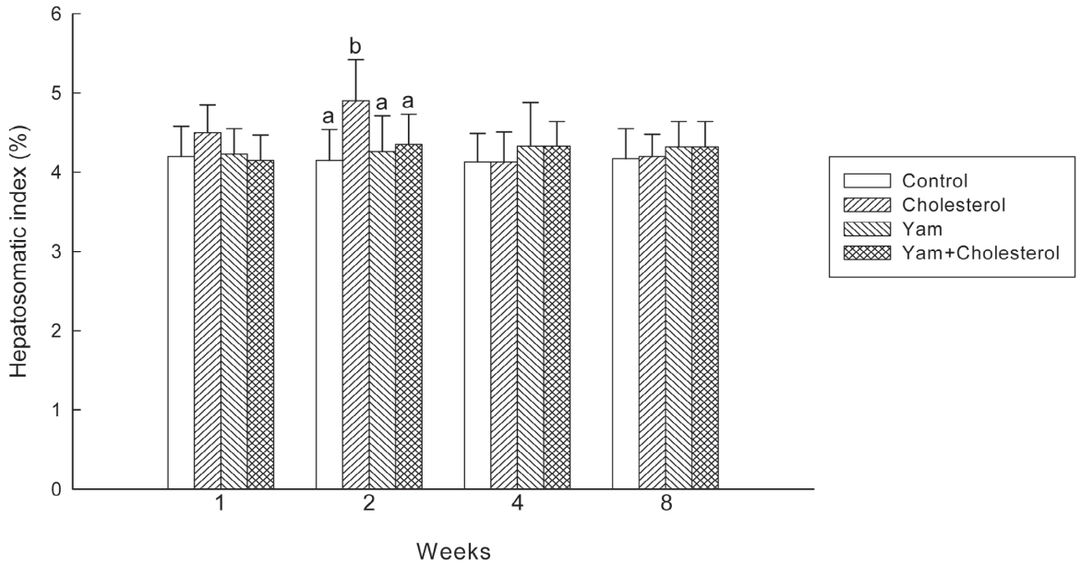

Fig 2. Effects of cholesterol and yam on hepatosomatic index of rats at 1, 2, 4 and 8 weeks. a-b: values in the same week with different superscript are significantly different (P< 0.05).

activities of the plasma in rats are shown in Fig. 5 and 6. After treatment for 1 week, the yam+cholesterol group presented higher AST and ALT activities than those of the other groups. The activities of AST in the rats of the yam group and the yam+cholesterol group are also higher than that of the other groups on 2 week. The activities of AST and ALT in the plasma were generally tested as indicators for liver function[23]. It means that yam could

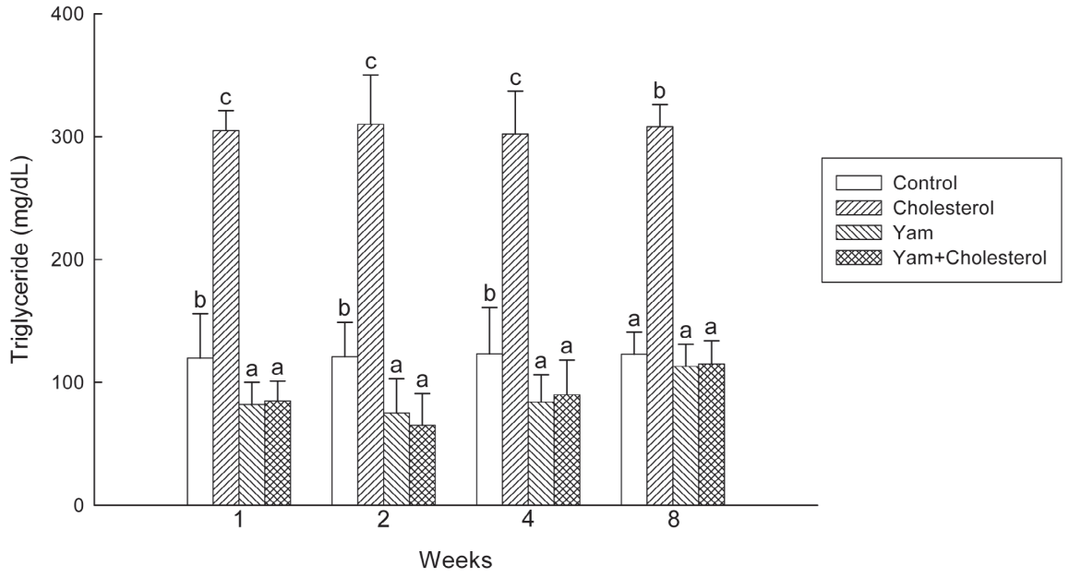

Fig 3. Effects of cholesterol and yam on triglyceride level in the plasma of rats at 1, 2, 4 and 8 weeks. a-c: values in the same week with different superscript are significantly different (P< 0.05).

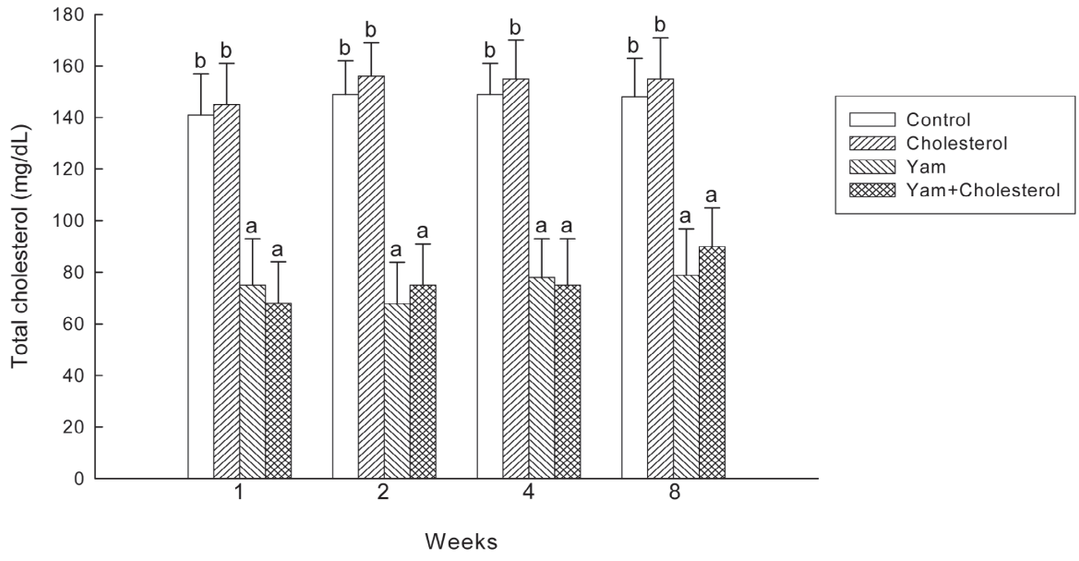

Fig 4. Effects of cholesterol and yam on cholesterol level in the plasma of rats at 1, 2, 4 and 8 weeks. a-b: values in the same week with different superscript are significantly different (P< 0.05).

induce a change of liver functions when the excess cholesterol was ingested at the same time, but excess cholesterol only did not induce any change. The reason for liver impairment is still unclear. Rule et al.[16] reported that the high activity of AST and ALT in the plasma was a symptom of hypercholesterol diet. On the other hand, cholesterol could induce the production of thiobarbituric acid reactive substances (TBARS) and thus damage the

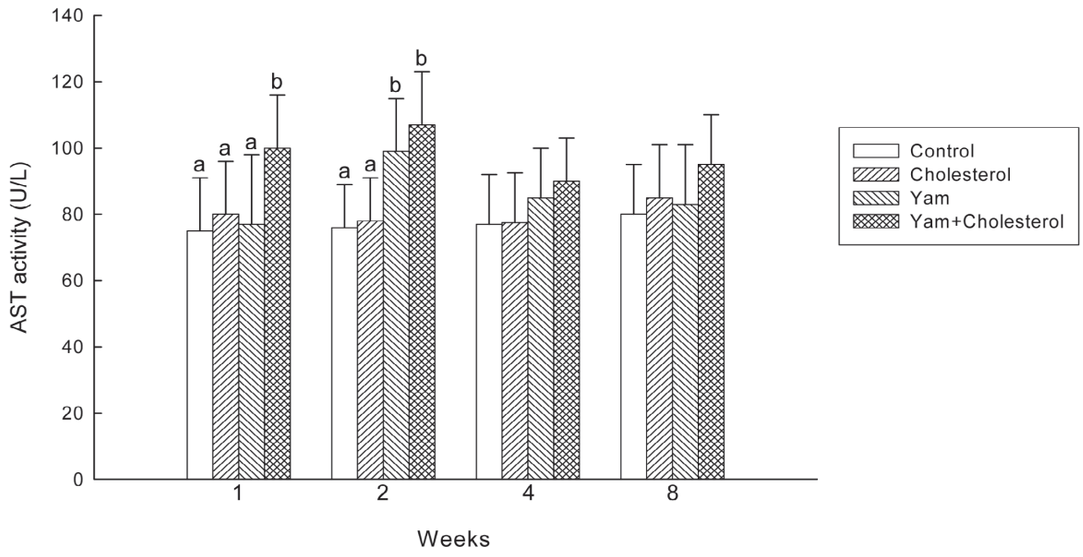

Fig 5. Effects of cholesterol and yam on activity of aspartate transaminase (ASP) in the plasma of rats at 1, 2, 4 and 8 weeks. a-b: values in the same week with different superscript are significantly different (P< 0.05).

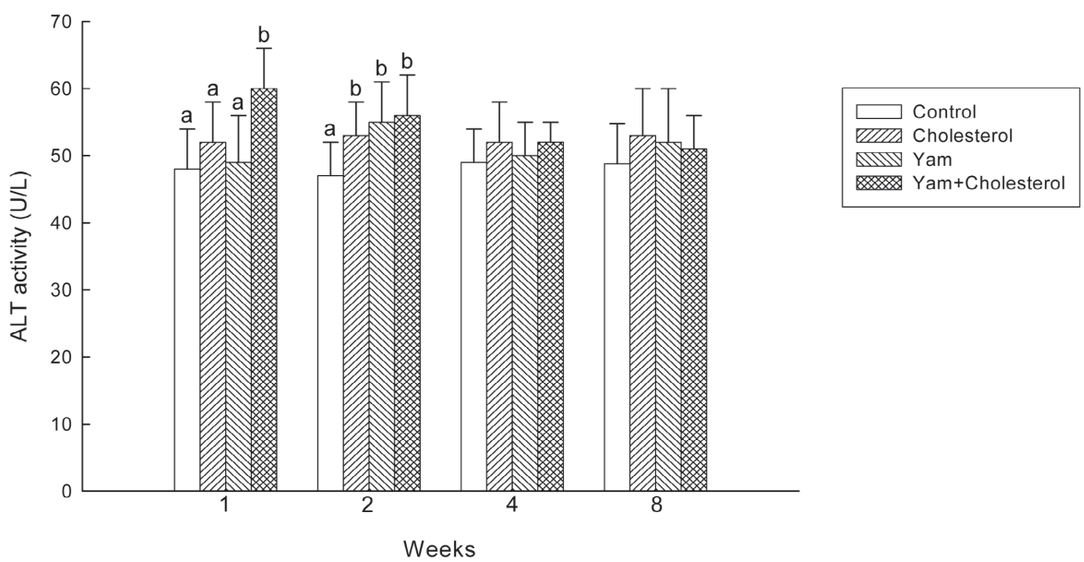

Fig 6. Effects of cholesterol and yam on activity of alkaline phosphatase (ALP) in the plasma of rats at 1, 2, 4 and 8 weeks. a-b: values in the same week with different superscript are significantly different (P< 0.05)

liver[24, 25]. Therefore, the change in liver function might be effected by excess cholesterol.

Summer the above results: the level of plasma triglyceride immediately increased, and then the liver enlargement occurred in the rats treated with one mega dose of cholesterol. The activities of AST and ALT in the plasma of rat were not affected by excess cholesterol. Therefore, the liver enlargement and high level of plasma triglyceride in rats are two major symptoms of hypercholesterol diet as in previous reports[26, 27]. On the other hand, yam immediately reduced the levels of plasma triglyceride and cholesterol, but an increase of AST activity followed in the plasma of rats treated with a dose of yam. However, a decrease of triglyceride level and increase of AST and ALT activities were found in the plasma of rats treated with excess cholesterol and yam. Thus, yam significantly inhibits the hypertriglyceridemia and liver enlargement of high fat, high cholesterol diets have been shown to accumulate oxidized lipids and related products in certain tissues (e.g. blood, liver arteries) and induces the expression of several inflammatory and oxidative stress-related proteins both in vitro[28-30] and in vivo[31-33]. The affected symptoms include liver enlargement, increase of plasma triglyceride and cholesterol and enzymatic activities of AST and ALT. These symptoms, caused by both a single mega dose of cholesterol and yam in rats, were quickly reduced, but were similar from those caused by hypercholesterol diet in humans. The causes of this difference require further studies.

REFERENCES

1. Coursey DG. Potential uitiltization of major root crops, with special emphasis on human, animal and industrial uses. In: Proc. 2nd Triennial Symp. Intl. Soc. Trop. Root Crops-Africa Branch, eds Mahungu. Douala: Cameroon; 1984.
2. Degras L. The yam-a tropical root Crop (2nd ed.). The Macmillan Press: London and Basingstoke; 1993.
3. Ihekoronye AI, Ngoddy PO. Processing of tropical roots and tuber crops. In: Integrated food science and technology for the tropics. MacMillan Publishers: London. 1985.
4. Okonkwo SNC. The botany of the yam plant and its exploitation in enhanced productivity of the crops. In G. Osuji (Ed.), Advances in yam research; the biochemistry and technology of the yam tuber. Enugu, Nigeria: Biochemical Soc: Nigeria and ASUT, pp. 3-29. 1985.
5. Onayemi O, Potter NN. Preparation and storage properties of drum-dried white yam (Dioscorea rotundata Poir) flakes. J. Food Sci. 39: 559-562, 1974.
6. Onayemi O. Some chemical factors a.ecting the quality of processed yam. J. Food Sci. 51:161-168, 1986.
7. Liu SY, Chang TW, Lin YK, Chen SF, Wang JY, Zu GL, Wang SC. Studies on the varietal characters, production potential, phytochemical properties, and antioxidant effect of Dioscorea spp. J. Agri. Res. 8: 1-22, 1999.
8. Lee SC, Tsai CC, Chen JC, Lin JG, Lin CC, Hu ML, Lu S. Effects of “Chinese yam” on hepatonephrotoxicity of acetaminophen in rats. Acta. Pharmacol. Sin. 23: 503-512, 2002.
9. American Heart Association, Heart and stroke statistics update. Dallas: Texas; 2000.

10. Hironaka K, Takad K, Ishibashi K. Chemical composition of mucilage of Chinese yam. J. Jpn. Soc. Food Sci. Technol. 37: 48-52, 1990.
11. Jenkins AL, Vuksan V, Jenkins DJ. Fiber in the treatment of hyperlipidemia. In: Spiller GA, ed. CRC handbook of dietary fiber in human nutrition, 3rd ed. CRC Press:New York, pp. 401-408. 2001.
12. Thewles A, Parslow RA, Coleman R. Effect of diosgenin on biliary cholesterol transport in the rat. Biochem. J. 291: 793-802, 1993.
13. Uchida K, Takase H, Nomura Y. Changes in biliary and fecal bile acids in mice after treatments with diosgenin and beta-sitosterol. J. Lipid Res. 25: 236-242, 1984.
14. American Institute of Nutrition, Report of the American Institute ad hoc committee on standards for nutritional studies. J. Nutr. 107: 1340-1348, 1977.
15. Puri SC, Mullen K. Multiple comparisons. In: Hall, G.K. (Ed.), Applied Statistics for Food and Agricultural Scientists. Medical: Boston, MA; 1980.
16. Rule DC, Liebman M, Liang YB. Impact of different dietary fatty acids on plasma and liver lipids is influenced by dietary cholesterol in rats. Nutr. Biochem. 7: 142-149, 1996.
17. Luria MH. Effect of low-dose niacin on high-density lipoprotein cholesterol and total cholesterol/high-density lipoprotein cholesterol ratio. Arch. Int. Med. 148: 2493-2495, 1988.
18. Alderman JD, Pasternak RC, Sacks FM, Smith HS, Monrad ES, Grossman W. Effect of a modified, well-tolerated niacin regimen on serum total cholesterol, high-density lipoprotein cholesterol and the cholesterol to high-density lipoprotein ratio. Am. J. Cardiol. 64: 725-729, 1989.
19. Chen HL, Wang CH, Chang CT, Wang TC. Effect of Taiwanses yam (*Dioscorea alata L. cv. Tainung No. 2*) on the mucosal hydrolase activites and lipid metabolism in Balb/c mice. Nutr. Res. 23: 791-801, 2003.
20. Chen HL, Wang CH, Chang CT, Wang TC. Effect of Taiwanses yam (Dioscorea japonica Thunb var, pseudojaponica Yamamoto) on upper gut function and lipid metabolism in Balb/c mice. Nutr. 19: 646-651, 2003.
21. Kritchevsky D, Story JA. Influence of dietary fiber on cholesterol metabolism in experimental animals. In: Spiller GA, ed. CRC handbook of dietary fiber in human nutrition, 2nd ed. CRC Press: New York; 1992.
22. Levrat-Verny MA, Behr S, Mustad V, Rémesy C, Demiqné C. Low levels of viscous hydrocolloids lower plasma cholesterol in rats primarily by impairing cholesterol absorption. J. Nutr. 130:243-248, 2000.
23. Ronald L, Koretz MD. Chronic hepatitis: science and superstition. In: Gitnick, G. (Ed.), Current Hepatology. Mosby-Year: Chicago; 1992.
24. Dietschy JM. Theoretical considerations of what regulates low-density-lipoprotein and high-density-lipoprotein cholesterol. Am. J. Clin. Nutr. 65: 1581S-1589S, 1997.
25. Illingworth DR. Management of hypercholesterolemia. Med. Clin. N. Am. 84:23-42, 2000.
26. Miller M, Bachorik PS, McCrindle BW, Kwiterovich POJ. Effect of gemfibrozil in men with primary low high-density lipoprotein cholesterol: a randomized, double-blind, placebo-controlled, crossover study. Am. J. Ment. Def. 94:7-12, 1993.

27. Hunninghake DB, Mellies MJ, Goldberg AC, Kuo PT, Kostis JB, Schrott HG, Insull WJ, Pan HY. Efficacy and safety of pravastatin in patients with primary hypercholesterolemia: II. Once-daily versus twice-daily dosing. Atherosclerosis 85:219-227, 1990.
28. Rajavashisth TB, Andalibi A, Territo MC, Berliner JA, Navab M, Fogelman AM, Lusis AJ. Induction of endothelial cell expression of granulocyte and macrophage colony stimulating factors by modified low density lipoproteins. Nature 344:254-257, 1990.
29. Cushing SD, Berliner JA, Valente AJ, Territo MC, Navab M. Minimally modified low density lipoprotein induces monocytes chemotactic protein I in human endothelial cells and smooth muscle cells. Proc. Natl. Acad. Sci. U S A. 87:5134-5138, 1990.
30. Parhami F, Fang ZT, Fogelman AM, Andalibi A, Territo MC, Berliner JA. Minimally modified low density lipoprotein-induced inflammatory responses in endothelial cells are mediated by cyclic adenosine monophosphate. J. Clin. Invest. 92:471-478, 1993.
31. Yla-Herttuala S, Palinski W, Rosenfeld ME, Parthasarathy S, Carew TE, Butler S, Witztum JL, Steinberg D. Evidence for the presence of oxidatively modified low density lipoprotein in atherosclerotic lesions of rabbit and man. J. Clin. Invest. 84:1086-1095, 1989.
32. Yla-Herttuala S, Lipton BA, Rosenfeld ME, Sarkioja T, Yoshimura T, Leonard EJ, Witztum JL, Steinberg D. Expression of monocyte chemoattractant protein 1 in macrophage-rich areas of human and rabbit atherosclerotic lesions. Proc. Natl. Acad. Sci. U S A. 88: 5252-5256, 1991.
33. Rosenfeld ME, Yla-Herttuala S, Lipton BA, Ord VA, Witztum JL, Steinberg D. Macrophage colony-stimulating factor mRNA and protein in atherosclerotic lesions of rabbits and human. Am. J. Pathol. 140: 291-300, 1992.

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山藥抑制餵食高膽固醇老鼠所引起之肝臟腫大和高膽固醇症

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研究台灣產山藥對於食用高膽固醇的老鼠之影響，以24隻雄性Wistar老鼠分別餵食高劑量膽固醇 (10%) 和山藥 (40%) 實驗發現，餵食高劑量膽固醇和山藥對老鼠的成長和體重有刺激增加的作用。餵食過量的膽固醇會造成有肝臟腫大的現象 ($P<0.05$)，但餵食山藥之後會減少肝臟腫大的症狀產生。以高劑量的膽固醇和山藥餵食老鼠可以減少餵食老鼠體內三酸甘油酯和膽固醇的含量。在第一週和第二週餵食高劑量的膽固醇和山藥對於老鼠的肝功能指標aspartate transaminase (AST) 和alanine transaminase (ALT) 會有上升的影響，但在第四週之後與對照組比較，則無差異性，由實驗結果顯示餵食山藥可減少老鼠服用高膽固醇所引起的肝臟腫大和高膽固醇症的現象產生。

關鍵詞：山藥、膽固醇、三酸甘油、高膽固醇症、肝功能。

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